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Around 15 million adults and 5 million children have been suffering from arthritis in the country. It is a common disease that affects inner system of the body in case of severity. There are 100 types of the disease but the symptoms, diagnosis and treatment of every type are different. Patients reach advance stage of the disease if they are ignorant of the disease. It is a curable disease. The disease affects hands and legs of patients. It attacks on the joints of hands and feet etc. It causes swelling and lining on the upper parts of the joints. It affects tissues too. At the last stage, the patient needs surgery. Many people experience some type of arthritis, while some types of arthritis can be genetic, other risk factors for developing arthritis include age, gender (women are more likely to have certain types of arthritis while men are more likely to have others), a previous joint injury, and obesity. Here are following three most common forms of arthritis:

Osteoarthritis: Osteoarthritis is the most common form of arthritis. It causes cartilage – the tissue that covers the ends of bones where they form a joint – to break down to the point of which bone grinds against bone, leading to pain and stiffness. Osteoarthritis generally appears in the knees, hips, feet and spine, and can either evolve over many years or be prompted by an injury or infection. People who have osteoarthritis experience pain, decreased range of motion, aches, pain when working, and a feeling of stiffness that sets in after you have rested. Sometimes, joints like the knees even emit clearly sounds when bent. With this form of arthritis, symptoms typically come and go. Osteoarthritis joint pain is worse in the morning, and improves with activity as the day goes on. If you have osteoarthritis, your healthcare provider will want you to manage your weight and stay active, which can help support and maintain the structures around the joint.

Physical therapy can also be helpful in teaching exercises that will help keep the muscle around that arthritis joint strong. If it is your knee that is painful, for example, you will want to be sure your quad and hamstring muscles are healthy and strong and that you have flexibility in those muscles so that the tendon’s and ligaments can work. In addition, patients often take anti-inflammatory medications (such as over-the-counter pain relievers) to ease symptoms.

Rheumatoid arthritis: This common form of arthritis is actually an autoimmune disorder. That means that the body’s immune system is forgetting the lining of the joints – which, in turn, prompts inflammation in the part of the joint that protects and lubricates. Once it becomes inflamed, pain and swelling occur. Rheumatoid arthritis (RA) causes joint pain and swelling, especially in the knuckles, heels or elbows. It also causes skin lumps, known as rheumatoid nodules, and stiffness that can last for hours or days. After a diagnosis of RA, people may be prescribed oral medications or injections to manage their symptoms. These drugs can include corticosteroids (such as prednisone), DMARDs (an acronym for disease-modifying anti-rheumatic drugs), and biologic injection to control the inflammation. Doctors recommend powerful anti-inflammatory drugs that work to change the inflammation pathway. But one caution is that these medications carry a risk of lowering your immunity, so patients have to be particularly vigilant about infections and may need to stop medications if they become ill.

Psoriatic arthritis: While the cause of psoriatic arthritis is not entirely clear, experts do know that it’s also an autoimmune disease that manifests in similar ways to rheumatic arthritis. The main difference is that when you have psoriatic arthritis, the skin can be involved, as well.

Between five percent and 20 percent of psoriasis patients will also have psoriatic arthritis. Some patients can have it with a lot of skin disease, where the body is very covered in rashes, while others have more joint symptoms and no active skin disease.

Symptoms of psoriatic arthritis include pain, swelling, redness in the joints (especially in the hands), nail changes, fatigue eye problems, skin rashes, and swelling and tenderness in fingers and feet.

To control inflammation, psoriatic arthritis patients will take similar medications as those who have RA. These include NSAIDs, DMARDs, biologic, as well as new oral treatments.

When the men were divided into obese and non-obese, the link between sugary drinks and worse knee damage held true only in the non-obese men. This suggests that soft drinks worsen knee osteoarthritis independently of the wear and tear on the joints caused by carrying around excess weight, Lu says. In people with osteoarthritis, the cartilage in a joint wears away in some areas. The function of cartilage is to reduce friction of cartilage to reduce friction in the joints and serve as a “shock absorber.” The wearing away of cartilage leads to pain and other symptoms. Nearly one in 100 people have evidence of knee osteoarthritis on x-ray. And nearly 19% of women and 14% of men over age 45 have joint pain, stiffness, and other symptoms of
knee osteoarthritis, according to a 2007 study in addition to obesity, known risk factors include:
* Older age
* Prior injury to the knee
* Extreme stress to the joints

What’s man who enjoys soda to do? “There’s an easy answer. Just don’t drink (sugary) soda, “Lu says. He notes that some studies have also linked soda to heart disease. Another expert says that’s going too far. “As with everything, enjoy soda in moderation. If you are (a man with) knee osteoarthritis and are drinking a lot of soda, this might be a reason to curb back,” says American College of Rheumatology spokesman Scott Zashin, MD. Zashin is a clinical professor of internal medicine in the rheumatology division at the University of Texas South Western Medical School in Dallas.

Dr. David, a foreign expert, said there were certain joints pains that stiffen muscles, which were manifested in hard skin as well as change in color of fingertips. Therefore, it is of utmost importance to correctly diagnosed the type of arthritis for proper treatment of the disease.

Terris Gibson from King’s College and Hospital, UK who said that gout is a very painful condition that affects the joints of the body. Big toe, ankle and knees are affected by this disease. It can occur because of the accumulation of uric acid in the body. The initial attack begins suddenly. Excessive weight, medication for high blood pressure and the consumption of too much alcohol can trigger this disease. If diagnosed, this disease can be treated with medications or injections. The best way to approach it is to treat the uric acid which is expelled in the urine. The treatment is long-term, but it is highly affected. The injections can be injected directly into the knees or bones and the uric acid should be managed by medicines.

Dr. D. Shaw from UK said that osteoporosis is the thing of the bones that can eventually lead to fracture of the bones. Worldwide one in every three women and one in every five men suffer from Osteoporosis after the age of 50. The disease can lead to broken spine / vertebrae or broken hips and 10% - 20% of the people die within a year. They slip and the bones are so fragile that they fracture. The people vulnerable to Osteoporosis are women and elderly people.

Osteoarthritis, RA, and psoriatic arthritis tend to be the most common forms of arthritis, there’s a long list of other types of arthritis. These include bursitis, carpal tunnel syndrome, gout, Raynoud’s phenomenon, and ankylosing spondylitis. Other conditions, such as lyme disease, lupus, fibromyalgia, and inflammatory bowel disease – can also include arthritis as one component of a more complex illness.

Arthritis usually occurs in adults, and advanced age is a risk factor for many different types. But children can also get a rare type of arthritis known as childhood or juvenile arthritis.

Because inflammation of the joints can be caused by so many different conditions, it’s important to see a doctor if you are experiencing pain and stiffness. A primary-care physician is a good first step, or you may be referred to a rheumatologist who can help diagnose and treat your specific joint problems.
Frequency and Outcomes of Undiagnosed Diabetes Mellitus in Patients Presenting with Acute Myocardial Infarction

Tanveer Ahmad¹, Umair Ali², Syed Tahir Shah³, Abad Khan² and Noor ul Hadi⁴

ABSTRACT

Objective: To find out frequency and outcomes of undiagnosed diabetes mellitus in patients presenting with acute ST elevation myocardial infarction (STEMI).

Study Design: Descriptive / Cross- Sectional Study

Place and Duration of study: This study was conducted at the Cardiology Department, Lady Reading Hospital, Peshawar from November 2018 to May 2019.

Materials and Methods: Patient of either gender having age ranging between 30-75 years old with acute STEMI who present within 12 hours of symptoms and with no past history of documented diabetes mellitus were included in the study. Venous blood samples for laboratory data, including random blood sugar, two fasting blood sugar and HBA1c using hitachi modular evo p800 machine was done.

Results: A total of 158 patients having acute STEMI were studied. Males were 68.4% (n=108). The mean age was 59.65 ±10.80 years. Frequency of undiagnosed diabetes mellitus was 31.64 % (n = 50). In non-diabetics stress hyperglycemia was found in 51.85 % (n=56) patients. Among various types of STEMI, anterior STEMI was more common presentation 34.1 % (n=54, p= 0.85). Mean HBA1c was 6.19 ± 1.87%. Frequency of Ventricular tachycardia (VT) was 22.2 % in which undiagnosed diabetics were n=18 (p=0.004). Ventricular fibrillation was present in 13.3 % patients with undiagnosed diabetics were n=14 (p=0.001). Frequency of AF was 13.9% (n=22) with undiagnosed diabetics having AF in n=13 (p=0.003). SVT was present in 5.7% (n=9) patients with not significant difference between two groups (p=0.017). Among various mechanical complications VSR was present in 10 % (n=16) of patients (p=0.001), cardiogenic shock in 11.1 % (n=18) patients (p=0.004), acute LVF was present in 15.8 % patients (p=0.017).

Conclusion: In our study we concluded that one third of patients having acute ST elevation myocardial infarction have undiagnosed diabetes mellitus (31.64 %, n = 50). The most common complication was ventricular tachycardia among electrical complication and LVF among mechanical complication.

Key Words: Diabetes Mellitus (DM), ST Elevation Myocardial Infarction (STEMI), Electrical Complications (EC), Mechanical Complications (MC)

INTRODUCTION

Diabetes is one of the most important health problem world is facing today. It gives rise to wide range of Complications including Coronary Artery Disease, Cerebral Vascular Disease, Renal Disease, Ophthalmopathy and Neuropathies, if not effectively treated. In 2010, an estimated 6.4% of the world's adult population had diabetes, the prevalence is projected to increase to 7.7% by 2030¹. In addition to known diabetics a significant portion of world population has undiagnosed Diabetes, and are at high risk of serious complications. One Study in Pakistan showed 62 % of the subjects with elevated serum glucose level at the time of admission had deranged glucose metabolism and 27.78 % of the total study population were diagnosed as having undiagnosed diabetes.²

Acute myocardial infarction is one of the serious and life threatening complications and occur very frequently in diabetic population. Numerous studies have identified an association between diabetes mellitus (both diagnosed and undiagnosed) and the incidence or development of coronary heart disease (CHD), including acute myocardial infarction.²,³

Diabetic individuals having coronary heart disease have poorer outcomes in terms of morbidity and mortality as
compared to non-diabetic CHD patients, prior identification of such patients for the development of de novo DM is expected to improve to overall outcomes in post-AMI patients. Elevated blood glucose levels are common in patients presenting with Acute Myocardial Infarction and are associated with a higher incidence of adverse clinical outcomes compared with normoglycemic patients. Patients with undiagnosed diabetes also have notably increased risk for moderate or severe GI bleeding post thrombolysis with increased need of in-hospital transfusion as compared non diabetics. These patients also have higher rates of all cause mortality at 30 days. Raised glucose level both at admission and fasting raises death, congestive heart failure, and cardiogenic shock in acute MI patients. Higher Fasting glucose levels at presentation were associated with a higher risk of post discharge mortality up to 6 months both after STEMI and NSTEMI.

In patients having no prior diabetes, insulin-based regimen of hyperglycemia after AMI is linked with better clinical outcomes. Randomized, controlled trials (RCTs) of intensive, insulin-based blood glucose treatment during hospitalization with AMI showed survival benefit. Persistence of hyperglycemia in acute AMI patients in 24–48 h after AMI results in worst prognosis. There is a strong association between diabetes and elevated glucose and short term and long term mortality. Patients with DM having AMI have about a 2 fold higher risk of short-term mortality as compared to non diabetic. Newly diagnosed glucose intolerance (IFG or AGT) after AMI have worse long-term adverse outcomes. Its adverse prognostic effect is as large as that of already diagnosed DM. Therefore clinicians should take into account the presence or absence of hyperglycemia for risk stratification of patients admitted with Acute Myocardial Infarction.

Taking into account the adverse effects of hyperglycemia and newly diagnosed diabetes in acute myocardial infarction, study is designed to find out the frequency and its outcomes in acute myocardial infarction patients.

**MATERIALS AND METHODS**

This descriptive cross sectional study was carried out at Cardiology Department, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar from 11 November 2018 to 11 May 2019. Patient with age range between 30-75 years old and either gender were studied. Patients having acute myocardial infarction who present within 12 hours of symptoms with no past history of documented diabetes mellitus were included in the study. Whereas patients of myocardial infarction having past history of diabetes mellitus, chronic renal failure (raised serum creatinine of more than 1.2mg/dl) or on chronic hemodialysis were excluded.

ST elevation myocardial infarction was defined as patients presenting with chest pain and new onset ST elevations in two contiguous chest leads or limb leads or patients with chest pain and new onset LBBB i.e patients with no past history of documented LBBB and positive Trop T or raised Trop I levels. Whereas undiagnosed diabetes mellitus was defined as patients with no past history of documented diabetes mellitus and anti-diabetic treatment with admission blood glucose level equal to or greater than 180 with following HBA1c equal to or greater than 6.5.

Sample size was determined using WHO software for sample size determination with 95% confidence level and 7% margin of error under. Non probability consecutive sampling technique was used. The study was carried out after approval from hospital’s research committee. After informed consent, all patients meeting the inclusion criteria were included in the study. All patients were subjected to detailed history, complete routine examination and baseline investigations. Venous blood samples for laboratory data, including random blood sugar, two fasting blood sugar and HBA1c using hitachi modular evo p800 machine was done. All patients were kept in ward till clinically stable and management protocol was observed for all included patients. In hospital complications like arrhythmias and structural complications were recorded during the hospital stay. All the above mentioned information including demographic features were recorded in a pre-designed proforma. Exclusion criteria were followed strictly to control confounders and bias in the study results.

Mean ± SD was calculated for numerical variables like age, random blood sugar, fasting blood sugar and HBA1c. Frequencies and percentages were calculated for categorical variables like gender and undiagnosed diabetes mellitus. Undiagnosed diabetes mellitus was stratified among age and gender to see effect modification. All results were presented in the form of tables and graphs. Statistical analysis was done with the Statistical Package for the Social Sciences software (SPSS 20.0) for Windows.

**RESULTS**

Total of 158 patients having acute ST elevation myocardial infarction with no past history of documented diabetes mellitus were studied. Among these patients, males were 68.4% (n=108) and female were 31.6% (n= 50)(p=0.5). The mean age was 59.65 ±10.80. (Figure 1)

Among various types of STEMI, anterior STEMI was present in 34.1 % (n=54, p= 0.85), anterolateral STEMI in 19.6 % (n=31, p=0.66), inferior wall STEMI in 23.4% (n=37, p=0.42), inferioposterior STEMI in 5.1 % (n=8, p=1). Inferior lateral in 7.59% (n=12, p=0.55), inferior and RVMI in 4.4% (n=7, p=0.70), and lateral wall STEMI in 5.7 (n=9, p=0.27) (Figure 2).
Mean RBS was 191.36 ±70.04 mg/dl, mean HBA1C was 6.19 ± 1.87, mean 1st FBS was 115.8 ± 48.71 mg/dl while 2nd FBS was 107.59±36.04 mg/dl. Frequency of undiagnosed diabetes mellitus was 31.64 % (n = 50). Out of them 36 were males (p=0.58). Frequency of non-diabetics was 68.4% (n=108) with 72 were males.

In electrical complications frequency of Ventricular tachycardia (VT) was 22.2 % in which undiagnosed diabetics were 36% (n=18/50), non-diabetics were 15.7% (n=17/108) (p=0.004). Ventricular fibrillation was present in 13.3 % patients (n=21) with undiagnosed diabetics were 28% (n=14/50) and non-diabetic patients were 10.18 % (n=11/108 (p=0.001). Total frequency of AF was 13.9 % (n=22), Undiagnosed diabetics had AF in 26% (n=13/50), while non-diabetics had 8.3% (n=9/108) (p=0.003). SVT was present in 5.7% (n=9) patients. Out of them 14% (n=7/50) were undiagnosed diabetics while 1.8% (n=2/108) were non diabetics (p=0.002). CHB was present in 15.8 % (n=25) patients [(Undiagnosed diabetics 26% (n=13/50) (p=0.033) while non-diabetics 11.11 % (n=12/108) (p=0.017)] (Figure 3).

Figure No.1: Gender wise distribution of total population (n=158).

Figure No.2: Frequency of different types of acute STEMI in undiagnosed diabetics and non-diabetics (n=158)

Among various mechanical complications VSR was present in 10 % (n=16) of patients [Undiagnosed diabetics 22% (n=11/50), non diabetics 4.6 % (n=5/108) (p=0.001)]. Cardiogenic shock was present in 11.1 % (n=18) patients, with undiagnosed diabetics 22% (n=11/50) and non-diabetes 6.4 % (n=7/108) (p=0.004). Acute LVF was present in 15.8 % (n=25) patients. Out of them 26% (n=13/50) were undiagnosed diabetics while 11% (n=12 /108 ) were non diabetics (p=0.017) (Figure 3).

DISCUSSION

Acute ST elevation myocardial infarction (MI) is a common medical emergency having higher mortality worldwide. Hyperglycemia is frequent in patients with acute myocardial infarction deteriorating cardiac function and increases in-hospital and long term morbidity and mortality irrespective of diabetic status. Hyperglycemia which is encountered in up to 50% to 60% of patients with AMI is linked with higher occurrence of major acute cardiac events (MACE) such as significant arrhythmias (supraventricular tachycardia (SVT), AF, VT, VF or heart blocks), cardiac pulmonary edema, hypotension and cardiogenic shock.

In this study, frequency of undiagnosed diabetes mellitus in patients presenting with ST elevation myocardial infarction and related complications were studied. The frequency of undiagnosed diabetes in patients presented with acute ST elevation myocardial infarction was found to be 31.6 % which is almost same as that found by Shafique Ahmed et al i.e. 27.78%2. Electrical and mechanical complications of acute ST elevation myocardial infarction were much more frequent in patients having undiagnosed diabetes mellitus as compared to patients who were diagnosed as non-diabetics at presentation as reported by Ghulap NN et al and Sinnaeve et al4,6. Among electrical complications of acute ST elevation myocardial infarction atrial fibrillation was 13.9% with patients having undiagnosed diabetes having frequency of 26% and those with no diabetes had frequency of 8.33%. Koracevic et al studied 543 patients of acute myocardial infarction, reporting hyperglycemia in 200 patients with
15% of atrial fibrillation. Similarly in a large cohort study, Kadri and coworkers reported AF 17.8% in patients with acute MI and underlying hyperglycemia. Frequency of atrial fibrillation in our study is almost in line with the international research work.

Ventricular arrhythmia including ventricular tachycardia and ventricular fibrillation was 22.2% and 13.3% respectively. In our study population, VT in undiagnosed diabetics and patients with no diabetes was 36%, and 15.74% respectively. Also VF in patients with undiagnosed diabetes and without diabetes was 28% and 6.48% respectively. Kadri et al reported ventricular fibrillation, which is less than half of the incidence of ventricular fibrillation in this study. The probable reason might be their large sample size and secondly, not all of our patients presented to hospital in time for proper thrombolysis, due to poor knowledge of acute MI and logistic problem, so the chances of ventricular arrhythmia were more in our patients, while Meisenger et al reported almost two third of incidence of ventricular fibrillation i.e. 9.5% as that in my study.

Khan et al studied our local population and reported the frequency of complete heart block as 6.4% as compared to 15.8 % total incidence in the present study including incidence in undiagnosed diabetics and patients without diabetes as 26% and 11.11% respectively. The sample size of my study was approximately same as that of Khan et al, but we reported different frequencies of complete heart block in our respective study. Supra ventricular tachycardia (SVT) was experienced as 14% in undiagnosed diabetics and 1.85 % in patients without diabetes mellitus.

Mechanical complications are well recognized complications of AMI. In patients with increased plasma blood glucose levels, the incidence of these complications increases with increasing severity of hyperglycemia. Cardiogenic shock occurred frequently among the mechanical complications, with frequency of 22%, and 6.48% in undiagnosed diabetics, and those with no diabetes respectively. Naber et al documented cardiogenic shock with incidence of 17.2 %.

Cardiac pulmonary edema, one of the mechanical complication included in our study was reported in 15.8% patients with undiagnosed diabetics and non-diabetics were 26% and 11.11 % respectively. While Meisenger et al reported 7.1% . On the other hand Ishihara et al reported almost half prevalence of cardiac pulmonary edema in patients of acute myocardial infarction with hyperglycemia. Ventricular septal rupture (VSR) which is one of the dread full complication of acute STEMI had total incidence of 10.18% in undiagnosed diabetics while it was 4.62% in non-diabetics.

The complications of STEMI i.e. electrical and mechanical complications didn’t have any significance when compared between undiagnosed diabetics and non-diabetics. When these complications were further analyzed in term of age and gender, there was no significant statistical difference.

Conventional risk factors associated with coronary artery disease like hypertension, smoking, dyslipidemia, obesity and family history were not considered in my study and there inclusion might have effect the outcome of patients presented with acute ST elevation myocardial infarction. Anemia, location and size of myocardial infarction were not considered which has significant effects on outcomes of myocardial infarction. The status of patient being non diabetic was decided on the basis of history given by patient or attendant. Oral glucose tolerance test was not used to decide about the diabetic status of patient.

In future if the conventional risk factors for coronary artery disease are taken in to account in patients of acute ST elevation myocardial infarction and comparative study is carry out between patients with risk factors and without risk factors, the results might be more controlled. The diabetic status of patient should be properly decided because the presence of diabetes in patients with acute ST elevation myocardial infarction is itself a bad prognostic factor.

CONCLUSION

In this study one third of patients having acute ST elevation myocardial infarction have undiagnosed diabetes mellitus (31.64 %, n = 50). Increased blood glucose levels in AMI patients are associated with increased adverse outcomes. The most common complication was ventricular tachycardia among electrical complication and LVF among mechanical complication.

Author’s Contribution:
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Final Approval of version: Tanveer Ahmad

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REFERENCES


Electrophysiological Variants of Guillain Barre Syndrome (GBS)

Muhammad Wazir Ali Khan, Asad Hussain and Hafiz Muhammad Zeeshan

ABSTRACT

Objective: This study aims at identifying frequency and distribution of common electrophysiological variants according to age and gender in our region.

Study Design: A Cross-sectional study

Place and Duration of Study: This study was conducted at the department of Neurology Sheikh Zayed Medical College/Hospital, Rahim Yar Khan from Jan 2015 to October 2020.

Materials and Methods: Patients clinically and electro diagnostically diagnosed as GBS in the last five years were included in the study. After using the electro diagnostic criteria, patients were categorized into three main variants: AMSAN (acute motor-sensory axonal neuropathy), AMAN (acute motor axonal neuropathy), and AIDP (acute inflammatory demyelinating polyneuropathy).

Results: 180 patients included in the study of which 62.22% were male and 37.78% were females. About 28.33% had AMSAN, 32.78% had AMAN, and 31.11% had AIDP, respectively. Males are affected more in each type. There was not much difference in the incidence of different variants in our region.

Conclusion: Different variants of GBS occur with slight variation in incidence depending upon the criteria used to classify as axonal or demyelinating variety.

Key Words: Guillain Barre Syndrome (GBS), Acute Motor Sensory Axonal Neuropathy (AMSAN), Acute Motor Axonal Neuropathy (AMAN), Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), Nerve Conduction Studies (NCS).

INTRODUCTION

Guillain-Barre syndrome (GBS) is an immune mediated acute, generalized paralytic polyradiculoneuropathy that is characterized by progressive weakness and diminished or absent deep tendon reflexes with intact sphincter control and without a sensory level.\(^1\)\(^2\) In about two thirds of cases, GBS is preceded by a symptomatic infection such as Campylobacter jejuni, Epstein-Barr virus, influenza, Mycoplasma pneumonia, Haemophilus influenza or cytomegalovirus.\(^3\) There has also been associations with influenza infections and vaccinations.\(^4\) GBS cases were also reported during the Zika virus outbreak in South America.\(^3\)

GBS associated with COVID-19 is also reported, but the strength and mechanism of association remains unclear.\(^5\)

Guillain-Barre syndrome (GBS) usually presents sporadically with global incidence reported around 0.6-2.4 cases per 100,000 populations. Men are affected by approximately 1.5 times than women.\(^7\)

Apart from clinical and laboratory findings, electro diagnostic studies (EDX) are helpful in classification of different subtypes of the disease. Electro physiologically, GBS has three major subtypes: acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor sensory axonal neuropathy (AMSAN). Predominant subtype of GBS differs according to the geographic area.\(^2\)

AIDP is the most commonly occurring subtype in North America and Europe, about 90 % of all cases. However, in Asia, Central and South America axonal variants of GBS i.e. acute motor axonopathy (AMAN) and acute motor sensory axonopathy (AMSAN) are found to represent 30% to 47% of cases.\(^8\)^{1,14} Nerve Conduction Studies (NCS) can be recorded by the end of the first week of illness and are most pronounced by the second week. The diagnostic yield of NCS can be increased by recording at least four motor nerves, three sensory nerves, F waves and H-reflexes.\(^10\)
The EDX findings supportive of AIDP include, prolonged distal motor latencies, reduced conduction velocities, conduction blocks at non-entrapment sites, temporal dispersion and prolonged F wave latencies. Another characteristic electro diagnostic feature of GBS is “sural sparing”. A normal sural sensory nerve action potential (SNAP) with abnormal upper extremity sensory nerve responses. This is very unlikely for other neuropathies than AIDP to manifest. Sural sparing, persists even in the later part of the disease. NCS in GBS is also helpful in assessing the need and duration of ventilatory support. Low compound muscle action potentials (CMAPs) are most predictive of a poor prognosis.

The studies on electrophysiological patterns and variants of GBS in Pakistan have shown a trend similar to other Asian countries. However, there is no study done in the South Punjab region to identify the variants of GBS. The purpose of this study is to identify the electrophysiological variants of GBS and find out the most common type in our region.

MATERIALS AND METHODS

This is an analytical cross sectional study conducted at the Department of Neurology Sheikh Zayed Medical College/Hospital Rahim Yar Khan. The study included patients who were diagnosed clinically and confirmed electro diagnostically to have GB syndrome. The data was collected from the last five years from January 2015 to October 2020. The patients were admitted from ER, OPD and Medical Wards. The patients underwent Nerve Conduction Studies at Neurophysiology Lab. The electro diagnostic criteria were used to identify patients with demyelinating or axonal types (Table 1) 15-19. Patients were identified as falling into three major variants of GBS as AIDP, AMAN and AMSAN. Patients who didn't fall into three major variants were classified as undifferentiated. Those patients found to have other diagnoses after electro diagnosis were excluded. The NCS was performed within one week of symptom onset. Most common variant and relationship to gender and age was identified. Percentage of patients with demyelinating and axonal variants also identified. The data was analyzed using the google sheets. The permission from the institutional ethical review board was taken before starting our study.

RESULTS

A total of 180 patients were included in the study after clinical evaluation and electro diagnostic studies. Out of which 112 (62.22%) were male and 68 (37.78%) were female. The age of patients range from 6 months to 90 yrs. Mean age was 26.9±20.2. There was no significant age difference between males and females when mean age was considered.

A total of 110 (61.11%) patients had axonal type of GBS including the pure motor and mixed variety. The patients with demyelinating variety were 56 (31.11%). 14 (7.78 %) patients were of undifferentiated type.

Table No.1: Electrodiagnostic Criteria for Guillain-Barré Syndrome

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>&lt;90% LLN (&lt;85%, if distal amp &lt;50% LLN)</td>
<td>&lt;90% LLN (&lt;85%, if distal amp &lt;50% LLN)</td>
</tr>
<tr>
<td>DML</td>
<td>&gt;110% ULN (&gt;120%, if distal amp &lt;LLN)</td>
<td>&gt;110% ULN (&gt;120%, if distal amp &lt;LLN)</td>
</tr>
<tr>
<td>TD</td>
<td>Unequivocal</td>
<td>Not Considered</td>
</tr>
<tr>
<td>CB</td>
<td>Not Considered</td>
<td>Proximal-to-distal amp ratio &lt;0.5 and distal amp &gt;20% LLN</td>
</tr>
</tbody>
</table>

Table No.2: Electrophysiologic Variants of GBS

<table>
<thead>
<tr>
<th>Total</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDP</td>
<td>56(31.11%)</td>
<td>33(58.93%)</td>
</tr>
<tr>
<td>AMAN</td>
<td>59(32.78%)</td>
<td>30(50.85%)</td>
</tr>
<tr>
<td>AMSAN</td>
<td>51(28.33%)</td>
<td>37(72.55%)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>14(7.78%)</td>
<td>11(78.57%)</td>
</tr>
<tr>
<td>Total</td>
<td>180(100%)</td>
<td>112(62.22%)</td>
</tr>
</tbody>
</table>

Of the total patients 56 (31.11%) patients had AIDP, 59 (32.78%) had AMAN and 51 (28.33%) were of AMSAN variety. Males were affected significantly more often than females. The most common type found was AMAN (32.78%). Of which 30 (50.85%) were males and 29 (49.15%) were females. The second common type was AIDP (31.11%) of which 33 (58.93%) were males and 23 (41.07%) were females.
DISCUSSION

Guillain-Barre syndrome (GBS) is a disorder of peripheral nerves of immune etiology which usually presents sporadically. The prevalence and incidence of different variants may vary in different regions. Although GBS is mainly diagnosed clinically, electrodiagnostic studies are the basis for classification into different variants. Some studies in Pakistan and other Asian countries have identified a similar percentage of the three major subtypes. In our study AMAN variety was slightly more common than AIDP. Overall, if the pure and mixed axonal varieties are considered, 61.11% had axonal type of GBS compared to 31.11% of demyelinating variety. In our study, AIDP accounts for 31.11% of cases and AMAN accounts for 32.78% of cases. In 2006 Zaheer M et al in Pakistan in their study found 36% AIDP cases and 12% Axonal variety. Another study in Pakistan showed a relatively similar pattern of GBS with demyelinating type in 46%, axonal in 31% and unclassifiable in the rest of their cases. Yadegari S et al in 2014 in Iran showed that the most common type of GBS was AIDP (63%) followed by AMAN (23%) and AMSAN (14%)%. In 2019 in Northern China Tian J et al showed that AMAN was the most common type in 55.8% and AIDP was 21.2%. A study in North India done on children with GBS found AMAN in 69.4% and AIDP in 25% children. A study of Chinese patients with GBS revealed AIDP in 32% and AMAN in 55%. The higher prevalence of AMAN has been reported from China and has been attributed to Campylobacter jejuni.

In our region and most Middle East and Asian countries, the axonal variants of GBS seem more prevalent than North America and Europe which include only 5% of GBS cases. Also the axonal variants are less common than Japan which have reported AMAN in 45-48% of their GBS cases. The slight difference in the incidence of different variants is identified in different studies even in the same geographic region. This may be attributed to the type of diagnostic criteria used for classification of different variants. The criteria we used is the common criteria to classify axonal and demyelinating varieties. In many studies males are more commonly affected than females which is also shown in our study.

Our study has certain limitations. There were patients who present with rapidly worsening severe disease and are directly shifted to ICU for ventilatory support. These patients could not undergo NCS studies in the initial week. Our study does not tell us about prognosis of different variants including need of ventilatory support and time of hospital stay. The accuracy of incidence of different variants of GBS can be improved by using different electrodiagnostic criteria and comparing their results. By developing a universal criteria, the true incidence of different variants can be identified in different geographic regions. This will help in better prognostication and planning for more aggressive treatment of vulnerable patients.

CONCLUSION

In our study the AMAN variant of GBS is slightly more common than the AIDP variant. The slight difference is also attributed to different criteria used to classify variants. Early identification of variants is helpful in planning treatment and prognostication of patients with severe disease.

Author’s Contribution: Concept & Design of Study: Muhammad Wazir Ali Khan
Drafting: Asad Hussain
Data Analysis: Hafiz Muhammad Zeeshan
Revisiting Critically: Muhammad Wazir Ali Khan, Asad Hussain
Final Approval of version: Muhammad Wazir Ali Khan

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

REFERENCES
Proton Pump Inhibitors Induced Hypomagnesemia in End Stage Renal Disease Patients
Shakeel Khan1, Usman Khalid2, Khawar Sultan1, Ahmad Shamim Khan1, Adnan Akhtar1 and Asma Hafeez1

ABSTRACT

Objective: To compare the severity of hypomagnesemia in end stage renal disease patients on hemodialysis taking proton pump inhibitors and standard therapy after three months of treatment.

Study Design: Randomized Controlled Trial (RCT) study.

Place and Duration of Study: This study was conducted at the Department of Nephrology, Pakistan Institute of Medical Sciences, Islamabad from May to Aug 2017.

Materials and Methods: This study involved 100 patients of both genders aged 18 years and above with end stage renal disease on hemodialysis. Patients were randomly allocated in two treatment groups. Group-A received PPI along with standard therapy of hemodialysis while those in Group-B received standard therapy of hemodialysis. The frequency of hypomagnesemia (<1.3 mEq/l) after 3 months of treatment was noted and compared between the two groups.

Results: The mean age of the patients was 50.89±10.20 years. Male to female ratio was found 1.7:1. The average blood urea, plasma albumin, serum creatinine, serum sodium, serum potassium, serum phosphate and serum calcium were not significantly different between two groups with p-value >0.05. Serum magnesium level was the only significant variable between two groups. The mean serum magnesium level was significantly lower in patients on PPI (1.48±0.26) versus control group (1.6±0.22) with p-value <0.05. The frequency of hypomagnesemia was significantly higher in patients on proton pump inhibitors (28.0% vs. 10.0%; p <0.05).

Conclusion: Proton pump inhibitors were found to be associated with hypomagnesemia in patients with end stage renal disease on hemodialysis.

Key Words: End Stage Renal Disease, Hemodialysis, Proton Pump Inhibitors, Hypomagnesemia

INTRODUCTION

Gastrointestinal symptoms are much common in CKD and ESRD patients than general population. 51% to 70.7% patients on hemodialysis experience upper gastrointestinal symptoms. There are many mechanisms which explain such a high prevalence of gastrointestinal problems in these patients.1 Uremic toxins, effect of dialysis, drugs and life style are some main underlying causative conditions.1

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Patients with high urea level are prone to erosive gastritis, ulcerative esophagitis and duodenitis.2 Recurrence of H. Pylori after eradication is also common in uremic patients.3 GI symptoms like nausea, vomiting, indigestion, bloating, abdominal pain, gastrointestinal reflux, diarrhea and constipation cause malnutrition and decrease quality of life.4

Magnesium (Mg) is an important cation required for a number of cellular functions.5 It is required for many enzymatic reactions like synthesis of adenosine triphosphate (ATP), ribonucleic acid (RNA) and deoxyribonucleic acid (DNA). It also takes part in cell permeability and neuromuscular excitability by regulating ion channels. It has role in cellular apoptosis and proliferation. It must be noted that both humoral immune and cellular immune responses have involvement of Mg.6 In body 50 to 60% of total magnesium is stored in bones, about 40% is in muscles and only 1% is found in extracellular fluid.7 Magnesium equilibrium is strongly maintained by absorption through intestine and renal excretion as well as its exchange with bone. Mg2+is absorbed passively through tight junctions between enterocytes and actively through the combined actions of transient receptor potential melastatin -6 and -7 (TRPM6/7).
channels, which are present in the apical membrane of enterocytes in the intestine. Proton-pump inhibitors (PPIs) are a widely used first line and evidence-based therapy for upper gastrointestinal disorders like dyspepsia, gastroesophageal reflux disease, peptic ulcer disease, upper GI bleeding and H Pylori associated disease. PPIs inhibit active proton pumps in gastric parietal cells and inhibit HCl production. PPIs when taken short-term exhibit excellent safety profile and clinically applicable adverse effects are rare. However, PPI therapy leads to hypergastrinemia, parietal cell hypertrophy leading to rebound acid hypersecretion, hypomagnesemia, osteoporosis and AKI. PPI-induced hypomagnesemia is primarily due to impaired intestinal absorption. Studies suggest that passive paracellular magnesium absorption is intact, but active transport via TRPM6/7 channels is disrupted. Although the pathophysiology has not been completely understood but it appears that a PPIs cause a decrease in pH of 0.5 of intestine lumen which alters TRPM6/7channel affinity for magnesium. Tamora et al. concluded that chronic use of PPIs can lead to severe hypomagnesemia. Perazella et al. confirmed the association between PPIs and hypomagnesemia in patients hospitalized at tertiary care medical centers. Alhosani et al. performed a study on 62 hemodialysis patients, which showed that 39% of patients had hypomagnesemia.

Hypomagnesemia is having specific clinical manifestation as it may lead to neuromuscular disturbances e.g., tetany, seizures, arrhythmias, hypoparathyroidism, osteomalacia, osteoporosis as well as concurrent metabolic disorders e.g. hypocalcaemia and hypokalemia. It was noticed significantly by Kanbay et al. that in CKD patients, future outcomes can be predicted by serum Mg level. In HD and CKD patients mortality rate increases with lowering of serum Mg levels. It has been reported by Sakaguchi et al. recently that in HD patients, high rate of non-cardiovascular and cardiovascular mortality can be predicted by hypomagnesemia.

There is limited literation on PPI induced hypomagnesemia, therefore we are taking up this study to know the severity of hypomagnesemia in dialysis dependent patients using PPIs in our center to know the hypomagnesemia burden in our population and to suggest alterations in medications to prevent serious morbidity and mortality.

MATERIALS AND METHODS

A randomized control study was conducted at department of Nephrology, Shaheed Zulfiqar Ali Bhutto Medical University PIMS Islamabad from May 2017 to August 2017. A study conducted by Alhosaini et al. in 2014 reported the proportion of hypomagnesemia in PPI group 55.2% whereas in control group 24.2%. taking the result of the above said study from the literature keeping power of test 80%, and level of significance 5% the minimum sample size for our study was 40 in each group (Total sample size=80). We fixed the sample size 50 in each group, taking total sample size 100 who were fulfil the inclusion/exclusion criteria. After approval from ethical committee. After detailed history and physical examination, a written consent was also taken from patients or guardians. Group-A patients were allowed to take a single dose of 40mg omeprazole in the morning on empty stomach. After 3 months of treatment all lab values were noted. The severity of hypomagnesemia (serum magnesium level < 1.3 mEq/l) in two groups was also examined. The data was entered and analyzed through SPSS version 23.0. The p value <0.05 was considered as significant.

RESULTS

Out of 100 patients there were 63% male and 37% female. The age of the patients ranged from 30 years to 70 years 50.89±10.2 years. Majority (33.0%) of the patients were aged between 51-60 years followed by 29% patients in the range of 41-50 years and 21% patients in the range of 61-70 years while only 17% patients were aged between 30-40 years. The age of patients was normally distributed as the p value of Kolmogorov-Smirnov test was >0.05. (Table 1)

| Table No.1: Normality test through Kolmogorov Smirnov test of normality for qualitative variables of the study |
| --- | --- | --- |
| Variable | Statistic | P value |
| Age in years | .06 | >0.05 |
| Serum Creatinine | .11 | <0.05 |
| Blood Urea | .14 | <0.05 |
| Serum Potassium | .13 | <0.05 |
| Serum Sodium | .28 | <0.05 |
| Serum Calcium | .08 | >0.05 |
| Serum Phosphate | .1 | <0.05 |
| Plasma Albumin | .12 | >0.05 |
| Serum Magnesium | .07 | >0.05 |

| Table No.2: Comparison of Non-Gaussian lab variables through Mann-Whitney U test between PPI and control groups |
| --- | --- | --- |
| Variables | Mann Whitney U Statistic | P value |
| PPI | Control |
| Serum Creatinine | 46.1 | 54.9 | >0.05 |
| Blood Urea | 46.66 | 54.34 | >0.05 |
| Serum Potassium | 49.18 | 51.82 | >0.05 |
| Serum Sodium | 48.98 | 52.02 | >0.05 |
| Serum Phosphate | 54.13 | 46.87 | >0.05 |
| Plasma Albumin | 49.14 | 51.86 | >0.05 |
We also test the normality of the lab variables from which serum creatinine, blood urea, sodium, serum potassium, serum phosphate and plasma albumin were not belong to normal distribution and was tested between groups with Mann-Whitney U test. The Mann-Whitney U test showed that the mean rank values of lab variables were not significantly different between two groups with p value >0.05. (Table 2).

Serum calcium and serum magnesium was the two lab variables which were belongs to normal distribution with p value >0.05. The independent sample t test showed that the mean serum calcium was not significantly different between two groups (with p value >0.05 whereas the mean serum magnesium was found the only lab variables which was significantly different between two groups with p value <0.05. (Table 3).

Table No.3: Comparison of Gaussian variables through independent sample t test between PPI and Control group

<table>
<thead>
<tr>
<th>Variables</th>
<th>PPI</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>Mean ± Standard deviation</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>50.62±10.01</td>
<td>51.16±10.49</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>Serum Calcium</td>
<td>8.31±1.14</td>
<td>8.59±1.32</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum Magnesium</td>
<td>1.48±0.26</td>
<td>1.60±0.22</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The frequency of hypomagnesemia was significantly higher in patients on proton pump inhibitors 28.0% versus 10.0% in control group with p value <0.05. (Table 4).

Table No.4: Stratification the result with respect of gender and age groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Categories</th>
<th>PPI</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>36</td>
<td>27</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>14</td>
<td>23</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>Yes</td>
<td>14</td>
<td>5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>36</td>
<td>45</td>
<td></td>
</tr>
</tbody>
</table>

Table No.5: Stratification the result with respect of gender and age groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Categories</th>
<th>Hypomagnesemia</th>
<th>PPI</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Yes</td>
<td>8</td>
<td>4</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>28</td>
<td>23</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Yes</td>
<td>6</td>
<td>1</td>
<td>&lt;0.05**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>8</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Age groups</td>
<td>30-40</td>
<td>Yes</td>
<td>3</td>
<td>0</td>
<td>&lt;0.05**</td>
</tr>
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<td></td>
<td></td>
<td>No</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>41-50</td>
<td>Yes</td>
<td>5</td>
<td>3</td>
<td>&gt;0.05**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>51-60</td>
<td>Yes</td>
<td>3</td>
<td>1</td>
<td>&gt;0.05**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>14</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>61-70</td>
<td>Yes</td>
<td>3</td>
<td>1</td>
<td>&gt;0.05**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>6</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

*Chi square test **Likelihood ratio test

We also stratified the result to find the reason of significant difference of proportion of hypomagnesemia between two groups. The proportion of hypomagnesemia was not equal in female patients and in younger age patients (30 to 40 years of age) between two groups. (Table 5).

DISCUSSION

Patients of Chronic kidney disease (CKD) are prone to develop upper gastrointestinal (GI) symptoms and mostly show erosive gastritis, ulcerative esophagitis, and duodenitis on biopsies. PPI’s (proton pump inhibitors) are commonly used for the management of upper GI related problems. However, there are potential side effects particularly the risk of hypomagnesemia with long term use.

In the present study, the mean age of the patients was 50.89±10.2 years. Majority (33%) of the patients were aged between 51-60 years followed by 29% patients in the range of 41-50 years and 21% patients in the range of 61-70 years while only 17% patients were aged between 30-40 years. The patients of ESRD were generally reported to the age.

There were 63 (63%) male and 37 (37%) female patients in the study. Many other also reported the same sex distribution which shows that there may be overall a high percentage of male patients as compare to female in ESRD.

In the present study, the mean serum magnesium level was significantly lower in PPI group. This was also reported as same in many recent studies. Alhosaini et al. previously reported similar significant difference in the mean serum magnesium level with and without PPI (1.37±0.1 vs. 1.7±0.2) mEq/I with p value <0.05. The same results were also observed in the study conducted in 2015 where the mean serum magnesium level among patients with and without PPI was 2.52±0.42 versus 2.68±0.46 mg/dl which was also non-significant at 5% level of significance.

We observed that the frequency of hypomagnesemia was significantly higher in patients treated with PPI. The proportion of hypomagnesemia was significantly high in PPI group with p value <0.05. The result of Gau et al. and Kim et al was strengthen our finding as in both studies reported significantly higher frequency of hypomagnesemia with PPI as compare to control group (23.2% vs. 10.7%; P <0.05) and (28.6% vs. 14.2%; P <0.05) respectively.

We also stratified our results to find out the reason behind this significance. The result showed that the proportion of hypomagnesemia was significantly higher in PPI group as compare to control group only in the patients having comparatively young age i.e. belong to (30 to 40 years of age) while in rest of the age groups the proportion of the hypomagnesemia was not statistically different including the age group (50-61 and 61-70 years) where the patients were generally belong to. Similarly, we observed that the proportion of hypomagnesemia was higher only in female patients whereas we found that majority of the patients were
male. In the light of above stratified results it’s recommended that few more trials should plan with more restrict inclusion criteria with respect of patient’s age group and specifically for female.

CONCLUSION

Proton pump inhibitors were found to be associated with hypomagnesemia in patients with end stage renal disease on hemodialysis. Serum magnesium level should be monitored to enable timely identification and correction of hypomagnesemia to avoid complications.

Author’s Contribution:
Concept & Design of Study: Shakeel Khan
Drafting: Usman Khalid, Khawar Sultan
Data Analysis: Ahmad Shamim Khan, Adnan Akhtar, Asma Hafeez
Revisiting Critically: Shakeel Khan, Usman Khalid

Final Approval of version: Shakeel Khan

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

REFERENCES


To Determine the Frequency of Maternal and Fetal Outcomes of Uterine Rupture at a Tertiary Care Hospital

Zubia Bugti, Naila Ahsan and Misbah Hayat

ABSTRACT

Objective: To determine the frequency of maternal and fetal outcomes of uterine rupture at a tertiary care hospital.

Study Design: Descriptive / cross sectional study

Place and Duration of Study: This study was conducted at the department of Gynae/Obstetrics Unit-I Sandeman Provincial Hospital Quetta for 10 months. January 2020 to October 2020.

Materials and Methods: The total sample size was 126 patients which were consecutively enrolled were having presenting with uterine rupture. Cases of ruptured uterus, who were either admitted with or who will develop this complication in the hospital, were included in the study. Diagnosis was made on history and examination and was confirmed on laparotomy. These cases were analyzed with regard to their clinical presentation, past history complications, management and outcome were noted as maternal mortality and perinatal outcome were still birth, early neonatal death, alive and perinatal mortality. The surgical procedure depended on general condition of the patients, parity, and desire for future child bearing, site, severity and extent of rupture.

Results: A total of 126 women having uterine rupture were enrolled in this study. Mean age was 29.58± 876(SD), Mode was 29, and Median was 28.5 with ranging between (16-45) years. Ranged between 16 to 45 years, the maximum number of cases 76(60.3%) were less than 30 years of age. This shows that according to this study uterine rupture was more common at the age <30 years. Regarding the parity, majority of patients 73[57.9%] in this study were primigravidas, followed by 49[3.9%] in parity group of multigravida, only four cases having follow on multigravida. Most of the cases coming in our hospital were un-booked accounted for 81[64.3%]. Regarding the risk factors in current pregnancy in women presenting with uterine rupture was most of the commons was observed Scarred Uterus 22[17.5%] and Scarred uterus with spontaneous labour was 25[19.8%]. Some cases follow Scarred uterus with augmentation with syntocinon was 11[8.7%] Transverse lie was 10[7.9%]. No risk factor could be identified in Scarred uterus with induction with prostaglandin E2. Maternal morbidity in women with uterine rupture was identified as in women having shock was 41[32.5%], 27 [21.4%] were anemic, 22 [17.5%] had Puerperal Sepsis, Whereas DIC was presented in 13[10.3%] respectively. Perinatal mortality was 15 [11.9%]. Regarding neonatal morbidity or alive was 47 [37.3%], fifty patients was still birth respectively.

Conclusion: This study concluded that prolonged neglected obstructed labour is the main cause of ruptured uterus followed by scarred uterus. Proper antenatal care and updated training courses of health care providers should be stressed to prevent this catastrophic but avoidable complications. Regular antenatal care, hospital deliveries and care during labor with quick referral to well-equipped hospitals may reduce the incidence of this condition.

Key Words: Maternal, Fetal Outcomes, Uterine Rupture

Citation of article: Bugti Z, Ahsan N, Hayat M. To Determine the Frequency of Maternal and Fetal Outcomes of Uterine Rupture at a Tertiary Care Hospital. Med Forum 2020;31(12):17-20.

INTRODUCTION

Uterine rupture is defined as breach in the integrity of the myometrial wall with spillage of uterine contents into the peritoneal cavity. The rupture may occur in a scarred or unscarred uterus, with the unscarred uterine rupture leading to exceptionally immense hemorrhage. Unfortunately, a ruptures uterus has been found to be most common cause of maternal and fetal demise in developing countries. The rate of caesarean delivery has risen from 6.7% in 1990 to 19.1% in 2014 worldwide, despite improvement in obstetrical procedures such as classic caesarean section, internal version, total breech extraction etc. This has also resulted in an increase in the frequency of uterine rupture, since women with previous caesarean sections have a greater possibility of a uterine rupture. Prevalence of uterine rupture is greater in patients who may have a history of caesarean
section include former classical incision, labour initiation or argumentation, macrosomia, greater maternal age, post-term delivery, short maternal stature, no prior vaginal delivery, and prior periviable caesarian section. The aim of this study is to determine the frequency of maternal and fetal outcome so as to highlight the grey areas where there might be a room for improvement of this avoidable catastrophe. This study will also help us to educate women about the consequences of poor maternal & parental outcome. Thus the implementation of regular antenatal visits and proper family planning should be emphasized to reduce the morbidity and mortality.

**MATERIALS AND METHODS**

This study was conducted at Gynae Unit-I SPH Quetta. The total sample size was 126 patients which were consecutively enrolled were having presenting with uterine rupture. Cases of ruptured uterus, who were either admitted with or who will develop this complication in the hospital, were included in the study. Patients having ruptured uterus due to congenital abnormality were excluded from the study. Diagnosis were made on history and examination and were confirmed on laparotomy. These cases were analyzed with regard to their clinical presentation, past history complications, management and outcome were noted as maternal (shock, anemia, puerperal sepsis, wound infection, mortality and perinatal outcome were still birth, early neonatal death, alive and perinatal mortality. The surgical procedure depended on general condition of the patients, parity, and desire for future child bearing, site, severity and extent of rupture.

**RESULTS**

A total of 126 women having uterine rupture were enrolled in this study. Mean age was 29.58± 876(SD), Mode was 29, and Median was 28.5 with ranging between (16-45) years Table 1. Ranged between 16 to 45 years, the maximum number of cases 76(60.3%) were less than 30 years of age. This shows that according to this study uterine rupture was more common at the age <30 years. Regarding the parity, majority of patients 73[57.9%] in this study were primigravida, followed by 49[3.9%] in parity group of multigravida, only four cases having follow on multigravida. Most of the cases coming in our hospital were un-booked accounted for 81[64.3%]. Regarding the risk factors in current pregnancy in women presenting with uterine rupture was most of the commons was observed Scarred Uterus 22[17.5%] and Scarred uterus with spontaneous labour was 25[19.8%]. Some cases follow Scarred uterus with augmentation with syntocinon was 11[8.7%] Transverse lie was 10[7.9%] Table 2. No risk factor could be identified in Scarred uterus with induction with prostaglandin E2.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scarred Uterus</td>
<td>22</td>
<td>17.50%</td>
</tr>
<tr>
<td>Scarred uterus with spontaneous labour</td>
<td>25</td>
<td>19.80%</td>
</tr>
<tr>
<td>Scarred uterus with augmentation with syntocinon</td>
<td>11</td>
<td>8.70%</td>
</tr>
<tr>
<td>Scarred uterus with induction with prostaglandin E2</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Grand Multiparity</td>
<td>4</td>
<td>3.20%</td>
</tr>
<tr>
<td>Injudicious use of oxytocin in unscarred uterus</td>
<td>2</td>
<td>1.60%</td>
</tr>
<tr>
<td>Obstructed labour</td>
<td>17</td>
<td>13.50%</td>
</tr>
<tr>
<td>Prostaglandin administration in Un- scarred uterus.</td>
<td>5</td>
<td>4.00%</td>
</tr>
<tr>
<td>Transverse lie</td>
<td>10</td>
<td>7.90%</td>
</tr>
<tr>
<td>Uterus repair</td>
<td>6</td>
<td>4.80%</td>
</tr>
<tr>
<td>Uterus Repair + Bilateral tubal ligation</td>
<td>4</td>
<td>3.20%</td>
</tr>
<tr>
<td>Uterus Repair + Bladder Repair</td>
<td>9</td>
<td>7.10%</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>11</td>
<td>8.70%</td>
</tr>
<tr>
<td>Total</td>
<td>126</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table No.3: Different categories of Maternal Morbidity in women presenting with uterine rupture**

<table>
<thead>
<tr>
<th>Maternal Morbidity</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock</td>
<td>41</td>
<td>85</td>
<td>126</td>
</tr>
<tr>
<td>Anemia</td>
<td>27</td>
<td>99</td>
<td>126</td>
</tr>
<tr>
<td>Puerperal Sepsis</td>
<td>22</td>
<td>104</td>
<td>126</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>4</td>
<td>122</td>
<td>126</td>
</tr>
<tr>
<td>DIC</td>
<td>13</td>
<td>113</td>
<td>126</td>
</tr>
<tr>
<td>Vesico vaginal fistula</td>
<td>12</td>
<td>114</td>
<td>126</td>
</tr>
<tr>
<td>Maternal Mortality</td>
<td>7</td>
<td>119</td>
<td>126</td>
</tr>
</tbody>
</table>

Maternal morbidity in women with uterine rupture was identified as in women having shock was 41[32.5%], 27 [21.4%] were anemic, 22 [17.5%] had Puerperal Sepsis,
DISCUSSION

Uterine rupture occurs extremely rarely - according to one study from France, the incidence of uterine rupture was found to be 6.2/10000 deliveries [6]. Another study shows the incidence to be 32/10000, with mean age of the patients to be 29.6± 5.6 years. This was a frightening result since it indicates that the risk is highest in women of young and optimum fertility age. Uncarried uteri have a lower risk of rupture. A study found the incidence rate to be 0.057%. Of those who did have a ruptured uterus, 76.9% were on term while 23.1% were preterm. The study suggests that a gravid woman with hypotension, abdominal pain, fetal distress, and vaginal bleeding, may be suspected of having a ruptured uterus. Uterine rupture during pregnancy is a rare event and frequently results in life-threatening maternal and fetal compromise. It can either occur in women with (1) a native, unscarred uterus or (2) a uterus with a surgical scar from previous surgery. While a scarred uterus has a higher risk of uterine rupture, the blood loss of the mother in either cases of a scarred or unscarred uterus were not found to be significantly different.

The normal, unscarred uterus is least susceptible to rupture. Grand multiparity, neglected labor, malpresentation, breech extraction, and uterine instrumentation are all predisposing factors for uterine rupture. Despite the odds being low, if uterine rupture does occur, the morbidity and mortality rate is rather high. A higher awareness of the issue, regular checkups and low threshold for intervention can allow a better management of the case.

It is found that 66% of cases occur in women who have had a previous caesarean section. A classical vertical and T-shaped incisions carry a higher risk of later uterine rupture than the standard modern low transverse approach and an inter-delivery interval of less than 18-24 months increases the risk. It is also found that the risk appears to be higher in pregnancies of gestational age greater than 40 weeks, and that prior uterine surgery (including myomectomy, curettage, induced abortion, manual removal of the placenta) also result in the prevalence in the occurrence of a uterine rupture. The aforementioned risk factors were found in about 90% of the cases of a uterine rupture. Trauma is also found to be a known cause of uterine rupture. As a matter of fact, it is the most common non-obstetrical cause of maternal mortality. A case study including seven patients shows that six out of seven patients were unable to survive a uterine rupture caused by trauma.

Nearly all cases of a ruptured uterus are reported to occur during the third trimester. Studies suggest that when a planned VBAC is induced, the uterine rupture risk is higher if prostaglandin is used than in a non-prostaglandin-based regimen. When a planned VBAC is augmented, the oxytocin dose should be titrated such that contraction frequency is no more than 4 in 10 minutes. Research supports a maximum oxytocin dose of 20 mU/minute in trials of labour, to avoid an unacceptably high (4 x greater) risk of uterine rupture. Labour induction using oxytocin, antepartum fetal loss, and prior miscarriage also increase the chances of a uterine rupture significantly.

The most direct prevention strategy for minimizing the risk of pregnancy-related uterine rupture is to minimize the number of patients who are at highest risk. According to the aforementioned studies, if a gravida falls into the category of having multiple previous cesarean deliveries, previous classic midline cesarean delivery, previous low vertical cesarean delivery, previous low transverse cesarean delivery with a single-layer hysterotomy closure, previous cesarean delivery with an interdelivery interval of less than 2 years, previous low transverse cesarean delivery with a congenitally abnormal uterus, previous cesarean delivery without a previous history of a successful vaginal birth, previous cesarean delivery with either labor induction or augmentation, previous cesarean delivery in a woman carrying a macrosomic fetus weighing >4000 g, or previous uterine myomectomy accomplished by means of laparoscopy or laparotomy, the patient is at a higher risk of uterine rupture. Decreasing the threat factors of extended labor, cervical dilatation, induction of labor, augmentation of labor with oxytocin, diabetes, and blood loss may lessen the prevalence of uterine rupture.

The most critical aspects of treatment in the case of uterine rupture are establishing a timely diagnosis and minimizing the time from the onset of signs and symptoms until the start of definitive surgical therapy. Once a diagnosis of uterine rupture is established, the mode of management for the mother is imperative. A surgery is the primary mode of management for the mother. As a rule, the time available for successful intervention after frank uterine rupture and before the onset of major fetal morbidity is only 10-37 minutes. Therefore, once the diagnosis of uterine rupture is considered, all available resources must quickly and effectively be mobilized to successfully institute a timely surgical treatment that

Table No.4: Classification of perinatal outcome in women presenting with uterine rupture

<table>
<thead>
<tr>
<th>Perinatal outcome</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Still Birth</td>
<td>50 [39.7%]</td>
<td>76 [60.3%]</td>
<td>126 [100%]</td>
</tr>
<tr>
<td>Early Neonatal Death</td>
<td>14 [11.1%]</td>
<td>112 [88.9%]</td>
<td>126 [100%]</td>
</tr>
<tr>
<td>Alive</td>
<td>47 [37.3%]</td>
<td>79 [62.7%]</td>
<td>126 [100%]</td>
</tr>
<tr>
<td>Perinatal Mortality</td>
<td>15 [11.9%]</td>
<td>111 [88.1%]</td>
<td>126 [100%]</td>
</tr>
</tbody>
</table>

Whereas DIC was presented in 13[10.3%] respectively Table 3. Perinatal mortality was 15 [11.9%]. Regarding neonatal morbidity or alive was 47 [37.3%], fifty patients was still birth respectively Table 4.
CONCLUSION

This study concluded that prolonged neglected obstructed labour is the main cause of ruptured uterus followed by scarred uterus. Proper antenatal care and updated training courses of health care providers should be stressed to prevent this catastrophic but avoidable complications. Regular antenatal care, hospital deliveries and care during labor with quick referral to well-equipped hospitals may reduce the incidence of this condition.

Author’s Contribution:
Concept & Design of Study: Zubia Bugti
Drafting: Nila Ahsan
Data Analysis: Misbah Hayat
Revisiting Critically: Zubia Bugti, Nila Ahsan
Final Approval of version: Zubia Bugti

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

REFERENCES

Socio-Demographic Details and Psychological Aspects of Parents of Thalassemia Major Children

Saba Haider Tarar¹, Toqeer Ahmed¹, Iftikhar Ahmed¹, Waseem Ahmed Khan² and Abubakar Ali Saad³

ABSTRACT

Objective: To determine the socio-demographic details and psychological aspects of parents of Thalassemia Major Children.

Study Design: Cross sectional / observational study.

Place and Duration of Study: This study was conducted at the Thalassemia Center, Divisional Headquarters Teaching Hospital, Mirpur, AJK for a period of 09 months from February 2020 to October 2020.

Materials and Methods: Permission from Hospital Ethics Committee was taken before the study. An informed written consent was taken from parents. A questionnaire was designed that contained questions regarding demographic details as well as psychological aspects of children suffering from Thalassemia major. The data was analyzed by using SPSS version 23.

Results: 65 parents of children with Thalassemia Major were enrolled in this study. Out of 65 children, 34(52.3%) were male and 31(47.7%) were female children. The age of children was divided into groups, 23(35.4%) were between 1-5 years of age, 21(32.3%) in 6-10 years, 15(23.1%) in 11-15 years and 06(9.20%) were more than 15 years of age. Education level of parents revealed, 8(12.3%) parents were totally illiterate, 47(72.3%) were under Matric pass, 08(12.30%) were Matric and 02(3.10%) parents were having Graduation level of education. 50(76.9%) parents reported consanguineous marriage while 15(23.10%) reported non-consanguineous marriage. Upon inquiry of parental screening, we found that 38 (58.5%) were not screened for carrier status and 27(41.50%) were screened.

37(56.90%) children were not attending any kind of school, 16(24.60%) were attending schools but with more leave days due to blood transfusions while 12(18.5%) were attending school normally. Majority of parents told that Hemoglobin should be kept between 7-8gm/dl before blood transfusion and 10gm/dl after blood transfusion. After recording demographic details, psychological aspects were explored by in depth interviews from the parents.

Conclusion: The existence of a chronic disease in a child leads to significant impact upon parents and that can predispose them to psychological disorders as well as financial problems.

Key Words: Thalassemia Major, Hemoglobin, Psychological, Pakistan

INTRODUCTION

Thalassemia is one of the most commonly encountered hemoglobinopathy in the world¹². Approximately 70,000 children are born annually with various forms of Thalassaemia³.

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Printed: December, 2020

Except for a minority who are cured by Bone marrow transplantation, children and adolescents need regular blood transfusions along with iron chelation throughout their life⁴,⁵. They have comparatively short life span and poor quality of life due to chronic illness⁶. Due to its high prevalence worldwide, Thalassemia Major is considered to be a serious public health problem. Its presence spans the Mediterranean basin, African countries, the Middle East countries, the Indian Sub-continent, South-East Asia, Melanesia and the Pacific Islands, with the incidence from only 02% to as high as 25% in some parts of the world⁷.

The mortality of Thalassemia is very high in poor and middle income countries reaching around 50,000 to 100,000 annually. Whereas, up to 07% of the world's population is a genetic carrier of this hemoglobin disorder⁸. Presently the estimated carrier rate is 5 to 7% in Pakistan. In future, the number of carriers is expected to rise up to 10 million. Due to limited local statistics and inadequate documentation, exact data indicating the
incidence and prevalence of the disease is not available. However, many studies indicate that the number of thalassemia major patients born each year is around 4000 to 9000\(^7\). The majority of Thalassemia children receive blood transfusions as the only treatment in Pakistan which creates a burden not only on health system but also on the affected families. These families are very much vulnerable to social, psychological and financial problems.

**MATERIALS AND METHODS**

This mixed method Study was carried out in the Thalassemia Centre, Divisional Headquarters Teaching Hospital, Mirpur, and Azad Kashmir. The study was carried out from 1\(^{st}\) February 2020 to 30\(^{th}\) October 2020. Permission from Hospital Ethics Committee was taken before the study. A total of 65 parents of children with Thalassemia Major were enrolled in this study after informed written consent. A non-probability convenient sampling technique was used. All Parents who brought their children for blood transfusion were added in the study. A self-designed Performa was used that had questions regarding demographic details and psychological aspects of children suffering from thalassemia major. The data was analyzed by using SPSS version 23.

**RESULTS**

A total of 65 parents of children with Thalassemia Major were enrolled in this study. Out of 65, 34(52.3\%) were male and 31(47.7\%) were female children. The age was divided into groups, 23(35.4\%) were between 1-5 years of age, 21(32.3\%) in 6-10 years, 15(23.1\%) in 11-15yrs and 06(9.20\%) were more than 15 yrs of age. As far as education status was concerned, 8(12.3\%) parents were totally illiterate, 47(72.3\%) were under Matric pass, 08(12.3\%) were Matric and 02(3.1\%) parents were having Graduation level of education. 50(76.9\%) parents reported consanguineous marriage while 15(23.10\%) reported non-consanguineous marriage. Upon inquiry of parental screening, we found that 38(58.5\%) were not screened for carrier status and 27(41.50\%) were screened. In this study, most of the children i-e 56.90\% were not attending any kind of school, 24.60\% were attending schools but with more leave days due to blood transfusions while 18.5\% were attending school normally.

Knowledge about Hemoglobin levels before transfusion, majority of parents told that it should be kept between 7-8gm/dl before blood transfusion and 10gm/dl after blood transfusion.

<table>
<thead>
<tr>
<th>Sr. #</th>
<th>Question Explored</th>
<th>Answers given by Parents:</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Do you have disturbed feeling?</td>
<td>Yes (n=59 90.8%)</td>
<td>0.002</td>
</tr>
<tr>
<td>2</td>
<td>Are you able to Concentrate upon work?</td>
<td>Not at all (n=12 18.5%)</td>
<td>0.061</td>
</tr>
<tr>
<td>3</td>
<td>Effect of child’s disease on your eating habits?</td>
<td>No effect (n=25 38.5%)</td>
<td>0.003</td>
</tr>
<tr>
<td>4</td>
<td>Effected sleep pattern or not?</td>
<td>Not at all (n=23 35.4%)</td>
<td>0.120</td>
</tr>
<tr>
<td>5</td>
<td>Effect of disease on economic status?</td>
<td>Not at all (n=4 6.20%)</td>
<td>0.004</td>
</tr>
<tr>
<td>6</td>
<td>Attend social Gatherings or not?</td>
<td>Normally (n=20 30.80%)</td>
<td>0.137</td>
</tr>
<tr>
<td>7</td>
<td>Effect on Relation with spouse due to disease?</td>
<td>Yes, badly effected (n=14 21.50%)</td>
<td>0.004</td>
</tr>
<tr>
<td>8</td>
<td>Do you take any Drug to relieve tension?</td>
<td>Yes (n=08 12.30%)</td>
<td>0.191</td>
</tr>
<tr>
<td>9</td>
<td>Would you go for termination if antenatal diagnosed?</td>
<td>Yes (n=35 53.80%)</td>
<td>0.078</td>
</tr>
<tr>
<td>10</td>
<td>Effect Thalassemia on family size?</td>
<td>Yes reduced size (n=18 27.70%)</td>
<td>0.065</td>
</tr>
<tr>
<td>11</td>
<td>Would you do marriage of children in family?</td>
<td>No (n=53 81.50%)</td>
<td>0.043</td>
</tr>
<tr>
<td>12</td>
<td>Any knowledge of thalassemia before your own child?</td>
<td>No (n=54 83.10%)</td>
<td>0.152</td>
</tr>
<tr>
<td>13</td>
<td>Any Knowledge about prenatal screening?</td>
<td>No (n=38 58.50%)</td>
<td>0.062</td>
</tr>
<tr>
<td>14</td>
<td>Have you opted prenatal diagnosis?</td>
<td>No (n=51 78.50%)</td>
<td>0.342</td>
</tr>
<tr>
<td>15</td>
<td>What are the management options?</td>
<td>Transfusion (n=19 29.20%)</td>
<td>0.143</td>
</tr>
</tbody>
</table>
In-depth exploration of psychological aspects of parents revealed that 59(90.80%) had disturbed feeling with an element of depression and deprivation and 06(9.2%) had normal feeling towards their children. This is comparable with a study done in Iran where patients with thalassemia were found to have a low Quality of life than their age fellows (P = 0.001) and depression was significantly higher in this group (P = 0.015)\textsuperscript{13}. 12(18.50%) parents reported that they are not at all able to concentrate upon their daily work and jobs due to their child’s illness, 32(49.20%) reported moderate difficulty in concentration while 21(32.30%) had normal concentration and ability to perform their daily duties. This is very high as compared with study done by Aziz et al where only 08% reported that the disease did not affect their daily jobs whereas 92% had an effect upon their work\textsuperscript{8}.

25(38.50%) parents reported normal eating habits, 35(53.80%) had moderate effect on eating habits while 05(7.70%) reported severe effect on their eating habits including loss of appetite, acid peptic disease and epigastric pain.

23(35.40%) parents had normal sleep pattern with some having severe fatigue during travelling for transfusions followed by deep sleep, 33(50.80%) had mild to moderate sleep loss and 09(13.80%) had severe insomnia due to depression and anxiety about their child.04(6.20%) had no impact of their child’s disease on economic status, 42(64.60%) had moderate impact while 19(27.70%) parents had major impact in terms of inability to meet travelling expenses as well as cost of chelation therapy. Zaheer et al also demonstrated that cost of treatment, unavailability of blood, hospitalization and traveling to the health centers is adding more to the anxiety of the parents. In his study, most of the parents confessed crying about the situation and having disturbed sleeping patterns\textsuperscript{14}.

20(30.80%) parents were not having any problem in attending social gatherings, 39(60.00%) had moderately restricted social life while 05(7.70%) parents had severely restricted social life due to very frequent transfusions, stigma of disease, depression and financial
problems. Aziz et al. conducted a study in Bahawalpur showed this rate to be 27%.
50(76.90%) had good relation with their spouse along with supportive attitude while 14(21.9%) were having problems in their relation with spouse in the form of financial support, bringing to thalassemia center for transfusion, abusive language, blame for disease and even divorce. 01(1.5%) refused to answer this question. Another study reported that 23% had family conflicts with their spouse.

The appropriate strategy to reduce Thalassemia is prevention. There are different ways to decrease the incidence of Thalassemia including population screening, parental education, prenatal diagnosis and genetic counseling. Turkey, Cyprus and Iran have implemented various strategies of Thalassemia prevention.

27.70% parents reported reduced family size due to fear of another Thalassemic child while 72.3% had no impact on family size. Upon inquiry about future marriage of effected children in family revealed 81.50% parents not willing for consanguineous marriage while 18.50% were willing for family marriage. An Iranian parent describes this phenomenon as “Life begins with joy and a lot of aspirations but it changes its face soon after the disease was diagnosed at birth of first child. The Thalassemic child is born among other healthy children and the happiness disappears. Our worries for the future of our Thalassemic children deprive us from life pleasure and the life color changes into gray, but because there are healthy children, it is not yet black”.

Inquiry about prior disease knowledge before their own Thalassemic child revealed that 83.10% parents had no idea about it while 16.90% had some idea from either relatives or community. 78.50% parents never opted for prenatal screening in further pregnancies either due to lack of knowledge or finances and 21.5% opted prenatal screening in further pregnancies. 58.50% were not knowing about availability of prenatal screening while 41.50% knew about prenatal screening. 55.4% parents didn’t go for termination after prenatal diagnosis while 44.6% opted TOP. Ishfaq et al. showed that the majority of the parents were illiterate and their monthly income was very low to bear the cost of the blood transfusion and medicines. Among the total respondents, 5.8% had the knowledge that Thalassemia is inherited disease while majority 94.2% respondents were not having the knowledge that thalassemia is an inherited disease.

Regarding disease awareness, 29.2% knew about blood transfusions, 58.50% knew about chelation therapy along with blood transfusions while 12.30% knew about bone marrow transplant as well. Parental awareness in other studies regarding the Thalassemia management was also inadequate and patients continue to suffer a slow and painful course ultimately leading to death.

**CONCLUSION**

Thalassemia being a chronic disease, significantly affects the families in all aspects. It is a preventable illness so parents should be supported both psychologically as well as financially.

**Recommendations:** Thalassemia awareness should be increased through health education of society. Counseling experts should be appointed at Thalassemia centers in Pakistan. Prenatal diagnosis should be provided to all effected couples in subsequent pregnancies.

**Author’s Contribution:**

- Concept & Design of Study: Saba Haider Tarar
- Drafting: Toqeer Ahmed, Abubakr Ali Saad
- Data Analysis: Waseem Ahmed Khan
- Revisiting Critically: Iftikhar Ahmed
- Final Approval of version: Saba Haider Tarar

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

**REFERENCES**

Determine the Outcome of Multiple Tract Percutaneous Nephrolithotomy for Renal Staghorn Calculus

Nizamud Din¹, Irfan Ahmed², Mumtaz Ali Shah³, Fazal Elahi¹, Fazal Akbar² and Rashidullah¹

ABSTRACT

Objective: To determine the outcomes of PCNL (multitract percutaneous nephrolithotomy) in patients presented with renal staghorn calculus.

Study Design: Descriptive case series study.

Place and Duration of Study: This study was conducted at the Department of Urology Saidu Teaching Hospital Swat and PIMS Islamabad, during from the period December 2018 to December 2019.

Materials and Methods: Two hundred and ten patients of both genders with renal staghorn calculi of >20 mm in size were included. Patients detailed demographics were recorded after taking written consent. Multiple tract PCNL was done after completion of all investigations. All patients were given prophylactic antibiotics. Stone clearance post-operatively was assessed by CT-KUB. Follow-up was taken at 1 month postoperatively. Data was analyzed by SPSS 24.0.

Results: There were 100 (47.62%) males while 110 (52.38%) were females. Mean age of 42.26±12.68 years. Mean BMI was 24.68±2.13 kg/m². Mean size of the stone was 24.88±4.73 mm. Postoperative complications found in 40 (19.05%) patients, in which 20 (9.52%) patients had fever, blood transfusion in 8 (3.81%) patients, wound infection in 6 (2.86%), hydrothorax in 4 (1.90%) patients and 2 (0.95%) patient had septic shock. Overall stone clearance rate in 6 (2.86%), hydrothorax in 4 (1.90%) patients and 2 (0.95%) patient had septic shock. Overall stone clearance rate with multiple tract PCNL was 87.92%.

Conclusion: It is concluded that multitract PCNL is safe and very effective treatment modality for staghorn calculi with higher stone clearance rate and fewer postoperative complications.

Key Words: Multiple tract percutaneous nephrolithotomy (PCNL), Renal staghorn calculus, Stone clearance.

INTRODUCTION

The stone-polluted stonic calculus is known as the renal calculus which has a branch structure with a large portion of the collector system [1]. This procedure also incorporates open operation, percutaneous nephrolithotomy, extracorporeal shock lithotripsy and a combination Staghorn calculus therapy option. The emphasis of staghorn computer management is to clear stones entirely, so that blockages are removed and the further formation of stones prevented, as well as causative organisms eradicated [2].

Despite this excellence in stone clearance, many international studies with suitable amounts of surgical complications and which have particular relevance to blood transfusion are documented[3]. Percutaneous nephrolithotomy is also controversial with numerous tract which may lead to additional complications such as serious bleeding from multitractal renal parenchyma trauma [4].

The effect of percutaneous nephrolithotomy on the transient deterioration of renal function is similar, however, either with a single or multi-acces tract. Thus the clearance of steel with a considerably complicated rates in percutaneous staghorn nephritomy with many accesses can be seen as an efficacious and competitive approach [6]. Therefore, many complex staghorn stones require many access in different sizes to reach and remove all parts of the stone [6], [4]. The discussion continues to see whether a single PCNL-loop procedure or sandwich treatment is to be carried out in which the initial PCNL is paired with the lithotripsy extracorporeal shock wave (SWL) and then another 2nd PCNL look or rather a PCNL-loop multitract to make the patient stone free in one session. In addition, the discussion continues. Later, the rate can be 84–95% without stone [7]. In addition, multitracting one-session PCNL would considerably
lower costs if multiple procedures of all forms were avoided \cite{8}. Compared to combination therapies, multitract PCNL has a comparable complication rate\cite{9}, although studies indicate that multiple tracts cause perioperative bleeding\cite{10}.

**MATERIALS AND METHODS**

This descriptive study was conducted at Department of Urology Saidu Teaching Hospital Swat and PIMS Islamabad, during from the period December 2018 to December 2019. Total 210 patients of both genders with renal staghorn calculi of >20 mm in size were included. Patients detailed demographics including age, sex, body mass index and size of stone were recorded after taking written consent. Patients ages were ranging between 18 to 70 years. Patients with uncontrolled bleeding disorders INR>1.5, ectopic pelvic kidney and urinary tract infection diagnosed on urine culture and sensitivity were excluded. Detailed medical history and examination, renal function tests (serum urea and creatinine), urine complete examination and urine culture, X ray KUB, ultrasonography and computed tomography (KUB) were done.

All the patients were received Multiple tract PCNL was. All patients were given prophylactic antibiotics. All procedures were performed under general anesthesia. Postoperative complications such as fever, blood transfusion, hydrothorax, septic shock and wound infection were examined. Stone clearance postoperatively was assessed by CT-KUB. Follow-up was taken at 1 month postoperatively. Data was analyzed by SPSS 24.0.

**RESULTS**

There were 100 (47.62%) males while 110 (52.38%) were females. Mean age of 42.26±12.68 years. Mean BMI was 24.68±2.13 kg/m². Mean size of the stone was 24.88±4.73 mm. (Table 1).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency No.</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (Years)</td>
<td>42.26±12.68</td>
<td>-</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>24.68±2.13</td>
<td>-</td>
</tr>
<tr>
<td>Mean Stone Size (mm)</td>
<td>24.88±4.73</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>100</td>
<td>47.62</td>
</tr>
<tr>
<td>Female</td>
<td>110</td>
<td>52.38</td>
</tr>
</tbody>
</table>

**Table No 2: Postoperative complications**

<table>
<thead>
<tr>
<th>Po complications</th>
<th>Frequency No.</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>20</td>
<td>9.52</td>
</tr>
<tr>
<td>Transfusion</td>
<td>8</td>
<td>3.81</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>6</td>
<td>2.86</td>
</tr>
<tr>
<td>Hydrothorax</td>
<td>4</td>
<td>1.9</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>2</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Postoperative complications found in 40 (19.05%) patients, in which 20 (9.52%) patients had fever, blood transfusion in 8 (3.81%) patients, wound infection in 6 (2.86%), hydrothorax in 4 (1.90%) patients and 2 (0.95%) patient had septic shock. (Table 2). 184 (87.92%) patients had successful treatment and found complete stone clearance while 26 (12.08%) had not complete stone clearance. (Figure 1).

**DISCUSSION**

Complex stones are very detrimental to the kidney as they cause inflammation, atrophy, renal failure and cancer. To obtain maximum clearance and to prevent second vision procedures such as ESWL or retrospective inner arrest surgery, multiple tracts are often required for treatment (RIRS). Nevertheless, some tracts frequently have a higher risk of bleeding \cite{11}. Moreover, multitract PCNL is very difficult to learn and needs a lot of expertise, even though device and technology have been developed over the recent decades \cite{12}. Some studies have shown that open or laparoscopic stone surgery is an effective way to treat complex renal stones and is related to a higher one-session stone-free rate \cite{13}. We conducted present study to determine the outcomes of renal staghorn calculi treated with multiple tract PCNL. In this regard 210 patients with staghorn calculi were enrolled. Majority 52.38% patients were females while males were 47.62%. Mean age of patients was 42.26±12.68 years. These results showed similarity to some previous studies in which females were high in numbers 55% to 60% and average age of patients was 45 years \cite{14-15}.

In present study stone clearance rate associated with PCNL was 87.92%. These results were comparable to many of previous studies in which multiple tract PCNL had high successful rate with stone clearance rate 85% to 92% \cite{7,16}. A study conducted by Rashid AO et al \cite{17} reported that out 65 patients received multitract PCNL and among them stone clearance rate was 85%.
A study conducted by Liang T et al. [18] regarding multiple tract PCNL for complex renal stone and they reported that complete stone clearance rate was 88.9%. Chan J et al. [19] used multiple tract PCNL for the treatment of renal staghorn calculi and in their study out of 117 patients 54.2% patients got complete stone clearance while 45.8% patients had partial stone clearance.

A study by Gadelmoula M et al. [20] regarding outcomes of PCNL for renal stone, in their study the stone clearance rate was 87.7% patients.

In our study postoperative complications found in 40 (19.05%) patients, in which 20 (9.52%) patients had fever, blood transfusion in 8 (3.81%) patients, wound infection in 6 (2.86%), hydrothorax in 4 (1.90%) patients and 2 (0.95%) patient had septic shock. Many of previous studies showed similarity to our study findings in which bleeding, fever, hydrothorax and septic shock were associated with PCNL [21–22].

CONCLUSION
The multiple tract PCNL is gold standard technique for staghorn calculi with reasonable operative duration, low morbidity and good success rate.

Author’s Contribution:
Concept & Design of Study: Nizamud Din
Drafting: Irfan Ahmed, Mumtaz Ali Shah
Data Analysis: Fazal Elahi, Fazal Akbar, Rashidullah
Revisiting Critically: Nizamud Din, Irfan Ahmed
Final Approval of version: Nizamud Din

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

REFERENCES
17. Rashid AO, Mahmood SN, Amin AK, et al. Multittract percutaneous nephrolithotomy in the
Early Graft Occlusion after Coronary Artery Bypass Grafting

Muhammad Sohail Saleemi¹, Nisar Ahmed¹, Zahid Rafiq¹, Muhammad Tahir Mohy-ud-din¹, Usama Khalid¹ and Abubakr Ali Saad²

ABSTRACT

Objective: To determine the frequency of premature coronary bypass graft occlusions after coronary artery bypass graft surgery.

Study Design: Descriptive case series study.

Place and Duration of Study: This study was conducted at the department of cardiovascular medicine, Chaudhary Pervaiz Ellahi Institute of Cardiology, Multan from March to September 2018.

Materials and Methods: This descriptive case series included 292 consecutive patients between one week to six months after coronary artery bypass graft surgery. The age range between 40 to 70 years and includes patients of both genders. The patients were scanned using a 128-section multi-detector computerized tomography scanner. Findings were interpreted by a consultant cardiologist. Frequency of venous and arterial graft occlusions and associated risk factors were noted.

Results: Mean age of the patients was 52.60 ± 7.72 years. Out of the 292 patients, 242 (82.88%) were male and 50 (17.12%) were female. In this study, 584 were vein conduits and 292 were arterial conduits. CT coronary angiogram identified graft closure in 69 (7.88%) out of 876 total grafts. Out of total 584 vein conduits 52 (8.90%) were occluded. On the other hand, out of total 292 arterial conduits 17 (5.82%) were occluded.

Conclusion: There is a substantial overall frequency of early graft occlusion including both arterial and vein conduits. In patients who underwent coronary artery bypass surgery, 7.88% had early graft occlusion.

Key Words: Graft occlusions, Coronary artery bypass grafting, Venous graft, Arterial graft

INTRODUCTION

Coronary arterial bypass graft surgery (CABG) is opted as a standard treatment modality in patients with complex coronary arterial involvement by the atherosclerotic disease process. Short and long term outcomes in patients undergoing revascularization by coronary artery bypass grafting are determined by the patency of graft conduits.¹ ¹,² ³ Now multi-slice CT scanner is used to evaluate grafts in post CABG patients while previously invasive coronary angiography was used for evaluation of grafts.⁴ ⁵ There is local damage particularly the endothelium of the harvested vascular conduit. This happens particularly when grafts are surgically harvested, and anastomosis is done. This localized damage particularly of the endothelial lining of the graft conduits leads to localized inflammation and platelet activation with resultant graft failure. This particularly happens in the first month after surgical procedure.⁶ In addition to physical damage, hypercoagulable state, and high intraluminal pressure to which vein conduits are exposed leads to its stretch and distention. All these factors lead to premature vein graft failure within one month of a cardiac surgical procedure.⁷ Two types of grafts (venous and arterial) are used for CABG surgery.⁸ Venous grafts degenerate and occlude early as compared to arterial grafts that remain patent for a longer duration.⁹ Grafts occlusion occur early in 8 to 12 percent grafts, unfavorably affecting short as well as long term outcomes in post CABG patients.¹ ¹ ¹² In one study, a total of 366 grafts, comprising of 250 vein grafts and 116 arterial conduits were assessed. In that study multi-slice, CT found total 32 (8.7%) early occluded grafts. The study showed that 26 (10%) of venous conduits were occluded. On the other hand, 6(5%) of 116 arterial grafts were occluded.¹³

To our best of knowledge there is limited worldwide and scarce local data available regarding the frequency of early grafts occlusion, so we planned to conduct this study to assess the incidence of graft occlusion. The study will look for premature vein and arterial graft occlusion within one month of a cardiac surgical
procedure. The results of the study will provide local area statistics about the premature graft occlusion and it will also help in appropriate management of such patients to improve post coronary artery bypass outcomes. Our local population differs ethnically, racially and socially from the western population, so different results can be expected in our population.

MATERIALS AND METHODS

This descriptive case series study was undertaken at the department of cardiovascular medicine, Chaudhary Pervaiz Ellahi Institute of Cardiology, Multan from 7th March to 6th Sept. 2018. The study was started after authorization of the ethical review board.

By using a WHO calculator, a sample size of 292 was calculated by taking 5% level of significance, 2.5% margin of error and taking occlusion of arterial grafts as 5% from previous studies.1 Total of 292 consecutive patients having a total of 876 grafts were included in the study. The total number of vein conduits was 584 (66.67%) and these were grafted to the right and left circumflex coronary vessels. Of out total 876 grafts 292 (33.33%) were left internal mammary arterial conduits and grafted to the left anterior descending artery. The patients were studied between one week to 6 months after CABG. Patients aging 40-70 years of both genders were included after informed consent. All patients underwent CT-coronary angiography for either symptoms or postoperative surveillance. Patients with hypersensitivity to contrast agent, and nephropathy defined as creatinine more than 2mg/dl were excluded from the study. Patient data regarding age, gender and risk factors for ischemic heart disease (IHD) was noted. All the patients were studied by utilizing 128-section multi-detect or cardiac tomography scanner. Findings were interpreted by consultant cardiologist and the presence or absence of graft occlusion was noted.

IBM SPSS version 20.0 was used for statistical analysis. Mean and standard deviation was calculated for age. Frequency and percentage were calculated for gender, risk factors of IHD and occlusion of venous and arterial grafts.

RESULTS

The age range in this study was from 40 to 70 years with a mean age of 52.60 ± 7.72 years (Table No 1). Most of the study cases 166 (56.85%) were within the age bracket of 40 to 55 years of age.

Table No. 1: Age distribution of the study patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean age±sd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years</td>
<td>40</td>
<td>70</td>
<td>52.6± 7.72</td>
</tr>
</tbody>
</table>

Out of the total 292 study patients, 242 (82.88%) were having male and 50 (17.12%) were having female gender (Table No 2).

Among the study patients 135 (46.23%) were diabetics, 210 (68.84%) were hypertensive, 183 (62.67%) were smokers and 183 (62.67%) had dyslipidemia (Table 3).

Table No. 2: Gender distribution of study patients

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>242</td>
<td>82.88%</td>
</tr>
<tr>
<td>Female</td>
<td>50</td>
<td>17.12%</td>
</tr>
<tr>
<td>Total</td>
<td>292</td>
<td>100%</td>
</tr>
</tbody>
</table>

In this study, 584 were vein conduits and 292 were arterial conduits. CT coronary angiogram identified graft closure in 69 (7.88%) out of 876 total grafts. Out of total 584 vein conduits 52 (8.90%) were occluded. On the other hand, out of total 292 arterial conduits 17 (5.82%) were occluded. Figure 1 shows the frequency and percentage of graft occlusion in venous and arterial grafts. Stratification of early graft occlusion with diabetes mellitus, hypertension, smoking and dyslipidemia showed p-value more than 0.05 depicting non-significant results.

DISCUSSION

For a long time, invasive Coronary artery angiography (CAG) was employed for assessment of grafts after CABG. Invasive CAG not only increases hospital cost but also has hazards of dreadful complications as ST-elevation MI leading to myocardial damage, ischemic/embolic neurological complications with resultant neurological complications, and ventricular arrhythmias. After the development of new noninvasive procedures like electron-beam tomography and helical scan computed tomography, these modalities are now being used increasingly for
assessing graft patency, but they have certain limitations which are multiple artefacts created due to motion of the patient, respiratory movements and metallic clips.\textsuperscript{14,16}

Bassri et al assessed and reported that out of 366 grafts including arterial and vein conduits. Two hundred and fifty were vein conduits and one hundred and sixteen were arterial conduits. Coronary angiography and graft study by cardiac tomography showed premature and early graft closure in 32 (8.7\%) of all the grafts. The study showed that 26 (10\%) of 250 venous conduits were occluded. While 6 (5\%) of 116 arterial conduits were occluded. The results were non-significant for venous vs arterial grafts.\textsuperscript{12} In our study we also found that early graft occlusion has no association whether the graft was arterial or venous. In a mean follow Benedetto et al done a meta-analysis of five studies. They demonstrated that the occlusion rate of arterial and venous conduits is almost the same. It was 14.1\% in the case of arterial conduits, while the rate of occlusion in venous conduits was 14.6\%. The study patients were followed for a mean period of twenty-two months.\textsuperscript{16}

Athanasiou et al demonstrated patency rates of 3678 arterial conduits and 7506 vein conduits. They recorded the patency at less than a year, between one to five years, and longer than five years, which they termed as short term, medium-term and long term follow up respectively.\textsuperscript{17} The study highlighted the fact that there was no statistically significant difference with an odds ratio of 1.04 when a short term comparison was done among arterial and venous conduits. The study also demonstrated that there was a statistically significant superior arterial conduit patency over the medium and long term period of follow up with an odds ratio of 2.06 and 2.28 respectively. Our study also showed similar results that there is no significant difference between early arterial and venous conduit occlusion. Our study has certain limitations. This is an observational study without long term follow-up with a small sample size. However, it paves a way for a larger study with longer follow up to assess the long term graft patency and also to assess the frequency of venous graft occlusion as compared to arterial graft occlusion.

**CONCLUSION**

There is a substantial overall frequency of early graft occlusion (venous and arterial) in post coronary artery bypass grafting patients (7.88\%).

**Acknowledgement:** Special thanks to Saima Dastgeer who is working as Assistant Professor in Department of Psychology, Govt. College of Home Economics Multan, for her valuable contribution in data analysis and proof reading of our study.

**Author’s Contribution:**

<table>
<thead>
<tr>
<th>Concept &amp; Design of Study:</th>
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<td>Muhammad Tahir Mohy-ud-din, Usama Khalid and Abubakr Ali Saad</td>
</tr>
<tr>
<td>Revisiting Critically:</td>
<td>Muhammad Sohail Saleemi, Nisar Ahmed</td>
</tr>
<tr>
<td>Final Approval of version:</td>
<td>Muhammad Sohail Saleemi</td>
</tr>
</tbody>
</table>

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

**REFERENCES**

Histomorphological Changes in Human Senile Cataractous Lenses with Diabetic and Non-Diabetic Patients: A Comparative Study

Asad Ali Zardari¹, Shazia Begum Shahani¹, Muhammad Yaqoob Shahani², Umbreen Bano², Mujeeb-ur-Rehman Sahito¹ and Pashmina Shaikh²

ABSTRACT

Objective: To determine the histomorphological changes in the human senile cataract, between diabetic and non-diabetic eyes and the correlation between anterior ocular segment biometry and HbA1c level.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Anatomy with collaboration of Sindh Institute of Ophthalmology and Visual Sciences (S.I.O.V.S) @ Eye Hospital Hyderabad, Sindh for the period of six months from April 2020 to October 2020.

Materials and Methods: This study was conducted on 385 patients aged more than 40 years who underwent intra-capsular cataract extraction who were included in study while those patients whose age less than 40 years. Data were analyzed using SPSS version 22.0

Results: A total of 385 patients of senile cataract extraction were selected. The frequency of cataracts was found 107(27.79%) among diabetic patients. There was a statistically significant difference concerning the increased incidence of senile cataract with HbA1C (mg/dL) in diabetic patients as compared to non-diabetic patients (p-value = <0.0001). The calcareous change was noted in 5 cases of 40 to 100 years’ age. Calcarious change and Collagen bundles were noted out of 278 cases of non-diabetic of 40 to 100 years’ age.

Conclusion: Duration of diabetes, age, and gender were found to be significant risk factors for predicting the grade of cataract in male or female diabetic patients.

Key Words: Histomorphological changes, senile cataractous lenses, diabetic Mellitus

INTRODUCTION

A cataract is considered to be primary reason for curable blindness that is caused by progressive loss of lens transparency and affects millions of people around world.¹ The prevalence of blindness in developing countries is 10-40 times higher than in developed countries². Across Western sub-Saharan Africa, age-standardized blindness incidence is still most widespread across people over age of 50 with a level of 6.0%.

In Eastern Asia, tropical Latin America, and Western Europe,³ highest reductions in age-standardized blindness are attributed to cataracts in people aged 50 years. It is likely to become an increasing problem as world population ages.⁴ The risk of cataract is now increasingly increasing⁴. Many clinicians are diagnosed between ages of 40 and 80 and cataracts are diagnosed fairly widespread, regardless of race or sex. Among developing countries, cataract is leading cause of blindness because of lack of medical care.⁵ A regional survey in Rawalpindi reveals that about 75% of population 75 years of age and over is prone to cataracts, which are biggest cause of vision impairment and blindness worldwide. Regular or flexible lenses are transparent.⁶

The zonular fibers are fixed in position and attach lens between equatorial lines and lens to a muscle tissue circle called ciliary body.⁷ Several culprits, from occupational, behavioral, UV radiation, medical and age factors have all been implicated.⁸ Obesity was at risk of mixed lens opacities at baseline and older age.⁹ Other risk factors include diabetes prolong exposure to sunlight and alcohol intake.¹⁰ In Memon AF et al.’s research, cataracts are
stated to be 4 times more frequent in diabetics and 2 times more frequently in people. In diabetic patients, nuclear sclerosis was most common type of cataract. The prevalence of type 2 diabetes mellitus is on rise, more so in Pakistan. The risk factors for cataract formation include long-term diabetic disorder, advanced age when clinically diagnosed; advanced retinopathy; diuretic therapy; low blood sugar control and even reduced fast glucose (IPG); Since incidence of type 2 diabetes mellitus (DM) is growing, occurrence of cataracts among diabetics should be examined. This research helps to understand how role of medical and biochemical factors affect development of cataracts. It highlights risk factors (age, sex, duration of diabetes, family history, RBS, glycosylated hemoglobin, serum cholesterol) both, biochemical and lifestyle variables and modulation of these variables may delay occurrence of cataract in population of type 2 diabetes mellitus. The present study aims to determine histomorphological changes in human senile cataract. between diabetic and non-diabetic eyes and the correlation between anterior ocular segment biometry and HbA1c level.

MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Anatomy with collaboration of Sindh Institute of Ophthalmology and Visual Sciences at Eye Hospital Hyderabad, Sindh for six months from April 2020 to October 2020. A total of 385 patients were included. Age more than 40 years, patients who undergone intra-capsular cataract extraction (both male and female) were included. Those with a record of eye injury, regional and systemic hormones, acute and ocular illness and those who have not given their permission were excluded. A detailed history was taken and an examination of patient admitted for cataract operation was done. After taking history morphometry of lens was done with help of ultrasonography, Cataractous lenses were obtained at time of operation. Cataracts are graded as cortical, vascular, subcapsular, or combined for morphological purposes. With written consent of participants, spontaneous levels of blood glucose and fasting blood plasma, and glycemia (HbA1c) were measured. The study was undertaken after ethical approval was granted by PUMHSW University Hospital Ethical Committees. Informed consent was taken from all participants.

Histological examination of senile cataractous lenses: The lens was washed with normal saline and lens was divided into 2 parts. Half was preserved in bovine fluid and a half was preserved in Mammannous fluid. The lens was processed for paraffin wax section and stained with Haematoxylin & Eosin for general Histological changes, Masson’s Trichrome- for collagen, PAS Staining- for glycogen, Sudan black B-for lipids. Microscope and after that photography of slides was taken on Kodak Gold color film,100ASA,21DIN.

Tissue processing: Tissues were placed in graded Alcohol 30%, 50%, 70%, and 90% for 2 minutes each. Tissues were embedded in molten paraffin wax using tissue blocks and allowed to cool and solidify. The sections were cleared in two changes of xylene for 3 minutes each. The sections were placed in graded alcohol 90%, 70%, and 50% for 2 minutes each.

Statistical Analysis: In SPSS version 22.0, frequencies and percentages have been determined to compare ratios of categorical variables such as age (in groups), race, and Chi-square (if needed). The mean ± standard deviation, "t" test was used to compare means among different ages such as ages, diameters, and thickness of lenses. All data was calculated on a 95% confidence interval. P-value ≤ 0.05 were considered as significant level.

RESULTS

A total of 385 patients of senile cataract extraction (both male and female) were selected based on inclusion criteria. The frequency of cataracts was found in 107(27.79%) among diabetics and 278(72.21%) among non-diabetics.

Age incidence: In this study, minimum age of patients with cataract was 40 years and maximum age was 100 years. The Mean age ± SD of diabetic patients was 52.2804 ± 6.84 years while mean ± SD of non-diabetic patients was 66.2590 ± 10.27 years. Out of 107 diabetic patients, frequency of cataracts in DM patients increased with age to 64(59.8%), 38(35.5%), 5(4.6%) in 41 to 50 years, 51-60, and >60 age groups respectively.

Gender: Among 385 patients, 236(61.5%) were females and 148(38.5%) were male patients. Senile cataract was seen as more common in female patients as compared to male patients. In diabetic females, there was an increased incidence of 66(62.3%) of senile cataracts as compared to decreased prevalence among diabetic males 40(37.7%). Cataract was significantly associated with gender concerning increased incidence of senile cataract in female diabetic patients (p-value = 0.040).

HbA1C: The mean HbA1C ± SD was 7.3914±1.018 mg/dl in diabetic patients. However, there was a statistically significant difference concerning increased incidence of senile cataract with HbA1C (mg/dL) in diabetic patients as compared to non-diabetic patients (p-value = <0.0001).

Duration of Diabetic Mellitus: In the present study, minimum duration of DM was 2 years and maximum duration of DM was 12 years. out of 107 diabetic patients, mean duration of DM ± SD was 4.56 ± 2.17 years. Cataract prevalence was also higher 105(98.1%) in subjects with shorter duration of diabetes (<10 years)
than in those 2(1.9%) with longer duration of diabetes (> 10 years).

Type of lens: In respect to regions of lens, Posterior sub-capsular cataract was commonest type in 79(73.8%) of cataract cases in diabetics followed by cortical cataracts 26(24.3%), mixed type 107(100%).

Histological findings: The nucleus showed an anteroposterior arrangement of primary lens fibers, surrounded periodically by secondary fibers. A decrease in thickness of capsule in cataracts at all planes was recorded when compared with normal lenses. The retention of broken lens cells debris and water in form of tiny globules was noted in 12 cases of 40 to 100 years of age.

The epithelial cells showed migration beyond the post-equatorial plane beneath posterior capsule out of 107 cases of diabetic Mellitus of 40 to 100 years of age and were accompanied by equatorial and posterior cortical degeneration with dystrophic calcification. Calcareous change was noted in 8 cases of 40 to 100 years ago.

Graph 1: Frequency of Diabetes Mellitus

<table>
<thead>
<tr>
<th>Region of lens</th>
<th>Diabetic n = 107</th>
<th>Non-diabetic n = 278</th>
<th>total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuclear Sclerotic Cataracts</td>
<td>2(1.9%)</td>
<td>190(68.3%)</td>
<td>192(49.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cortical Cataracts</td>
<td>26(24.3%)</td>
<td>48(17.3%)</td>
<td>74(19.2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Posterior Subscapular Cataracts</td>
<td>79(73.8%)</td>
<td>38(13.7%)</td>
<td>117(30.4%)</td>
<td></td>
</tr>
<tr>
<td>Mixed type</td>
<td>107(100.0%)</td>
<td>278(100.0%)</td>
<td>385(100.0%)</td>
<td></td>
</tr>
<tr>
<td>HbA1C Level</td>
<td>7.3914 ± 1.018</td>
<td>5.6990 ± 1.312</td>
<td>7.6105</td>
<td>0.001</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>3.8857 ± 0.57</td>
<td>4.0943 ± 0.54</td>
<td>4.0297</td>
<td>0.001</td>
</tr>
<tr>
<td>Anterior Chamber (AC)</td>
<td>6.2955 ± 33.34772</td>
<td>3.0863 ± 1.87549</td>
<td>7.5018</td>
<td>0.011</td>
</tr>
<tr>
<td>Vitrous</td>
<td>16.0283 ± .68</td>
<td>15.7332 ± .83</td>
<td>15.8659</td>
<td>0.001</td>
</tr>
<tr>
<td>Total Length (TL)</td>
<td>22.7508 ± 6.13</td>
<td>30.1737 ± 126.095</td>
<td>22.9605</td>
<td>0.54</td>
</tr>
<tr>
<td>Morgagnian Globules</td>
<td>31(29.0%)</td>
<td>17(6.1%)</td>
<td>48(12.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Morgagnian Globules + Dystrophic Calciication</td>
<td>14(13.1%)</td>
<td>29(10.4%)</td>
<td>43(11.2%)</td>
<td>0.473</td>
</tr>
<tr>
<td>Morgagnian Globules + Collagen bundles</td>
<td>12(11.2%)</td>
<td>12(4.3%)</td>
<td>24(6.2%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Epithelial Migration</td>
<td>93(86.9%)</td>
<td>76(27.3%)</td>
<td>169(43.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Collagen Bundles</td>
<td>13(12.1%)</td>
<td>12(4.3%)</td>
<td>25(6.5%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Morgagnian Globules + Collagen Bundles + Migration of Epithelium</td>
<td>13(12.1%)</td>
<td>13(4.7%)</td>
<td>26(6.8%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Migration of epithelium + Dystrophic Calciication</td>
<td>16(15.0%)</td>
<td>17(6.1%)</td>
<td>33(8.6%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Morgagnian Globules + Dystrophic Calciication + Collagen Bundles</td>
<td>24(22.4%)</td>
<td>30(10.8%)</td>
<td>54(14.0%)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Histological findings

Figure No.1: Anterior part of normal human lens stained with H & E x 410

Figure No.2: Morganian globules and Collagen bundles stained with H and E x250.

Figure No.3: Dystrophic calcification stained with H & E x 250.

Figure No.4: Dystrophic calcification and Epithelial migration within anterior cortex of lens substance stained with H and E x 250.

Figure No.5: Dystrophic calcification stained with H & E x 250.

Figure No.6: Dystrophic calcification stained with H & E x 250.
Figure No.7: Dystrophic calcification, Collagen bundles, and organian globules within anterior cortex of lens substance stained with H and E x 250

Figure No.8: Dystrophic calcification and Collagen bundles stained with H & E x 250.

Table No.2: Distribution of patients according to Descriptive statistics of Duration of DM (n = 107)

<table>
<thead>
<tr>
<th>Descriptive statistics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4.56</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>2.17</td>
</tr>
<tr>
<td>Mode</td>
<td>3.00</td>
</tr>
<tr>
<td>Median</td>
<td>4.00</td>
</tr>
<tr>
<td>Range</td>
<td>2 to 11 years</td>
</tr>
<tr>
<td>Minimum</td>
<td>02</td>
</tr>
<tr>
<td>Maximum</td>
<td>12</td>
</tr>
<tr>
<td>Duration of DM:</td>
<td></td>
</tr>
<tr>
<td>&lt; 10 years</td>
<td>105(98.1%)</td>
</tr>
<tr>
<td>&gt; 10 years</td>
<td>02(1.9%)</td>
</tr>
</tbody>
</table>

DISCUSSION

This study showed that the average age of patients with diabetes in cataracts was 61±10, which is identical to Raman and his colleague's Indian study, and higher than that of Janghorbani's average age at 49.2 years. In both diabetic and non-diabetic cataracts, both forms of cataracts (atomic, cortical, post capsular, and mixed cataracts) are discovered with a higher prevalence for diabetics, and radioactive cataract in non-diabetics. This was consistent with Beaver Dam Eye Study and Blue Mountains Eye Study which demonstrated a statistically significant correlation of Post-capsular cataract with diabetes.

We found glucose in all of the diabetic nuclei with a mean concentration of 21.24 mg/dl and a mean concentration of non-diabetes of 12.30 mg/dl in this biochemical research portion. This finding is compatible with Pirie who has observed that diabetic cataract lenses have igneous sorbitol and glucose and fructose levels compared to non-diabetic lens, most likely at same frequency as high glucose levels in diabetic comedy.

The Park Young M et al. notes that nuclear consistable cuboidal sloshed capsular has been observed to have an equivalent cuboidal epithelial cell monolayer firmly attached to anterior capsule. According to previous studies using extraction lens abnormal permeability of lens around sac to induce cataract, which is due to histologic analysis of cell membrane damage and consequent expansion of space between lens fiber, and Some were also abnormal shape changes in lens capsule confirmation.

Further, duration of diabetes was found to be a significant independent predictor of cataract for patient with insulin-dependent diabetes mellitus.

CONCLUSION

In many cases lens capsules were ruptured spaces between lens fibers increases in some area. The duration of diabetes, age, or gender was found to be a significant risk factor for predicting the grade of cataract in male or female diabetic patients. The present study revealed that the decreased energy available for normal functioning of the lens in old age resulted in degenerative and sclerotic changes.

Author's Contribution:
- Concept & Design of Study: Asad Ali Zardari
- Drafting: Shazia Begum Shahani, Muhammad Yaqoob Shahani
- Data Analysis: Umbreen Bano, Mujeeb-ur-Rehman Sahito, Pashmina Shaikh
- Revisiting Critically: Asad Ali Zardari, Shazia Begum Shahani
- Final Approval of version: Asad Ali Zardari

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

REFERENCES

1. Comparative Biometric Study. The Anatomical Record 2016;299:1308-12.
Prevalence of Refractive Errors in Urban Area among School Boys

Zulfiqar Ali¹, Nadia Nazir¹, Soufia Farrukh¹, Abdul Rehman², Muhammad Javaid Iqbal³ and Imran Nazir⁴

ABSTRACT

Objective: To study the prevalence of refractive errors among school boys in urban area.

Study Design: A cross sectional study

Place and Duration of Study: This study was conducted at Ophthalmology, Bahawal Victoria Hospital, Quaid e Azam Medical College, Bahawalpur during November 2017.

Materials and Methods: The study population comprised of 462 students from class 6th to Class 10th. Ocular examination process was thoroughly explained to the study participants while all the study instruments/equipments were transported to school one day prior to the actual ocular examination. Standard “Snellen Chart” was used for screening of visual acuity. Children having visual acuity < 6/6 in any of the eye were further confirmed for refractive error with the use of pinhole. Objective refraction was made using auto-refractor and retinoscopy while confirmation was done applying subjective refraction.

Results: Among a total of 460 students, age range was between 9 to 18 years while the mean age ±SD was recorded to be 14.3±1.8 years. History of glasses was noted among 58 (12.6%) students. There were 253 (55.0%) who had history of glasses in their parents. Findings of our study revealed frequency of refractive errors in 98 (21.3%) students. Among 98 children with refractive errors, myopia in 58 students (59.2%) was the commonest type of refractive error followed by astigmatism in 28 students (28.6%) and hypermetropia in 12 students (12.1%).

Conclusion: Myopia was the commonest type of refractive error in school going boys followed by Astigmatism and hypermetropia.

Key Words: Refractive errors, myopia, astigmatism, boys


INTRODUCTION

Prevalence of blindness in pediatric population ranges between 0.3% to 1.5% per 1000 children in developing countries. Uncorrected refractive errors are known to be the commonest reason of visual impairment worldwide. WHO estimated around 285 million people to have visual impairments, out of which, around 40 million are having blindness while 250 million have low vision. Commonest causes for visual impairment are considered to be refractive errors followed by cataract seen in 43% and 33% cases respectively. Researchers have proposed that more than 90% causes of blindness are either preventable or treatable.

Among children, refractive errors are considered to be one of the commonest problems faced. In children and adults age groups, refractive errors present multiple issues like educational loss, economic hurdles, less productivity as well as impairment in quality of life. Lack of services along with less affordability and poor access to healthcare services are some of the major issues linked to non-correction of refractive errors among pediatric age groups. But, this does not mean that developed communities cannot have unidentified or uncorrected refractive errors in pediatric age groups. Untreated visual problems are of special interest among children as they affect educational achievements as well as put emotional burden on the parents and families. Vision problems can be addressed with help of various available options like eye glasses, medications or vision therapies. Children themselves have increased chances of developing social or emotional problems due to unidentified or untreated vision issues. Studies have shown variation in the prevalence of refractive errors among school going children. This study was planned to determine the prevalence of refractive errors among boys in an Urban school of District Bahawalpur.

MATERIALS AND METHODS

This cross sectional study was conducted in a boys school of Bahawalpur City. Boys from Class 6th to
Class 10th were included during November 2017. Request was made to school administration and after getting the formal permission, ocular examination of the students was done in the school. Approval from “institutional ethical committee” was taken for this research. Informed consent was sought from all study participants.

Ocular examination process was thoroughly explained to the study participants while all the study instruments/equipments were transported to school one day prior to the actual ocular examination. Two ophthalmologists along with 2 optometrists did ocular examination and refraction. Standard “Snellen Chart” was used for screening of visual acuity. Children having visual acuity < 6/6 in any of the eye were further confirmed for refractive error with the use of pinhole. Objective refraction was made using auto-refractor and retinoscopy while confirmation was done applying subjective refraction. A special proforma was made to record study data.

SPSS version 26.0 was used for data handling and analysis. Study data was represented as frequency and percentages.

**RESULTS**

Among a total of 460 students, age ranged between 9 to 18 years while the mean age±SD was recorded to be 14.3±1.8 years. Table (1) is showing characteristics of study participants. Class 10th followed by 9th and 8th had the most number of students in the present study having 106 (23.0%), 102 (22.2%) and 94 (20.4%) students respectively. History of glasses was noted among 58 (12.6%) students. There were 253 (55.0%) who had history of glasses in their parents. Table No.1: Characteristics of Students Participated

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class-wise Distribution</td>
<td></td>
</tr>
<tr>
<td>6th</td>
<td>82 (17.8%)</td>
</tr>
<tr>
<td>7th</td>
<td>76 (16.5%)</td>
</tr>
<tr>
<td>8th</td>
<td>94 (20.4%)</td>
</tr>
<tr>
<td>9th</td>
<td>102 (22.2%)</td>
</tr>
<tr>
<td>10th</td>
<td>106 (23.0%)</td>
</tr>
<tr>
<td>History of Glasses</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>58 (12.6%)</td>
</tr>
<tr>
<td>No</td>
<td>402 (87.4%)</td>
</tr>
<tr>
<td>History of Glasses among any of the Parents</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>253 (55.0%)</td>
</tr>
<tr>
<td>No</td>
<td>207 (45.0%)</td>
</tr>
</tbody>
</table>

Findings of our study revealed frequency of refractive errors in 98 (21.3%) students while remaining 362 (78.7%) had normal vision (Figure No.1). Figure (2) is showing distribution of students with refractive errors in terms of types of refractive errors. Among 98 children with refractive errors, myopia 58 (59.2%) was the commonest type of refractive error followed by astigmatism 28 (28.6%) and hypermetropia 12 (12.1%).

**DISCUSSION**

Among children, refractive errors are associated with short-term as well as long term problems like loss in education, poor educational grades, loss of professional opportunities, economic difficulties as well as poor quality of life. Visual impairments caused by unaddressed refractive errors are considered to be a public health issue while correction of refractive errors adopting spectacles are known to be the best cost effective interventions. Researchers have shown that screening at mass levels among children of school going age can be a successful way of identifying and treating uncorrected refractive errors. In the present study, frequency of refractive errors was noted to be 21.3% among students. Our findings are showing a higher prevalence of refractive errors when compared to other local studies (8.9% and 10%).

Studies from Malaysia noted prevalence of refractive errors among children to be 7.7% while researchers from Nepal and Iran noted that to be 8.6% and 3.5% respectively. A recent local study found prevalence of refractive errors to be 9.4% among children. In this study, among 98 children with refractive errors, myopia 58 (59.2%) was the commonest type of refractive error followed by astigmatism 28 (28.6%) and hypermetropia 12 (12.1%). Our findings are close to a recent local study from Faisalabad which showed that Myopia was the commonest type of refractive error observed among 51.5% children. Another local study revealed Myopia to form 42.1% of refractive errors among children. Data from Ethiopia also showed that myopia was the most frequent type of refractive error among children. Our findings were somewhat different to a local study from LandiKotal where researchers noted hypermetropia to be the most common type of refractive error among the children.
frequent type of refractive error.\textsuperscript{12} Data from Vietnam has also shown that myopia was the commonest cause of impaired vision among school going children.\textsuperscript{19} Some other researchers have also concluded that Myopia is the most frequent type of refractive error among children.\textsuperscript{20}

The present study has some limitations as well. As this study was conducted among school going children, our findings cannot be generalized. As this study was conducted among male students. We were unable to find out any gender based differences regarding prevalence and types of refractive errors. High prevalence of refractive errors among school going children is alarming so the government and stakeholders should form alliance to plan regular screening programs for the timely identification and treatment of refractive errors among school going children. There screening programs can provide low cost assistance to children and their families who are suffering with refractive errors. Awareness programs and relevant educational activities can also be planned to increase awareness and knowledge about refractive errors among general population.

**CONCLUSION**

Prevalence of refractive errors was high among school going children. Myopia followed by Astigmatism was the commonest types of refractive errors. Regular screening programs for the timely identification and treatment of refractive errors should be conducted.

**Acknowledgement:** The authors would like to thank Muhammad Aamir (Research Consultant, Bahawalpur) for his valuable assistance in statistical analysis of this research.

**Author’s Contribution:**
- Concept & Design of Study: Zulfiqar Ali
- Drafting: Nadia Nazir, Soufia Farrukh
- Data Analysis: Abdul Rehman, Muhammad Javaid Iqbal and Imran Nazir
- Revisiting Critically: Zulfiqar Ali, Nadia Nazir
- Final Approval of version: Zulfiqar Ali

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

**REFERENCES**


Effectiveness of Pre-Procedural Antimicrobial Mouthwash Rinse with a Simple Water Rinse on the Dry Socket after Third Molar Extractions

Tauseef Ahmed, Amna Rehman, Navid Rashid Qureshi, Muhammad Athar Khan, Samir Azeem, and Ikram Alam

ABSTRACT

Objective: To compare the effectiveness of pre-procedural antimicrobial mouthwash rinse with a simple water rinse on the dry socket after third molar extractions at a tertiary care hospital, Karachi.

Study Design: A Randomized Control Trial Study

Place and Duration of Study: This study was conducted at the Oral and Maxillofacial Surgery Department, Liaquat College of Medicine and Dentistry, Darul-SEhat Hospital, Karachi from October 2019 to April 2020.

Materials and Methods: A total of 140 patients were selected who fulfilled the inclusion criteria and divided in two groups, (n=70) in controlled and (n=70) in experimental group. Both groups underwent the extractions of mesioangular impaction of Mandibular third Molars on either side under local anesthesia. Pre-procedural antimicrobial mouth rinsing was done only in experimental group. Presence of dry socket was assessed on follow up (third post op day) by scoring intensity of pain on VAS and presence of exposed bone clinically.

Data had been analyzed using SPSS version 17.0. Mean and standard deviation will be calculated for age. Frequency and percentages will be calculated for gender, effectiveness in both groups. Chi-square test will be applied to compare the effectiveness in both groups.

Results: The mean age was 34 years with standard deviation of ± 9 years. In control group 39 were female compared with 45 subjects females in preprocedural antimicrobial mouth rinsing group. Chi-square test showed the significant difference for VAS between groups (p<0.001) and also significant difference for exposed bone (p = 0.018).

Conclusion: We concluded that the use of preprocedural antimicrobial mouth rinsing with chlorhexidine mouthwash before the extractions of mandibular third molars seems to be an appropriate option for the reduction of alveolitis.

Key Words: Alveolar Osteitis, Chlorhexidine, Mandibular third molar, Postoperative complication


INTRODUCTION

Tooth extraction is a common procedure in Dentistry. The normal healing response to the procedure results in a significant loss of bone and collapse of the surrounding gingiva. Studies reported bone remodeling of post-extraction socket previously, utilization of various materials and wound healing were measured as time until healing was completed with epithelial closure. Tooth extraction healing normally takes approx. six months about everything that is going on in the dental socket is completed. Socket healing on the third and fourth weeks were characterized by small bone marrow spaces and a gradual transformation of the trabecular bone to one of cortical-compact nature, over six weeks of time woven bone is formed with in socket and about in six months this is replaced by mature bone. The typical characteristics of resorbing, resting and formatting surfaces were detected in all phases of socket healing. In addition to normal healing, a substantial percentage of extraction sites suffer postoperative complications. Many materials were used previously to fill and/or cover extraction socket in an attempt to enhance healing or prevent post-op complications associated with extractions.
The application of antiseptics to the skin or mucous membranes before surgery or injections has been practiced for many years. The goal of such application is to reduce the number of microorganisms on the surface to prevent their entry to underlying tissues, which could cause bacteremia, septicemia, or local harmful infections. The use of an antimicrobial mouth rinse by the patient before dental procedures is based on a similar principle of reducing the number of oral microorganisms. This reduction also reduces the number of microorganisms that may escape a patient's mouth during dental care through aerosols, spatter, or direct contact. In a study carried out by Ragno and Szkutnik 0.2% chlorhexidine mouthwash produced a reduction of dry socket after extraction of impacted third molars (17.5% as opposed to 36% in a control group. Incidence of localized alveolitis following third molar extraction in preprocedural antimicrobial mouth rinse group were found to be less than in untreated control group. Chlorhexidine is a cationic polybiginamide (bisdiguanide). It is used primarily as its salts (e.g., the dihydrochloride, diacetate and digluconate). It is on the World Health Organization's List of Essential Medicines, a list of the most important medication needed in a basic health system. Chlorhexidine appears to be relatively safe with little effect on the wound healing process, and its use may favor healing of open wounds in risk for infection. However, the results from studies to date are insufficient to draw conclusions about the use of chlorhexidine on open wounds. More human trials need be performed to assess its efficacy and safety. Clinical and experimental studies have described an increased local fibrinolytic activity as a principal factor for the etiology of dry socket. Chlorhexidine is a cationic polybiginamide (bisdiguanide). It is used primarily as its salts (e.g., the dihydrochloride, diacetate and digluconate).

Dry socket was first described as a complication of disintegration of the intra-alveolar blood clot, with an onset 2 to 4 days after extraction. It is clinically characterized by a putrid odor and intense pain that radiates to the ear and neck. Pain is considered the most important symptom of dry socket. It can vary in frequency and intensity, and other symptoms, such as headache, insomnia, and dizziness, can be present. Clinical and experimental studies have described an increased local fibrinolytic activity as a principal factor for the etiology of dry socket.

Chlorhexidine is a cationic polybiginamide (bisdiguanide). It is used primarily as its salts (e.g., the dihydrochloride, diacetate and digluconate). It is on the World Health Organization's List of Essential Medicines, a list of the most important medication needed in a basic health system. Chlorhexidine appears to be relatively safe with little effect on the wound healing process, and its use may favor healing of open wounds in risk for infection. However, the results from studies to date are insufficient to draw conclusions about the use of chlorhexidine on open wounds. More human trials need be performed to assess its efficacy and safety.

### MATERIALS AND METHODS

A Randomized Control Trial Study was conducted at Oral and Maxillofacial Surgery Department, Liaquat College of Medicine and Dentistry, Darul-Sehat Hospital, Karachi from 31st October 2019 to 30th April 2020. By using WHO sample size calculator taken P 1= 17.5%, P 2=36%, Power of test= 80 %, Level of significance = 5 %, estimated sample size n= 70 in each group. A total of 140 patients were selected consecutively who fulfilled the inclusion criteria (age 20—50 years, both gender, mesioangular impaction of lower wisdoms, asymptomatic patients) and divided in two groups, (n=70) in controlled and (n=70) in experimental group. After detailed history and examination the relevant pre-operative information will be recorded for each patient. Both groups underwent the extractions of mesioangular impaction of Mandibular third Molars on either side under local anesthesia. Patients in experimental group (B) were asked to take 20 ml of antimicrobial mouth wash while patients in control group (A) 20 ml simple water into mouth and swish the liquid around for 30 seconds and then spit the liquid from mouth thoroughly. Rinse once again in same manner, so total time of swishing will be one minute. Extractions were performed under LA (2% xylocaine with epinephrine 1:80,000) with dental instruments. Postgraduate dental surgeons experience with 2 years will perform third molar extractions. No intra-operative or postoperative antibiotics will be given to both groups. Pain will be evaluated on 3rd postoperative day. Patients will be instructed to mark the severity of pain by VAS on the Proforma sheet and oral cavity will be examined by the same surgeon on 3rd postpone day. Absence of dry socket will be labelled as effectiveness +ve. Presence or absence of Dry socket will be confirmed if (A) there is the presence of exposed underlying bone on clinical examination. (B) Patients having moderate to severe postoperative pain score on Visual Analogue Scale (VAS) within 3 days after extraction. Presence of both point A and B will be labeled as dry socket.

All the collected data was entered in the SPSS version 21. Mean and standard deviation was calculated for age. Frequency and percentages were calculated for gender and effectiveness in both groups. Chi-square test was applied to compare the effectiveness in both groups and p-value <0.05 as significant. A written informed consent was obtained from each subject in the study. The study had approval of the Research and Ethics Committee of the hospital.

### RESULTS

A total of 140 patients were included in this study fulfilling the inclusion criteria. In group A, mean age was 34.8 ± 9.2 years, while in group B, mean age was 33.7 ± 8.8 (Table 1). In group A, 31(44.2%) patients were male and 39 (55.7%) were females while in group B, 25(35.7%) patients were male and 45(64.2%) patients were females (Table 1).

When compared the pain on VAS Scale at third day of follow up, we found no pain in 4 subjects, v/s 25 subjects in control group and preprocedural antimicrobial mouth rinsing group, mild pain in 30 subjects, v/s 25 subjects in control group and preprocedural antimicrobial mouth rinsing group, severe pain in 11 subjects, v/s 3 subjects in control...
group and preprocedural antimicrobial mouth rinsing group, as given in Figure 1. Table 2 shows effectiveness in both groups. In group A, effectiveness was present in 47(67.1%) patients, and absent in 23(32.8%) patients. In group B, effectiveness was present in 59(84.2%) patients, and absent in 11(15.7%) patients (p=0.018). Table 2 showed stratification of outcome variable with respect to age (20-35). In group A, effectiveness was present in 26(32.9%) patients and absent in 2(3.27%) patients. While in group B, effectiveness was present in 33(41.7%) patients and absent in 11(13.9%) patients. While in group B, effectiveness was present in 21(34.4%) patients and absent in 12(19.67%) patients. (p=0.060). Table 2 showed stratification of outcome variable with respect to age (36-50). In group A, effectiveness was present in 21(34.4%) patients and absent in 12(19.67%) patients. While in group B, effectiveness was present in 26(42.6%) patients and absent in 2(3.27%) patients (p=0.060).

Table No.1: Demographic Characteristics of Study Participants (n=140)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>34.8 ± 9.2</td>
<td>33.7 ± 8.8</td>
</tr>
<tr>
<td>Female</td>
<td>39(55.7%)</td>
<td>45(64.2%)</td>
</tr>
</tbody>
</table>

Table 2: Effectiveness with respect to Age and Gender (n=140)

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Yes</th>
<th>No</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (20-35) Years</td>
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<td></td>
</tr>
<tr>
<td>Groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>47(67.1%)</td>
<td>23(32.8%)</td>
<td>0.018</td>
</tr>
<tr>
<td>B</td>
<td>59(84.2%)</td>
<td>11(15.7%)</td>
<td></td>
</tr>
<tr>
<td>Age (36-50) Years</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>26(32.9%)</td>
<td>11(13.9%)</td>
<td>0.060</td>
</tr>
<tr>
<td>B</td>
<td>33(41.7%)</td>
<td>9(11.3%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>20(35.7%)</td>
<td>11(19.6%)</td>
<td>0.529</td>
</tr>
<tr>
<td>B</td>
<td>21(37.5%)</td>
<td>4(7.1%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>27(32.1%)</td>
<td>12(14.2%)</td>
<td>0.465</td>
</tr>
<tr>
<td>B</td>
<td>38(45.2%)</td>
<td>7(8.3%)</td>
<td></td>
</tr>
</tbody>
</table>

Figure No.1: Pain Scale on VAS

DISCUSSION

Tooth extraction is followed by healing of alveolar bone which is a complex process. Delayed and disturbed healing of the extraction site is reported to occur in approximately 1 to 11.5% of patients. Its prevalence is substantially increased after Mandibular Third Molar extractions, with incidences varying between 25% and 30%. Adeyemo and colleagues, found localized osteitis 26 (8.2%), acutely infected alveolus 5(1.6%), and an acutely inflamed alveolus 4 (1.2%) in 311 patients. These complications were more in females than males (p=0.003). Most complications were found in molars (60%) and premolars (37.1%). This has been noticed that localized osteitis caused severe pain in all cases, while infected and inflamed alveolus caused mild or no pain. Thirty patients (12%) among those without healing complications experienced mild pain. Apart from alveolar osteitis (AO); post extraction alveolus healing was also complicate by acutely infected alveoli and acutely inflated alveoli. We found that when patients were recalled after 3 days, out of 70 patients in group A (control) 23 showed an evidence of dry socket(pain+ exposed bone clinically) while only 11 patients showed an evidence of dry socket(pain+ exposed bone clinically) in group B (with anti-microbial mouth wash). Incidence of dry socket in group A 32.8% while in group B 15.7%, with p = value (p= .018). In total 60% were female. In group A out of 70, 39 patients were female and 31 were male similarly in group B, 25 patients were male and 45 were female.

Dry socket prevention is determined by the medical and dental history of the patient, physical examination findings, pertinent laboratory examination results, and the presence of contributing factors. To avoid complications, strict guidelines for maintaining an aseptic field during the procedure and the correct indication and use of the surgical technique must be followed. In addition to avoiding these factors, the prevention of dry socket has been studied in relationship to some antifibrinolytics agents, antibiotics, analgesics, antisepic agents, and combinations of these substances. Mouthwash with chlorhexidine digluconate at 0.12% has been an efficient antiseptic for the prevention of dry socket. Some studies have shown
important reductions in the incidence of dry socket after extraction of mandibular third molars logic saline10, 11, 24 Our study shows statistically significant difference was observed in terms of time taken for closure of socket and nature of bone deposition in patients with preprocedural antimicrobial mouthwash rinse before third molar extraction.

This study also shows the stratification of outcome variable with respect to two age groups, one from (20-35) years and the other one is from (36-50) years. Our study shows statistically significant difference was observed in reduction of dry socket with use of preprocedural antimicrobial mouth rinsing.

The limitations of our study was small sample size so that the result of the study can be generalized. Currently pre-procedural antimicrobial mouth rinsing proved to be as efficient as other commercially available antibiotic which meets this entire requirement to fasten healing process without any complication.

Needs is to draw an attention towards its regular use of in dental practice before extraction of tooth. It is cost effective, easily available of which should be included in the list of medicaments. Research is under way assessing the antioxidant and anti-inflammatory activities in chlorhexidine with a view to being able to select for marketing. Further research is still to be done to identify the role that stimulate the immune response and stimulate wound tissue growth, and the component responsible for releasing bacteria from skin cells and mucosa.

CONCLUSION

We concluded that the use of preprocedural antimicrobial mouth rinsing with chlorhexidine mouthwash before the extractions of mandibular third molars seems to be an appropriate option for the reduction of alveolitis.

Author’s Contribution:
Concept & Design of Study: Tauseef Ahmed
Drafting: Amna Rehman, Navid Rashid Qureshi
Data Analysis: Muhammad Athar Khan, Samir Azeem and Ikram Alam
Revisiting Critically: Tauseef Ahmed, Amna Rehman
Final Approval of version: Tauseef Ahmed

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

REFERENCES


The Role of C – Reactive Proteins as Indicator of Antibiotic Therapy among Patients with Acute Exacerbation of Chronic Obstructed Pulmonary Disease

Muhammad Mujtaba Ali¹, Rashid Ali² and Hafiz Muhammad Taha Waqas³

ABSTRACT

Objective: This study was conducted to define role of CRP as indicator of antibiotic therapy among patients with COPD.

Study Design: Descriptive case series Study

Place and Duration of Study: This study was conducted at the Department of Pulmonology, Shalamar Medical and Dental College Lahore from June, 2019 to January, 2020.

Materials and Methods: The study included 100 cases fulfilling inclusion criteria. Serum CRP levels were measured in all patients and were categorized as: low CRP (<40 mg/L) and high CRP (>40 mg/L). Patients in both groups received antibiotic therapy (Levofloxacin 500mg twice daily per oral) for 7 days. Patients were assessed for clinical success (absence of dyspnea and sputum).

Results: High CRP level was observed in 65(65%) patients and low in 35(35%) patients. Clinical success was achieved among 14(40%) patients in low CRP group and 56(86.2%) patients with high CRP group (p<0.05).

Conclusion: Majority of patients had high CRP level (>40mg/L). So, CRP level can be used as an indicator for commencement of antibiotic therapy among patients with acute exacerbation of COPD.

Key Words: Chronic obstructive pulmonary disease; C-reactive Proteins; antibiotic therapy

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the 4th principal reason of mortality globally. It is a escapable and curable ailment, for which physicians have to inaugurate a impulsive and precise verdict and management, comprising teaching for prophylaxis. COPD is a chief source of morbidity and mortality worldwide. The exact incidence of COPD all over the world is basically unidentified, however approximations have wide-ranging from 7-19%. It is generally a progressive illness, categorized by exacerbation of symptoms. Exacerbations signify a substantial financial problem, however, additional significantly, it can lead to augmented lung function deterioration, in addition to amplified mortality. In the attention of refining the analysis of COPD, numerous kinds of biomarker have been measured that are connected to respiratory pathophysiology. An acute phase protein i.e. CRP is hepatic in origin and formed in response to IL-6 stimulation. CRP is elevated in most disorders related with inflammation, infection or tissue destruction, for which it is a sensitive marker. CRP in blood is stated to be higher during exacerbation compared with the baseline state. So far, there are no clear guidelines regarding the use of antibiotics in acute exacerbation of COPD. The disease burden is still very high in our population and a large number of patients with exacerbations are attended in primary care, and definitive evidence to support the use of antibiotics in such patients is lacking. Many studies in the past had shown relationship of CRP with acute exacerbation of COPD, but its clinical utility as indicator of antibiotic therapy is still debatable.

Objective of the study was to determine the frequency of patients showing CRP > 40 mg/L among patients presenting with exacerbation of COPD and to compare the clinical Success Rate of Antibiotic therapy among
COPD patients with low CRP (<40) versus high CRP (>40).

MATERIALS AND METHODS

This Descriptive case series Study was conducted in in Department of Pulmonology, Shalamar Medical and Dental College Lahore from June, 2019 to January, 2020. The study included 100 patients of both gender, between 20 – 80 years of age, with acute exacerbation of COPD. We excluded all the patients with antibiotic use in the previous 2 weeks, Bronchial asthma, pulmonary neoplasm, History of surgery on respiratory tract i.e. tracheotomy, Patients on steroid use and Patients with history of hypersensitivity to b-lactams, clavulanate or lactose.

Demographic features, history and physical examination were noted. All the patients had their serum CRP level done. The patients were categorized to have low CRP (i.e. < 40 mg/L) and high CRP (i.e. >40 mg/L). The patients in both groups had received antibiotic therapy (Levofloxacin 500 mg per oral OD) for a period of 7 days. After 7 days of treatment, the patients were assessed for the absence of dyspnea and absence of sputum and were labeled as clinical success. All the collected data was entered into SPSS version 20 and analyzed. Study variables were analysed by simple descriptive statistics. Mean and standard deviation were calculated for numerical variables (age), CRP level and duration of COPD. Frequency and percentage were calculated for gender, number of patients with low & high CRP, presence of clinical success (yes or no) was presented as frequency distribution and percentage. Both the groups were compared each other for the clinical success. Effect modifiers like smoking (pack years smoking) during year, duration of COPD were controlled by stratification of data with clinical success. p-value* was calculated for gender, number of patients with low & high CRP levels, presence of clinical success (yes or no) was stratified with effect modifier (duration of smoking) and with effect modifier (duration of COPD) of patients with low and high CRP levels.

RESULTS

Table No.1: Distribution of patients by CRP level and Comparison of patients by clinical success among patients with low (<40mg/L) and high (>40mg/L) CRP level

<table>
<thead>
<tr>
<th>CRP level</th>
<th>No. of patients (%)</th>
<th>Clinical Success N(%)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 mg/L</td>
<td>35 (35%)</td>
<td>14 (40%)</td>
<td>0.001**</td>
</tr>
<tr>
<td>&gt; 40 mg/L</td>
<td>65 (65%)</td>
<td>56 (86.2%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100 (100%)</td>
<td>70 (70%)</td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>46.51±7.79</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Chi-square test
** Statistically significant

There were total one hundred patients included in this study. The mean age of the patients was 65.04 ± 14.75 years [range 46 – 80]. There were 85 (85.0%) male patients and 15 (15.0%) female patients (M:F; 5.2:1). The mean distribution of patients by duration of smoking (pack-year) was 56.22±8.99. The mean distribution of patients by duration of COPD was 11.89±3.78 years. Distribution of patients by CRP level and Comparison of patients by clinical success among patients with low and high CRP levels, Stratification of data (clinical success) with duration of smoking and COPD were shown in table 1, 2 & 3, respectively.

Table No.2: Stratification of data (clinical success) with effect modifier (duration of smoking)

<table>
<thead>
<tr>
<th>Duration of Smoking (Pack years smoking)</th>
<th>Clinical success n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 – 30 (n=12)</td>
<td>8 (66.7%)</td>
</tr>
<tr>
<td>31 – 40 (n=18)</td>
<td>11 (61.1%)</td>
</tr>
<tr>
<td>41 – 50 (n=45)</td>
<td>35 (77.8%)</td>
</tr>
<tr>
<td>51 – 60 (n=25)</td>
<td>16 (64%)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.517**</td>
</tr>
</tbody>
</table>

* Chi-square test
** Statistically not significant

Table No.3: Stratification of data (clinical success) with effect modifier (duration of COPD)

<table>
<thead>
<tr>
<th>Duration of COPD (years)</th>
<th>Clinical success n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 5 (n=22)</td>
<td>18 (81.8%)</td>
</tr>
<tr>
<td>6 – 10 (n=67)</td>
<td>47 (70.1%)</td>
</tr>
<tr>
<td>11 – 15 (n=11)</td>
<td>5 (45.5%)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.732**</td>
</tr>
</tbody>
</table>

* Chi-square test
** Statistically not significant

DISCUSSION

The most common decision a pulmonologist has to make when treating a patient with an acute exacerbation in COPD is whether to prescribe antibiotic therapy. This prospective study investigated the role of CRP as an indicator of antibiotic therapy and revealed an important observation that commencement of antibiotic therapy with elevated CRP (> 40mg/L) may be more beneficial (more clinical success). The mean age of the patients in our study was 65.04±14.75 years with an age range of (46 – 80) years. In a study by Arslan RS, et al, the mean age of patients was 63.70±7.81 years. In another study by Iqbal S, et al, the mean age of patients was 59.3 years ±10.76SD while in literature; the mean age of patients has been reported as 70 years ± 8.0SD years and 62.1 years ± 9.8SD. In the study conducted in China, the mean age reported is 73.4 years.

There was a male dominancy in our study (85% were male and 15% were female). This male dominancy has
also been observed in other studies. In study by Iqbal S, et al\textsuperscript{15} there were 67.10\% male with a male to female ratio of 2.03:1. In an Indian study, there were 80.7\% male.\textsuperscript{17} In another study, there were 87.9\% male patients with acute exacerbation of COPD.\textsuperscript{18} The reason for male dominancy in our study is related to prevalence of smoking in our population. Smoking is more common in males with resulting in higher incidence of COPD. In our study, we included all the patients who were smokers. The female patients in our study were also smokers. This reflects that smoking is not very uncommon among female in our population.

Smoking history was present in all of the patients included in the study. However, there has been found variability in frequency of smoking among different authors. Ahmad H, et al\textsuperscript{19} found that 37.5\% patients in their study were smokers. Alam SE\textsuperscript{20} et al, reported that prevalence of smoking was 21.6\%. COPD varies with age and smoking status, occurring rarely in individuals more than 40 years old, and less frequently in non-smokers. In our study, the majority of smokers (45\%) had history of 41-50 years pack smoking. The mean duration (pack years) was 56.22±8.99 pack-years. Arslan RS,\textsuperscript{14} documented a mean smoking history (Pack-years) 59.89±6.60 years among their study population. Nearly all physicians acknowledge that the first step in patient management is the cessation of smoking.\textsuperscript{21} The mean duration of COPD was 11.89±3.78 years in our study while in study by Ahmed H,\textsuperscript{22} et al the mean duration of 8.81(± 5.72 SD) years. We observed that a CRP level of < 40 mg/L was observed in 35\% of the patients, while majority of the patients had high level of CRP. In our study, the cut off value was 40 mg/L, which was similar to that of study by Llor et al.\textsuperscript{11} However, Peng C, et al\textsuperscript{7} also used a cut of value as low as 15.6mg/L among patients with a sensitivity of 81.5\% and a specificity of 77.8\%.

In our study, the clinical response was achieved in 86.2\% patients with CRP >40mg/L and 40\% among patients with CRP <40mg/L. The results were statistically significant (p<0.05). A study by Llor\textsuperscript{11} et al have shown that the clinical success rate among patients with a CRP <40 mg/L was 87.6\%, while only 34.5\% of patients with a CRP >40 mg/L experienced clinical success (p <0.05). The clinical success rate (87.6\%) achieved in with an antibiotic is quite comparable with that of observed in previous placebo-controlled trials, particularly 68\% in the study by Anthonisen and colleagues,\textsuperscript{23} 80\% in the study by Daniels and colleagues,\textsuperscript{90} and 86.4\% in the study by Allegra and colleagues,\textsuperscript{24} all of which included patients with severe COPD.

In our study, we selected levofloxacin as an antibiotics. Amoxicillin, trimethoprim/sulfamethoxazole, tetracycline, and erythromycin were not chosen because failure rates with their use may almost double in outpatients with COPD exacerbations compared with amoxicillin/clavulanate, azithromycin, or ciprofloxacin.\textsuperscript{24} Our study had certain limitations. This was carried out in a single centre and in a limited population size.

**CONCLUSION**

The results of the study demonstrate use of antibiotic therapy among patients with elevated CRP level (>40mg/L) showed better clinical response as compared to that of low CRP level. So, elevated CRP level (>40mg/L) may be used as an indicator of antibiotic therapy among patients with acute exacerbation of COPD. However, there is still need of double blind randomized controlled trial to document its role.

**Author’s Contribution:**

Concept & Design of Study: Muhammad Mujtaba Ali

Drafting: Rashid Ali, Hafiz Muhammad Taha Waqas

Data Analysis: Hafiz Muhammad Taha Waqas

Revisiting Critically: Muhammad Mujtaba Ali, Rashid Ali

Final Approval of version: Muhammad Mujtaba Ali

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

**REFERENCES**

Challenges and Difficulties Associated with Physiology Learning in Undergraduate Medical Students in Integrated Curriculum

Sadaf Fatima¹, Syed Tousif Ahmed², Shazia Hashmat², Haider Abbas³, Zahra Safiuddin³ and Kevin Borges⁴

ABSTRACT

Objective: To find out the difficulties and challenges associated with learning of Physiology in undergraduate medical students in integrated curriculum.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Ziauddin Medical College, Ziauddin University, July 2017 to June 2018.

Materials and Methods: The study participants included 1st, 2nd, 3rd year medical students. There were 147 MBBS students in this study. A questionnaire was distributed to each student. The questionnaire included 23 items from why is Physiology hard for students to learn? It included items related to subject, teaching and learning of Physiology. The medical students were asked to select a response for each item on likert scale from 1 to 5. The Physiology learning responses were compared between 1st, 2nd & 3rd MBBS students.

Results: The medical students thought that characteristics of discipline including well defined syllabus (90.7%), understanding of physiological phenomena (88.8%), and use of scientific terms (89.3%) were more important aspects. Regarding the teaching factors including integration (84%), use of active learning methods (81.7%), use of graphs and flow charts by teachers (80%), teachers' response to student questions (88.4) were found to be more important. In relation to student learning important factors was rote learning than understanding (92%), time commitment (83.6%), and not taking guidance from other students (80.4). The comparison was done between MBBS 1st 2nd and 3rd year medical students. A significant difference was found in factors including basic concepts (0.01), passing exams by using short books (0.01) and integration (0.002).

Conclusion: The medical students provided perspective regarding the difficulties in learning physiology and the reasons of these difficulties.

Key Words: Physiology, Teaching, Learning, Integrated Curriculum


INTRODUCTION

In creating 21st century physicians, the primary goal is to educate future doctors who can completely incorporate the new sciences and technology into humane patient care. Recently many medical schools are designing innovative medical curricula in their bachelor programs. Many medical schools are progressing towards a more student centered approach to learning and assessment. Integration is established as a vital educational strategy in medical education. Integration promotes better retention of knowledge and the skill to execute basic science principles in the appropriate clinical context. During first two years of medical school, basic science content provides an essential foundation for clinical experiences. Basic science concepts forms schema for clinical reasoning and therefore they work as building blocks for any clinical decision making. This knowledge helps students to rebuild the relationship between features and diagnosis of disease. Recently many medical schools have started to modify their preclinical curricula to indicate the importance of basic science to practice. The coherence between basic and clinical science is provided by early patient contact in
the first year simultaneous with basic science teaching and by clinical principles mingled into basic science courses\textsuperscript{10}. Understanding the applicability of basic science education in the establishment of patient assessment, diagnosis, and treatment is critically important to competent medical practice\textsuperscript{11}.

Physiology is one of the basic science disciplines taught at undergraduate level in traditional & integrated curriculum, in medical, dental and other health professional education\textsuperscript{12}. Its importance lies in its application in clinical practice\textsuperscript{13}. The close association of physiology with clinical medicine is highlighted in the preclinical years, and also in hospital practice later\textsuperscript{14}. Being one of the mandatory basic science disciplines, Physiology is also experiencing changing trends in teaching. Student centered learning methods have been found to be most helpful in concept building of physiological sciences\textsuperscript{14}. As the knowledge of Physiology is the basis of good clinical practice, a questionnaire was designed to study the different aspects of Physiology learning. The objective of the study was to find out the difficulties and challenges associated with learning Physiology in undergraduate medical students in integrated curriculum.

MATERIALS AND METHODS

The study design was cross sectional. The study was conducted at Ziauddin Medical College. The study was conducted in 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} year medical students. There were 147 MBBS students in the study. The participants were selected by convenient sampling technique. The time duration of study was one year, from July 2017 to June 2018. The study was approved by Ethics review board of Ziauddin University. After getting the ethics approval, the participants were enrolled in the research study. Informed consent was obtained from each participant.

In order to study the challenges associated with Physiology learning, questionnaire was distributed to 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} year medical students. The questionnaire included 23 items from why is Physiology hard for students to learn? The students were asked to select a response for each item on likert scale from 1 to 5. The medical students provided their opinion about the difficulties in learning physiology and the reasons of these difficulties. The questionnaires were collected and the data was analyzed.

The data were analyzed using SPSS version 20. The results of all quantitative data were expressed as mean ±SD. The comparison of qualitative data was expressed by Chi Square test. In all statistical analysis, only p-values ≤ 0.05 were considered significant.

RESULTS

There were 147 MBBS students in the study. The mean age of students was 19.99± 1.3 years (male 36% & female 64%).

Table I showed the cumulative percentage of items included in the questionnaire as marked by MBBS students. The medical students thought that characteristics of discipline including well defined syllabus (90.7%), understanding of physiological phenomena (88.8%), and use of scientific terms (89.3%) were more important aspects.

Table No. 1: The cumulative percentage of Physiology learning responses of MBBS students

<table>
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<tr>
<th>Q.No.</th>
<th>Option</th>
<th>Cumulative %age</th>
</tr>
</thead>
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<td></td>
<td>B</td>
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<tr>
<td></td>
<td>C</td>
<td>15.6</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>87.9</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>4.5</td>
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</table>
Regarding the teaching factors including integration (84%), use of active learning methods (81.7%), use of graphs and flow charts by teachers (80%), teachers’ response to student questions (88.4%) were found to be more important. In relation to student learning important factors was rote learning than understanding (92%), time commitment (83.6%), and not taking guidance from other students (80.4).

Table 2 showed the comparison of Physiology learning responses between 1st, 2nd and 3rd year MBBS. The frequency, percentage and chi square value of each item is mentioned in the table. Table II included items related to basic concepts, scientific terms, new researches in medical science, interaction between systems, well defined physiology syllabus, understanding physiology, commitment of time for learning physiology, importance of case study, passing physiology exams by short books, teaching physiology by giving concepts, correlating different topics, guiding students about learning resources, use of graphs & flow charts in teaching, integration of physiology teaching, covering large content in lecture, responding to student questions and use of active learning methods.

Table No.2: Comparison of Physiology learning between 1st, 2nd and 3rd year MBBS students

<table>
<thead>
<tr>
<th>Q.No.</th>
<th>n</th>
<th>Year</th>
<th>Frequency</th>
<th>Percentage</th>
<th>Chi square</th>
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</table>
DISCUSSION

In this study, challenges and difficulties associated with Physiology learning were studied. Table II showed comparison of Physiology learning responses between MBBS 1st, 2nd and 3rd years. There was a significant difference found in Item 1, 11 and 18. Item 1 was regarding knowledge of basic concepts of physics and chemistry. It is known that transfer, the capability to use something learned in one context in another context, is difficult, and this evidently contributes to students' lack of ability to use their prerequisite knowledge (chemistry and physics) in learning physiology. This is consistent with the study done by Michael15. He asked the physiology faculty to fill the questionnaire regarding difficulty in studying physiology and Calthorpe et al16 who asked the students to mark the difficult topics according to the modules. Item 11 was related to passing physiology exams by reading short books. Physiology tutors expect more than only retention of knowledge from their students. Our study findings are same as Michael15 study and Miller et al17 study. Students believe that learning and memorizing is the same thing. It was also mentioned in Sonmez18 et al and slominski19 et al. The memory of students' knowledge of human physiology has been identified by numerous physiology educators to be wildly inconsistent20. Item 18 was regarding teachers integrating physiology teaching with other skills. The educators need to employ creative teaching strategies that involve the students in active learning21. In active learning, the higher thinking processes of students are stimulated21. In rest of the table items, significant difference was not observed.

Physiology was rated as one of the most difficult courses by medical students, and its knowledge is generally not enough at a senior level of their medical education20. To acquire the physiology concepts, a variety of cognitive processes, such as memorization, comprehension, analysis, classification, summarization, calculation, multidisciplinary connections, and clinical application is required, and it is inevitable that students with different cognitive levels and study styles learn at different paces20. Causal reasoning, use of graphs and
sectionalize were remarkably important than any other aspect of teaching in making physiology hard to learn. There is a significant difference between teaching and learning. The fact is, there is too much teaching and inadequate learning. Teaching is not only passing the information to students about what we know, but it is instead, to show the students how we learn. Teachers expect “understanding” or the ability to “think” about physiological mechanisms. It is reported that students generally enter the physiology classroom lacking the expected prior knowledge and skills. It is also noticed that students, both pre and post instruction, have serious misconceptions about physiological phenomena. Students find it difficult to interpret graphs and to acquire a conceptual understanding of phenomena.

There is an urgent requirement for teaching reforms to improve the teaching efficacy of human physiology in medical schools. The duty of teachers is to help students learn physiology. The more they understand about learning, the better they acknowledge the causes of problems that students have in learning physiology and the better they can do their job.

CONCLUSION

The medical students provided perspective regarding the difficulties in learning physiology and the reasons of these difficulties.

Author’s Contribution:

Concept & Design of Study: Sadaf Fatima
Drafting: Syed Tousif Ahmed, Shazia Hashmat
Data Analysis: Haider Abbas, Zahra Safiuddin, Kevin Borges
Revisiting Critically: Sadaf Fatima, Syed Tousif Ahmed
Final Approval of version: Sadaf Fatima

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

REFERENCES

9. Dominguez I, Zumwalt AC. Integrating the basic sciences in medical curricula: focus on the basic scientists Adv Physiol Educ 2020 44:119-123
15. Michael J. What makes physiology hard for students to learn? Results of a faculty survey Adv Physiol Edu 2007; 31:34-40
17. Miller SA, Perrotti W, Silverthorn DU, Dalley AF, Rarey KE. From college to clinic: Reasoning over
memorization is key for understanding anatomy 
18. Sonmez H. A Review about the Use of the 
Memorization Strategy during the Learning 
Process by Students. Int J languages, Edu 
19. Slominski T, Grindberg S, Momsen J. Physiology 
is hard: a replication study of students’ perceived 
learning difficulties Adv Physiol Educ 2019;43: 
121-127.
20. Shang F, Liu CY. Blended learning in medical 
physiology improves nursing students’ study 
21. Majeed F. Effectiveness of case-based teaching of 
physiology for nursing students. J Taibah Univ 
22. Anderson GL, Passmore JC, Wead WB, Falcone 
JC, Stremel RW, Schuschke DA. Using “Active 
Learning” Methods to Teach Physiology. Med Sci 
23. Khalil MK, Elkhider IA. Applying learning 
theories and instructional design models for 
effective instruction. Adv Physiol Educ 2016;40: 
147-156.
24. Versteeg M, Loon MHV, Meijer MW, Steendijk P. 
Refuting misconceptions in medical physiology 
Role of Bevacizumab (Avastin) in Diabetic Macular Edema
Muhammad Awais Ashraf¹, Ghulam Abbas¹ and Adeel Ahmed Siddiqui²

ABSTRACT

Objective: To evaluate the efficacy of injection Bevacizumab (Intravitreal) in management of diabetic macular edema (DME).

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the completed at Ophthalmology department Nishtar Hospital Multan from March 2019 to March 2020.

Materials and Methods: Study was conducted on 60 eyes of 60 patients presented with diabetic macular edema. Intravitreal bevacizumab injection of 1.25 mg was administered 3.5 mm from the limbus under topical anesthetic drops. Follow up was done at 1st day and at 1 month duration after injection. Macular thickness was measured at every follow ups visit. SPSS version 23 was used for analysis of data. P value ≤ 0.05 was considered as significant.

Results: The mean pre Avastin macular thickness of the patients was 391.43±30.91 µm and after Avastin OCT at one month was 308.66±25.82 µm. Difference was found significant statistically, (p=0.000).

Conclusion: Diabetes leads to macular edema and retinopathy which is a hurdle in macular grid laser in such cases. Intravitreal injection of bevacizumab minimizes the exacerbation of macular edema in diabetic cases.

Key Words: Bevacizumab, Vascular Endothelial Growth Factor (VEGF), Macular thickness, Diabetic macular edema (DME).


INTRODUCTION

Angiogenesis either physiological or pathological propagated by vascular endothelial growth factor which is a proangiogenic cytokine¹. In condition of hypoxia vascular endothelial growth factor (VEGF) stimulate the endothelial cells which played an important role in pathophysiology of certain ophthalmic diseases which may include neurovascular age related degeneration, diabetic retinopathy, retinal vein occlusion²,³. This whole procedure results in loss of vision after hemorrhage, edema and retinal detachment after fibro vascular proliferation⁴. Anti VGEF therapy brings a revolution in treatment modalities of ocular disease⁵. First of all Pegaptanib was used and after that bevacizumab, Ranibizumab and Afibercept were used successfully⁶.

Older therapeutic methods were photo dynamic therapy and neovascularization with laser photoocoagulation, although these modalities were non physiologic and destructive in use⁷. In comparison to these methods, VEGF therapy is more potent and successful to inhibit the level of VEGF.

Now treatment of retinal diseases with anti VEGF is famous worldwide in clinical practice⁸. Number of injections increasing day by day in united states as in 2001 about 4215 injections were used in 2011 about 2.5 million injections. Similar ratio of increase in injections was noted in United Kingdom and Canada⁹. After anti VEGF therapy some local complications may occur like intraocular complications, ocular hemorrhage, rhegmatogenous retinal attachment and raised intraocular pressure¹⁰.

MATERIALS AND METHODS

This prospective study was conducted at the department of Ophthalmology Nishtar Hospital Multan from March 2019 to March 2020. The hospital's ethics review board approved the all aspects of study. Patients who received anti VEGF therapy during the study period were included in the study. Informed written consents were obtained from patients before the start of procedure. Non probability consecutive sampling technique was used. Sample size was calculated by using an online software Openepi.com. Patients of the presumed or established endophthalmitis were enrolled in the study. Patients with any degree of intraocular inflammation who required Intravitreal antibiotics were labeled as
presumed endophthalmitis. Positive gram stain and culture was used to approve the endophthalmitis. Patients in which endophthalmitis develops secondary to some other etiology or who did not fulfill the criteria of endophthalmitis were excluded from the study. All Intravitreal injections were performed in well-designed operating rooms with standard protocols. A 29 gauge needle was used for administration in infra temporal quadrant. It was about 4 mm distance from the limbus. Conjunctival anaesthesia was given with 4% lidocaine and 0.5% proparacaine. 5% povidone iodine solution was used to prepare eyelashes and eyelids. Patient's mouth and nose covered with surgical self adhesive drape. Sterile lid speculum was also used. Injections were administered by an ophthalmologist having 5 years experience in this procedure. Every patient was dealt after changing surgical sterile gloves and complete hand sepsis. Use of face masks and cessation of conversation at the time of injection administration was assured. A vitreous fluid of all patients sent to laboratory for microbial culture. Empiric treatment was started. Treatment modified according to the culture results.

SPSS version 23 was used for data analysis. Mean and standard deviation was calculated for categorical data. P value less than or equal to 0.05 was considered as significant.

### RESULTS

Sixty patients were included, in this study. Intravitreal Injection of Bevacizumab was given to these sixty patients’ sixty eyes. There were more males than females i.e. n=35 (58.3%) and n=25 (41.7%), respectively. The mean age of the patients was 52.91±3.25 years. The mean duration of diabetes of the patients was 12.61±4.15 years. n=11 (18.3%) eyes insulin dependent patients’ and n=49 (81.7%) eyes were non-insulin dependent patients’. n=39 (65.0%) patients were controlled diabetes on medicine where as n=21 (35.0%) patients were found to be uncontrolled diabetes by medicine. (Table 1).

### Table No.1: Baseline Characteristics of the Patients

<table>
<thead>
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<th>Variable</th>
<th>Gender</th>
<th>Presence</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>n=35</td>
<td>(58.3%)</td>
</tr>
<tr>
<td>Female</td>
<td>n=25</td>
<td>(41.7%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.91±3.25</td>
<td></td>
</tr>
<tr>
<td>duration of diabetes (years)</td>
<td>12.61±4.15</td>
<td></td>
</tr>
<tr>
<td>Insulin dependent patient</td>
<td>n=11</td>
<td>(18.3%)</td>
</tr>
<tr>
<td>Insulin independent patient</td>
<td>n=49</td>
<td>(81.7%)</td>
</tr>
<tr>
<td>Controlled diabetes patient</td>
<td>n=39</td>
<td>(65.0%)</td>
</tr>
<tr>
<td>Un-controlled diabetes patient</td>
<td>n=21</td>
<td>(35.0%)</td>
</tr>
</tbody>
</table>

The mean pre Avastin macular thickness of the patients was 391.43±30.91 micrometers and post Avastin OCT after one month was 308.66±25.82 micrometers. The difference was statistically significant, (p=0.000). (Figure 1). It was seen that macular thickness after one month of injection was decreased in n=55 (91.7%) cases and increased in n=5 (8.3%) cases. Reduction in macular thickness was found as > 10% in n=46 (76.7%) cases, < 10% in n=9 (15.0%) cases and increased in n=5 (8.3%) cases. (Table 2).

### Table No.2: Reduction in Macular Thickness

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</tr>
<tr>
<td>Yes &lt; 10%</td>
<td>n=9 (15.0%)</td>
</tr>
<tr>
<td>Increased</td>
<td>n=5 (8.3%)</td>
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</table>

### DISCUSSION

In patients of vitreous hemorrhage or media opacity it is difficult to perform laser therapy. Patients with neovascular glaucoma or iris neovascularization often present corneal edema or hyphema which is a hurdle in laser treatment\(^1\). Despite grid laser therapy in some cases macular thickness continue to increase in size. But in such cases Bevacizumab shows rapid and dramatic results and observed very effective that resolve complete macular edema in couple of days. Better outcomes associated with good diabetic control and compliance towards follow ups\(^2\).

The mean age of the patients in our study was 52.91±3.25 years. A similar study was conducted by Mason et al\(^3\) on 30 patients having mean age of 47.7 ± 12.5 years; another study was conducted by Avery et al\(^4\) and observed mean age of 58 years which much higher than our study. Arevalo JF et al\(^5\) reported a close enough observation of 53.2 years mean age in his study. Patients of these studies having diabetic retinopathy show variation in age limits may be due to geographical settings.

In our study mean duration of diabetes was 12.61±4.15 years. A study by EI Haddad et al\(^6\) reported that age of patient and duration of diabetes also associated with retinopathy but by logistic regression model lost the significance of diabetic duration which proves that it is not an independent risk factor. In a study by Ateeq A et al\(^7\) reported mean duration of diabetes was 10.15 ± 3.2 years. This study also reveals that prevalence rate of
diabetic maculopathy is higher in cases with prolonged duration of diabetes.

In our study 18.3% eyes were insulin dependent and 81.7% eyes were non insulin dependent. In a study by Ateeq A et al17 reported 18.5% were insulin dependent and 81.5% patients were non-insulin dependent. Regarding outcomes of study macular thickness after Bevacizumab a significant decrease in macular thickness (91.7%) was observed. Another similar study was conducted by Haritoglou et al18 on diabetic macular edema treated with Bevacizumab 1.25mg and observed a significant decrease in macular edema (33%). Baseline macular thickness was 498.96±123.99 micrometers and after 1 month of injection thickness was 334.40±121.76 µm.

Another study was conducted by Ozkiriş et al19 and concluded that Intravitreal administered of bevacizumab improves the thickness of macular edema and visual acuity, that why bevacizumab labeled as primary treatment of macular edema in diabetic cases. Joshi et al20 observed in his study that hypertension and previous history of laser treatment are two main contributing predictor of Intravitreal injection of bevacizumab. But improvement in macular thickness reduction is observed.

CONCLUSION

Diabetes leads to macular edema and retinopathy which is a hurdle in macular grid laser in such cases. Intravitreal injection of bevacizumab minimizes the exacerbation of macular edema in diabetic cases.

Author’s Contribution:
Concept & Design of Study: Muhammad Awais Ashraf
Drafting: Ghulam Abbas
Data Analysis: Adeel Ahmed Siddiqui
Revisiting Critically: Muhammad Awais, Ashraf, Ghulam Abbas
Final Approval of version: Muhammad Awais, Ashraf

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

REFERENCES


Objective: To determine the frequency of Hypothyroidism in patient with Hepatitis C infection

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Liaquat National Hospital, Karachi from Oct 2018 to April 2019.

Materials and Methods: All patients who met the inclusion criteria and visited the Department of Gastroenterology at Liaquat National Karachi Hospital were included in the report. After acceptance by ethics and informed and written consent. Brief history was taken, clinical examination was done and blood sample was sent for Thyroid stimulating Hormone (TSH), free T4 (FT4) to access the outcome i.e. frequency of Hypothyroidism in patient with Hepatitis C infection.

Results: 97 patients with Hepatitis C infection were included. 46 patients of which were (i.e., 47.4%) males & 51 patients (i.e., 52.6%) were female patients with the age of 33.96±7.247 years. Hypothyroidism was seen in 25 patients (25.8%).

Conclusion: In 25.8 percent of patients with HCV infection, HCV infection itself induces biochemical thyroid dysfunction prior to treatment.

Key Words: Hepatitis C virus, hypothyroid, chronic hepatitis C

INTRODUCTION

A global health issue is hepatitis C occurs due to the (HCV) hepatitis C virus. 3 to 4 million people are newly infected with HCV per year. The World Health Organization, estimated and presented the fact that there are around 180 million HCV patients in the world.1 In case of chronic HCV, which causes extrahepatic disorders, including hypothyroidism, in addition to hepatic complications.2 Some studies have shown that the hepatitis C virus and the autoimmune thyroid are basically liver thyroid diseases. The far more common thyroid disorder noted in patients with HCV infection is Hashimoto's thyroiditis (HT). In chronic hepatitis C (CHC) patients, IFN-alpha therapy is associated with the development of thyroid dysfunction, typically revealing preexisting subclinical thyroid problems.4 Shen Y et al. reported a study involving 1735 HCV infected patients and 1868 Non HCV infected patients pooled Anti-thyroid antibody prevalence tended to be higher in HCV infected subjects and the Hypothyroidism prevalence by HCV was reported 3.10 (95% CI: 2.19-4.40) in HCV infected subjects.5 In Pakistan local study reported by Shafiq M I et al. that thyroid dysfuntion in upto 27% of HCV positive patients.6 Batol N et al. reported a study among 557 ELISA positive HCV patients 9.0% were Hypothyroidism.7 Only few studies are available on frequency of Hypothyroidism in patients with HCV infection in Pakistani population. The aim of the study is to determine the frequency of hypothyroidism in HCV infected patients, which may help the future researchers for the early detection and treatment of the disease.

Operational Definitions

Hypothyroidism: was labeled as positive when TSH level is > 4.0 mIU/l and Free T4 <11.0 pmol/l.

Hepatitis C Infection: Patients with hepatitis C infection having positive serology of anti HCV antibodies were confirmed by ELISA method.

MATERIALS AND METHODS

This cross sectional study was conducted at the department of Gastroenterology, Liaquat National Hospital, Karachi.
Hospital, Karachi. Duration for this research was six months (from 19th Oct 2018 to 19th April 2019). One hundred patients were required to achieve objective of research. Sample size calculated on the basis of the prevalence of Hypothyroidism in patients with Hepatitis C infection 27% = confidence level= 95%, Absolute 8% precision was required; therefore, sample size was calculated to be 97. Non probability consecutive sampling technique was utilized for the data collection. Patients of either gender between the age of 16-50 years with Hepatitis C infection as per operational definition (for >6 months) and who were not on any treatment for HCV were included in the research. Thyroid patients already taking medications and having treatments or had gone through surgeries, even those who are diagnosed were excluded. Similarly Hepatitis C infected patient previously treated was also excluded. Other co-morbid conditions such as heart failure, renal failure, malnutrition, malabsorption was excluded (because all are effect modifier and can produce bias in my study). Patients were selected from Gastroenterology Out-Patient Department (OPD), Liaquat National Hospital, Karachi. An informed consent was obtained from patients for including them in study and using their data in research. Based on history, examination and previous-investigations, patients were evaluated for inclusion and exclusion criteria. History was taken for Hepatitis C infection and a request was sent attached with performa for serum Anti- HCV antibodies by ELISA method and serum Thyroid Stimulating Hormone (TSH), free T4 (FT4) was determined by radio-immune assay technique in the institutional laboratory. Hypothyroidism was considered if TSH is greater than 4.0 mIU/l and FT4 less than 11.0 pmol/l. This information and data regarding age and sex was entered in the performa (attached as annexure) by the principal investigator. During clinical examination of the patients, patients comfort was taken care of. In order to control the bias, exclusion criteria were followed by principal investigator strictly and the investigations were done through the institutional laboratory. Data was analyzed on SPSS version 22. Mean and standard deviation was calculated for age & duration of HCV. Male and female ratio was calculated. Frequency and percentage was calculated for patients having Hypothyroidism. Data was stratified in different age groups, gender and duration of HCV to control effect modifiers. Post stratification chi-square test was applied by taking P= < 0.05 as significant.

RESULTS

A total of 97 patients with Hepatitis C infection were selected to conduct this study. The mean age of 33.96±7.247 years. The distribution of age is presented in Fig.1. The descriptive statistics of age is presented in Table-1.

46 patients (47.4%) were males & 51 patients (52.6%) were females (as shown in Table-2). The mean duration of HCV was 18.21±18.682 months. The distribution of duration of HCV is presented in Graph-2. The descriptive statistics of duration of HCV is presented in Table-1. In our study hypothyroidism was seen in 25 patients (25.8%), as shown in Table-3 The frequencies of age groups, gender, duration of HCV was calculated according to hypothyroidism. The results are presented in Table-4, Table-5 & Table-6 respectively. In our study hypothyroidism in HCV infected patients was more common in age group of 35-50 years, predominant in female gender, was more common in patients with duration of 7-24 months of HCV.

<table>
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<th>Statistics</th>
<th>Age (years)</th>
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<td>Minimum</td>
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<td>7</td>
</tr>
<tr>
<td>Maximum</td>
<td>55</td>
<td>48</td>
</tr>
<tr>
<td>Mean + Std. Dev.</td>
<td>33.96 ± 7.247</td>
<td>18.21 ± 11.682</td>
</tr>
</tbody>
</table>
In the general population, the occurrence of TD is approximately 5 percent, with a higher rate of hypothyroidism than hyperthyroidism14,15. According to our findings, while the overall prevalence of TD was far much higher than in the common people, in HCV patients there was a trend of comparatively more hypothyroidism (9.0 percent) than hyperthyroidism (6.3 percent). This finding is consistent with other studies that have reported a higher incidence of hypothyroidism relative to hyperthyroidism in patients with HCV14-16. According to the new meta-analysis, the patients of HCV were three times more vulnerable than control subjects to hypothyroidism17. Taking into account the high occurrence of TPO-Ab in patients with HCV (local), anticipated that this hypothyroidism is likely to be autoimmune15. Conformation, however, is important since HCV infection is also documented in non-autoimmune hypothyroidism.18 Several devices for the stimulation of autoimmune thyroiditis through HCV have been suggested in various studies, such as molecular impression among viral antigens and self-antigens, stimulation of (bystander mechanism) autoreactive T cells through local infection induction, induction of peculiar expression on thyroid cells of MHC, (class II molecules), viral changes stimulation in self-antigen appearance. The HCV that induces thyroid autoimmunity in a predisposed person, on the other hand, is still mysterious. Two theories, i.e. molecular simulation and an observer activation, provide the authentic evidence of the production of thyroid autoimmunity in patients already having hepatitis C virus among the above-mentioned mechanisms. The theory of molecular mimicry proposed that a similar classification of nucleotides among self-proteins and the viral proteins may induce a cross-over immune reaction to self-antigens counterfeit by proteins of "infectious agents"20-21 Although HCV was unable to spread a virus to thyroid cells, the other parts of the body were also infected by a virus coat that is essentially a protein; a major physiological effects. For example, 2 proteins (structural) of HCV, i.e. E1 and E2, are able to bind to certain molecules of the body surface, i.e. CD81, which assist in viral entry21. Local inflammation caused by viral infection according to the bystander activation hypothesis; as an outcome, stimulation occurs of autoreactive T lymphocytes that have been repressed by peripheral tolerance mechanisms by Treg cells (regulatory T cells) 21. The bystander activation mechanism is supported by recent facts as the main process through which hepatitis C infection induces autoimmune thyroiditis. Therefore, the association between thyroid autoimmunity and hepatitis C virus infection has been shown to be triggered by thyroid HCV infection as a result of the release of pro inflammatory mediators, such as IL-8, and the

### Table No.2: Frequency distribution of Gender

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<th>Gender</th>
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<tbody>
<tr>
<td>Male</td>
<td>46 (47.4%)</td>
</tr>
<tr>
<td>Female</td>
<td>51 (52.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>97 (100%)</td>
</tr>
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### Table No.3: Frequency distribution of Hypothyroidism

<table>
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<th>Hypothyroidism</th>
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<tbody>
<tr>
<td>Yes</td>
<td>25 (28.5%)</td>
</tr>
<tr>
<td>No</td>
<td>72 (74.2%)</td>
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<td>Total</td>
<td>97 (100%)</td>
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### Table No.4: Hypothyroidism According to Age

<table>
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<th>Age</th>
<th>Hypothyroidism</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>16-34 years</td>
<td>8(8.24%)</td>
<td>36(37.11%)</td>
<td>44(45.36%)</td>
</tr>
<tr>
<td>35-50 Years</td>
<td>17(17.52%)</td>
<td>36(37.11%)</td>
<td>53(54.63%)</td>
</tr>
<tr>
<td>Total</td>
<td>17(17.52%)</td>
<td>72(74.2%)</td>
<td>97(100%)</td>
</tr>
</tbody>
</table>

### Table No.5: Hypothyroidism According to Gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Hypothyroidism</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9(9.3%)</td>
<td>37(38.1%)</td>
<td>46(47.42%)</td>
</tr>
<tr>
<td>Female</td>
<td>16(16.5%)</td>
<td>35(36.1%)</td>
<td>51(52.57%)</td>
</tr>
<tr>
<td>Total</td>
<td>25(25.8%)</td>
<td>72(74.2%)</td>
<td>97(100%)</td>
</tr>
</tbody>
</table>

### Table No.6: Hypothyroidism according to duration of hepatitis C virus (HCV)

<table>
<thead>
<tr>
<th>Duration of HCV</th>
<th>Hypothyroidism</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>7-24 Months</td>
<td>19 (19.58%)</td>
<td>61 (62.88%)</td>
<td>80 (82.47%)</td>
</tr>
<tr>
<td>25-48 Months</td>
<td>6 (6.18%)</td>
<td>11 (11.34%)</td>
<td>17 (17.52%)</td>
</tr>
<tr>
<td>Total</td>
<td>25 (25.8%)</td>
<td>72 (74.2%)</td>
<td>97 (100%)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The goal of this research was to determine the prevalence of thyroid dysfunction in patients with HCV infection who visited the Liaquat National Hospital, Karachi. As compared to the Batool et al8 study in which improper thyroid functioning was observed at the rate of 15.2 percent HCV patients. Our findings presented that thyroid dysfunctioning is figured in almost 25.8 percent of the patients. The above figure is consistent with research performed in other states showing thyroid improper functioning in 7% -15% of patients which are untreated with HCV 2-5. In interferon-free HCV patients, a recent study of such studies recorded a 10-15 percent incidence of TD148. Our prior outcome of an eminent incidence of TPO-Ab i.e., (26.8 percent) in patients who confirms high incidence of TD9. Local studies have identified a prevalence of TD ranging (7% to 22%) in patients of HCV prior to interferon therapy in other cities in Pakistan10-13
production of thyroid autoimmunity via the bystander activation phase\(^7\).

Due to the high occurrence of thyroid autoimmunity among females, majority studies have reported a higher threat or occurrence of TD affecting females effecting from HCV equally compare to the male patients 22,23. Female HCV patients in this report had a greater risk and occurrence of TD comparatively from male patients i.e., (16.1% Vs 12.5%), yet the variance was not substantial. The outcome is close to that of a indigenous study11 and confirmed by our prior result of a compatible occurrence of TPO-Ab specifically in patients with HCV in men and women10. Although other studies also report a non-significant gender gap in the incidence of TD,\(^24, 25\). The most likely explanation likely to be the reason of the low number of male patients included in this study (less than one-third female patients). The ratio of TD in them may be decreased towards a substantial level by a growing number of male patients. Even if male patients be more than females, a former Chinese study showed a greater occurrence of TD in female patients.\(^26\).

In females, thyroid autoimmunity is improved compared with male subjects168. Different studies have documented a similar pattern in HCV infected patients,\(^26, 27\.

Local studies in Pakistan have testified TD in HCV patients (20%) after treatment with IFN-alpha and ribavirin\(^28, 29\). Local studies showed that TD in 20% patients of HCV subsequent treatment with IFN-alpha and ribavirin\(^28, 29\). This high incidence can be hypothesized to be due to pre-existing in TD patients. The pre-treatment screening is also suggested for every patient effecting from HCV scheduled for IFN-alpha therapy.

**CONCLUSION**

It is observed that HCV itself induces biochemical thyroid dysfunction in 25.8 % patients prior to treatment.

**Author’s Contribution:**

**Concept & Design of Study:** Hafeez Yaqoob  
**Drafting:** Shahid Karim, Muhammad Tanweer Khalid  
**Data Analysis:** Hamid Ali, Afsheen  
**Revisiting Critically:** Faryal, Ghulam Mujtaba  
**Final Approval of version:** Hafeez Yaqoob

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

**REFERENCES**

Safe Blood to Save Life: A Study to Assess the Knowledge, Attitude, and Practice Regarding Blood Donation among Undergraduate Medical Students

Sofia Waheed Khan¹, Maheen Rana¹, Sahar Mudassar¹, Nasim Aslam Ghumman¹, Ayesha Khalid² and Yusra Rashid³

ABSTRACT

Objective: To explore the Knowledge, Attitude and Practice regarding blood donation among undergraduate medical students in Rashid Latif Medical College, Lahore.

Study Design: Descriptive / cross sectional study

Place and Duration of Study: This study was conducted at the Rashid Latif Medical College, Lahore from July to September 2019.

Materials and Methods: A total of 347 students who were present on the day of the survey and expressed their consent for participation were enrolled in the study. A structured validated questionnaire was used as a study tool.

Results: A total of 347 undergraduate medical students responded to the questionnaire, 191 were in Group A and 156 were in Group B. In Group A 29 (15%) donated blood, while in Group B donors are only 5%. Majority of the students in both groups know their blood groups. Knowledge about the blood donations among medical students is inadequate.

Conclusion: Inadequate knowledge indicates a need to incorporate topics of transfusion medicine in undergraduate curricula. Opportunities for blood donations should be created regularly to increase the sense of social responsibility among medical students.

Key Words: Blood donation, Medical Students, Knowledge, Attitudes, Practice

INTRODUCTION

Safe blood transfusion is one of the most essential needs in preventing people from various serious and life threatening medical conditions. It is the most important intervention for surgeries, trauma, blood disorders and chemotherapy. ¹ There is always a need for safe blood to save life. Millions of lives can be saved by this intervention each year. ² Although millions of blood units are collected each year but demands are still increasing. ³ Globally from all types of blood donors, around 92 million units of blood donations are collected annually.

According to World Health Organization (WHO), at least 1% of the nation's population should voluntarily donate blood in order to meet the basic requirement for blood and its products. ⁴ In Pakistan, the requirement of blood bags for transfusion is more than 1.5 million per year. ² ⁵ but unfortunately the rate of blood donation is less than one percent and it is insufficient to meet the requirements of such country where thalassemia and anemia are the main concerns. Blood which is donated by the friends and relatives accounts for 90%, while around 10% blood is donated by professional donors. ² The percentage of voluntary donors is still very less in developing country like Pakistan. So there is a need to create awareness among young students which are energetic, receptive and motivated potential blood donors. They are the good source of voluntary blood donors. ³ Medical students can be used as best model to lead this initiative. ¹ These students with positive attitude and good practice may influence their peer groups and general public. ⁴ Therefore, the objective of this study is to explore the Knowledge, Attitude and Practice among undergraduate medical students regarding blood donation in Rashid Latif medical college, Lahore.

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Printed: December, 2020
MATERIALS AND METHODS

A descriptive cross-sectional study was conducted among undergraduate Medical Students at Rashid Latif Medical College, Lahore from July to September 2019. A total of 347 students who expressed their consent for participation, were enrolled in the study. Group A comprised of 191 students of third year and fourth year MBBS. Group B comprised of 156 students of first year and second year MBBS. The nature and purpose of study were explained to them. Anonymity of participants was maintained. A structured validated questionnaire was used as a study tool. Which was based on WHO guidelines on blood donation. It include four parts, the first part enquires about socio-demographic data. The second part consist of reasons for donation and non-donation. The third part deals with knowledge of blood donation, while the fourth part includes questions about attitude of the students towards blood donation. All students were interviewed to fill the Performa.

For assessment of the seven knowledge questions, one score was given for correct answer, and zero score was given for incorrect answer. The total scoring of knowledge ranged between 0-7. The respondents whose scores were more than 50% of the total scores (i.e., ≥ 4) were considered to have adequate knowledge. While for 09 questions about attitude was assessed by agree and disagree responses. For each agree one score was given and for disagree zero score was given. The students with a total score equals to 50 percentile (median) were labeled as having positive attitude. Data was entered into and analyzed using SPSS software version 22. Percentages were used for categorical data. While mean and standard deviation were used for analysis of variables and difference was measured through t-test. P-value < 0.05 was considered as significant. The study was approved by the ethical research committee of Rashid Latif Medical College.

RESULTS

A total of 347 undergraduate medical students responded to the questionnaire; 191 were in Group A and 156 were in Group B. All responders were single in their marital status. In group A 29 (15%) donated blood and 162 (84.8%) never donated blood, while in group B donors are only 5%. Majority of the students in both group have knowledge about their blood groups. (Table No.1)

Out of 37 students who donated blood 75.8% donated once, 17.2% donated twice and only 6.8% donated more than 3 times. The main reason for donation is for the relative or friends 59.4% (Fig #1). While the main cause for non-donation is that they were never asked to donate (28%). (Table No.2). Out of seven knowledge questions group a students answer 3 out of 7 (more than 50%) than Group B. Both groups have inadequate knowledge about blood donation. Group A students have positive attitude toward blood donation 70.4% of the total studied participants. Majority of the students will donate blood in emergency situations and when friend need it (96%).

Table No.1: General characteristics of study population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>98(51.3%)</td>
<td>92(59%)</td>
<td>0.154</td>
</tr>
<tr>
<td>Female</td>
<td>93(48.7%)</td>
<td>64(41%)</td>
<td></td>
</tr>
<tr>
<td>Age , mean ± SD</td>
<td>23±1.26</td>
<td>20±1.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Donors, n(%)</td>
<td>29(15%)</td>
<td>8(5%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Know about their blood group n(%)</td>
<td>171(89.5%)</td>
<td>142(91%)</td>
<td>0.641</td>
</tr>
</tbody>
</table>

Table No. 2: Causes of Non-Donation

<table>
<thead>
<tr>
<th>Questions</th>
<th>Students (n=310)%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never thought about blood donation</td>
<td>30(9.6%)</td>
</tr>
<tr>
<td>Never asked to donate</td>
<td>86(28%)</td>
</tr>
<tr>
<td>Not enough time</td>
<td>12(3.9%)</td>
</tr>
<tr>
<td>Don’t know where to donate</td>
<td>14(4.5%)</td>
</tr>
<tr>
<td>Fear of side effects</td>
<td>14(4.5%)</td>
</tr>
<tr>
<td>Fear of drawing blood</td>
<td>10(3.2%)</td>
</tr>
<tr>
<td>Fear of transmitted diseases</td>
<td>81(26%)</td>
</tr>
<tr>
<td>Fear of sight of blood</td>
<td>4(1.2%)</td>
</tr>
<tr>
<td>Health issues</td>
<td>17(5.5%)</td>
</tr>
<tr>
<td>No specific cause</td>
<td>17(5.5%)</td>
</tr>
<tr>
<td>Multiple reasons</td>
<td>36(11.6%)</td>
</tr>
</tbody>
</table>

Table No.3: Respondents with correct knowledge questions

<table>
<thead>
<tr>
<th>Items</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=191)</td>
<td>(n=156)</td>
<td>(n=347)</td>
<td></td>
</tr>
<tr>
<td>Blood volume donated in every donation</td>
<td>78(40.8%)</td>
<td>20(13)%</td>
<td>98(28)%</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Time interval between two successive donations</td>
<td>61(31.9%)</td>
<td>33(21)%</td>
<td>94(27)%</td>
<td>0.02*</td>
</tr>
<tr>
<td>Suitable age for donation</td>
<td>7(37%)</td>
<td>51(32%)</td>
<td>122(35%)</td>
<td>0.38*</td>
</tr>
<tr>
<td>Minimum weight for donation</td>
<td>79(41.3%)</td>
<td>64(41)%</td>
<td>143(41%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Should blood be tested before donation?</td>
<td>181(95.5%)</td>
<td>146(93)%</td>
<td>327(94)%</td>
<td>0.64</td>
</tr>
<tr>
<td>Do all surgical procedures need blood donations?</td>
<td>177(92%)</td>
<td>74(47%)</td>
<td>251(71%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Could infections be transmitted by blood?</td>
<td>173(90%)</td>
<td>77(49)%</td>
<td>250(71%)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>
DISCUSSION

Blood donation is the core component of health care facilities, in this study we have explored the knowledge, attitude and practice of blood donation among young students who are the healthy and enthusiastic donors. We also sought out causes for donations and non-donations. In the present study the prevalence of blood donors among the students are 10% which is in concordance with the studies reported in the past, Iraq (14.7%), Thailand (11%) and Nigeria (15%)\(^3\). The main cause of donation in our study is a friend or relative need followed by moral satisfaction. While other studies reported that the main reason for donation is moral satisfaction. In a country like Pakistan where family bounds are strong our youth donate blood whenever needed. In our study the cause for non-donation is that they were never asked to donate which is in line with the study reported in Iraq,\(^7\) from Faisalabad\(^2\) and Karachi,\(^1\) second main cause is the fear of blood transmitted diseases reported by 26% of medical students. The reason for this is awareness about transmitted infections like hepatitis and HIV. In our study majority of the students were aware of their blood groups which is comparable from a study from Lahore.\(^12\)

Knowledge about most of the blood donation related questions are inadequate which is in line with other studies.\(^1,7\) In our study students have inadequate knowledge about volume of donated blood, time interval, suitable age and weight to donate blood which is in line with the study reported from Iraq. But overall knowledge about the blood donation is observed in 63% of students, which is in line with study conducted in Central India (52.5%) and South India (62%).\(^8,9\) While it is high in Nigeria (85%).\(^10\) This may be due to sociodemographic differences.

Our students showed positive attitude towards blood donation which is in concordance with other studies. The positive thing that we observed in our study that students don’t want any incentive for donation which is comparable to other study from Pakistan.\(^13\) In contrast to our study, participants need incentives for donation.\(^13\) The positive attitude of youth towards blood donation is a significant finding in our study, a need is to motivate students. The gap between the demand and supply can be narrowed by giving them opportunities for donations. The shortcoming in this study was to include any comparative group from other non-medical students.

CONCLUSION

There is a need to conduct seminars to increase awareness and motivation towards voluntary blood donation among students. Inadequate knowledge indicates a need to incorporate topics of transfusion medicine in undergraduate curricula. Opportunities for blood donations should be created regularly by conducting blood donation camp, this will increase the Sense of social responsibility among medical students.

Author’s Contribution:
Concept & Design of Study: Sofia Waheed Khan, Maheen Rana
Drafting: Ayesha Khalid, Yusra Rashid
Data Analysis: Nasim Aslam Ghumman, Maheen Rana, Sahar Mudassar
Revisiting Critically: Ayesha Khalid, Yusra Rashid
Final Approval of version: Sofia Waheed Khan, Sahar Mudassar

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

REFERENCES
2. Tariq S, Jawed S. Knowledge and attitude of blood donation among female medical students in...
8. Giri PA, Phalke DB. Knowledge and attitude about blood donation amongst undergraduate students of Pravara Institute of Medical Sciences Deemed University of Central India. Annals of Tropical Med Publ Health 2012;5(6):569.
Histological Comparison of Honey with Formocresol in Partial Pulpotomy of Deciduous Molars

Babra Marium Anwari¹, Mubashir Rasheed², Shazia Naz¹, Rabia Ijaz Yousaf³, Ayesha Bashir³ and Nadia Khan¹

ABSTRACT

Objective: The objective of this study is to histologically evaluate the repair of pulpal tissue after partial pulpotomy by covering the pulp tissue with Formocresol or with Honey.

Study Design: Randomized controlled trial study.

Place and Duration of Study: The study was conducted in de’Montmorency College of Dentistry, Lahore in six months from January 2018 to June 2018.

Materials and Methods: Since the study population were minors, a written informed consent was taken from the parent/guardian after explaining the procedure to them. 140 deciduous molars were randomly assigned for partial pulpotomy with Honey or Formocresol. The treated teeth were radiographically and clinically examined seven days and 60 days prior to extraction. The extracted teeth were then evaluated histologically for pulpal response.

Results: Honey is more effective in a long term therapy. Results prove that Formocresol gave instant relief but was effective only in short term treatments.

Conclusion: There is prospective of honey as an active biologic pulp dressing agent without affecting the normal function. It is a natural harmless material with a long shelf-life that can replace formocresol.

Key Words: Honey, Formocresol, Pulpotomy, Molar


INTRODUCTION

Endodontic treatment of deciduous teeth due to its bizarre internal geometric features such as connections involving furcation and horizontal anastomoses is regarded as highly complicated. This is particularly true for the deciduous first molars with and the mesiolingual canal as the least accessible canal for the mandibular first deciduous molar and the least accessible distobuccal canal in the maxillary first molar. Since the foremost reason of restoration in the pulpectomy procedure is the elimination of organic contents from the canal, a comprehensive knowledge of the root canal morphology is undoubtedly helpful.

The root canals of deciduous teeth differ greatly from those of permanent teeth, and treatment is complicated by apical resorption to allow for eruption of the succadaneous tooth. Surely it is agreed that the best pulpotomy technique should leave the radicular pulp vital and healthy and totally enclosed inside an odontoblast-lined dentin chamber. The ideal pulp dressing material must be bactericidal, nontoxic to the pulp and neighboring structures, encourage healing of the radicular pulp without hindering with the physiological course of root resorption. Haghgoo R¹. Fuks AB². The pioneering medicament used for pulpotomy was formocresol, a mixture of formaldehyde and cresol. Bijimole J³.

Formocresol pulpotomy has enjoyed a long-standing clinical utilization and accomplishment. Neamotollahi H⁴, there are concerns such as inconsistence, variability in success rate, mutagenic, cytotoxic, allergenic, and some other potential health hazards. Jabarifar SE⁵. It is recommended that a move should be made not only for the reasons relating to the possible toxicity of formaldehyde but to reveal a more modern, biologic approach to pulp therapy in the deciduous dentition. Waterhouse PJ⁶.

Facts based dentistry is being used more and more as a tool to make, assess, and interpret studies to produce clinical guiding principles and conclusions. Bekiroglu N⁷. Honey (Hy) has been used as a natural medication for centuries for the treatment of a variety of disorders as it reduces pain, inflammation, and in duration of

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Printed: December, 2020
affected area. Ahuja A\textsuperscript{8}. Natural honey is known to be harmless to the tissues. It is sterile in nature and has antiseptic, antibacterial and hygroscopic properties. Khan SA\textsuperscript{9}.

**MATERIALS AND METHODS**

The study was a randomized controlled trial conducted in de’Montmorency College of Dentistry, Lahore. Since the study population were minors, a written informed consent was taken from the parent/guardian.

140 cases were collected from the OPD of Paediatric Dentistry Department, de’ Montmorency College of Dentistry, Lahore. On clinical examination a tooth with a large carious lesion with normal pulp or reversible pulpitis that showed on periapical radiographs the succadaneous tooth to be at Nolla stage seven or eight of tooth development was included. They were divided into two major groups which were further sub-divided into two sub groups.

Teeth were clinically evaluated, radiographed, pulpotomy procedure according to the specified protocol performed and then extracted. Half of the patients had extractions done on the 0\textsuperscript{7}th day and the other half on the 60\textsuperscript{th} day in both the groups.

Same criteria applied for analyzing histologic, clinical and radiographic features 0\textsuperscript{7}th day and 60\textsuperscript{th} day after PP. Any tooth requiring extraction before the schedule was considered a failure and was excluded from the study. The procedure began with a thorough medical history and any implications related to the anticipated treatment. The dental history and characteristics of associated pain were helpful in determining pulpal status. History of any traumatic injury to the facial area was explored in depth and recorded for future medical, dental, legal, and insurance purposes.

Each tooth was randomly assigned to either Formocresol (GP FC) or Honey Groups (GP Hy). A total of 140 teeth were a part of the study. All teeth in the study were anaesthetized by block injection, using 2\% lidocaine with 1:100,000 epinephrine. The tooth was isolated and it was critically maintained to evade bacterial contamination of pulp during the procedure and any succeeding seepage after the restoration. No instrument used previously was re-introduced to the surgical field.

The procedure included removal of the carious tooth structure and part of roof of pulp chamber with a new sterile bur at high speed and water spray.

**RESULTS**

In Group-Hy mean age of patients was 10±0.851 years. Minimum and maximum age in this group was 9 and 11 years respectively. In Group-FC mean age of patients was 9.99±0.860 years. Minimum and maximum age of patients in this group was 9 and 11 years.

In Group-Hy there were 26(74.28\%) male and 9(25.72\%) female patients while in Group-FC there were 24(70.58\%) male and 11(31.42\%) female patients. At 7\textsuperscript{th} day in Group-Hy 33 patients radiological findings were at grade-1 while 1 patient had grade-2 and 1 patient had grade-3 radiological findings. In Group-FC 31 patients had grade-1, 3 patients had grade-2 and 1 patient had grade-3 radiological finding. At day 7 radiological finding were same in both treatment groups. p-value=0.588 While at 60\textsuperscript{th} day in both treatment groups radiological findings were same. [Grade-1=Group-Hy:33, Group-FC:30, Grade-2: Group-Hy:1, Group-FC:3, Grade-3: Group-Hy:1, Group-FC:2 ] i.e. p-value=0.478

Success rate as per operational definition in Group-Hy was observed in 31(88.6\%) patients and in Group-FC success of treatment was seen in 34(97.1\%) patients at 7\textsuperscript{th} day. It was observed that success rate in Group-FC was high as compared to that of Group-Hy but statistically this difference was not significant. i.e. (p-value=0.164) At 60\textsuperscript{th} day success was again seen in both treatment groups. At this point in Group-Hy success of treatment was seen in 33(94.3\%) patients and in Group-FC in 30(85.7\%) only. Success rate in Group-Hy patients was high as compared to that of Group-FC patients but in terms of p-value this difference was not statistically significant. (p-value=0.232)

In both treatment groups success rate was 91.4\%. No statistically significant difference was seen for success when overall success was determined.

![Figure No.1: Age distribution of patients](image)

There were 51 patients in the age group 9 years and in the age group 10 years there were 39 patients. In the age group 11 years there were 50 patients.

At 7\textsuperscript{th} day in Group-Hy07 33 patients radiological findings were at grade-1 while 1 patient had grade-2 and 1 patient had grade-3 radiological findings. In Group-FC07 31 patients had grade-1, 3 patients had grade-2 and 1 patient had grade-3 radiological finding. At day 7 radiological finding were same in both treatment groups. p-value=0.588 While at 60\textsuperscript{th} day in both treatment groups radiological findings were same. [Grade-1=Group-Hy60:33, Group-FC60:30, Grade-2:
Group-Hy60:1, Group-FC60:3, Grade-3: Group-Hy60:1, Group-FC60:2 ] i.e. p-value=0.478 (Table 1).

**Table No.1: Radiographic findings in groups at 7th day & at 60th day**

<table>
<thead>
<tr>
<th>Radiographic Findings</th>
<th>7th Day</th>
<th>60th Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-Hy07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-FC07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-Hy60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-FC60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>33(94.3%)</td>
<td>33(94.3%)</td>
</tr>
<tr>
<td>2</td>
<td>1(2.9%)</td>
<td>1(2.9%)</td>
</tr>
<tr>
<td>3</td>
<td>1(2.9%)</td>
<td>2(5.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Chi-Square Test</td>
<td>1.063</td>
<td>1.476</td>
</tr>
<tr>
<td>p-value</td>
<td>0.588</td>
<td>0.478</td>
</tr>
</tbody>
</table>

**Group-Hy= Honey Group- FC= Formocresol**

At 7th day and 60th day histological grades were not having a statistically significant difference in both treatment groups (Table 2).

**Table No.2: Histological grade in treatment groups at 7th day & at 60th day**

<table>
<thead>
<tr>
<th>Histological Grade</th>
<th>7th Day</th>
<th>60th Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-Hy07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-FC07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-Hy60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-FC60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>52(19.4%)</td>
<td>31(88.6%)</td>
</tr>
<tr>
<td>1</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>2</td>
<td>2(2.5%)</td>
<td>3(8.6%)</td>
</tr>
<tr>
<td>3</td>
<td>1(2.9%)</td>
<td>1(2.9%)</td>
</tr>
<tr>
<td>4</td>
<td>0(0%)</td>
<td>1(2.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Chi-Square Test</td>
<td>1.20</td>
<td>2.15</td>
</tr>
<tr>
<td>p-value</td>
<td>0.549</td>
<td>0.540</td>
</tr>
</tbody>
</table>

**Group-Hy= Honey Group- FC= Formocresol**

**Table No.3: Success rate in treatment groups at 7th day & at 60th day in relation to age of patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>Time</th>
<th>Success</th>
<th>Group-Hy</th>
<th>Group-FC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 Years</td>
<td>7 Days</td>
<td>Yes</td>
<td>11(100%)</td>
<td>13(100%)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>11</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>14(100%)</td>
<td>12(92.3%)</td>
<td>0.290</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>0(0%)</td>
<td>1(7.7%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>14</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>10 Years</td>
<td>7 Days</td>
<td>Yes</td>
<td>9(81.8%)</td>
<td>10(100%)</td>
<td>0.156</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>2(18.2%)</td>
<td>0(0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>8(88.9%)</td>
<td>7(77.8%)</td>
<td>0.527</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>1(11.1%)</td>
<td>2(22.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>11 Years</td>
<td>7 Days</td>
<td>Yes</td>
<td>11(84.6%)</td>
<td>11(91.7%)</td>
<td>0.588</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>2(15.4%)</td>
<td>1(8.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>13</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>11(91.7%)</td>
<td>11(84.6%)</td>
<td>0.588</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>1(8.3%)</td>
<td>2(15.4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>12</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Patients in age group 9 years among them it was seen that success rate in both treatment groups at 7th day and at 60th day did not differ significantly. Same trend was seen in patients who were 10 and 11 years old. But at 7th day success rate was observed to be high in Group-FC and at 60th day success rate was high in Group-Hy. So it can be said that at short term follow up success rate was high in Group-B but not statistically significant and for long term follow up success rate was high in Group-A but not statistically significant. (Table 3)

**DISCUSSION**

There is no qualm that a reparative, biologic, pragmatic approach to vital pulp therapy in pediatrics is welcome. The devitalization path and investigations to find substitutes for replacing the devitalizing medicaments is not only looked for but is very imperative.

In this study, the clinical and histologic success rates of pulpotomy using Honey in comparison with Formocresol were examined over a period of 07 days and 60 days. Although the teeth treated with Honey demonstrated a slightly lower success rate (88.6%) than those treated with Formocresol (97.1%) at 07th day. A slightly higher success rate of Honey (94.3%) than those treated with Formocresol (85.7%) at 60th day was observed. No statistically significant difference in success rates were found between the groups when overall success was determined (P > 0.05).

Verification of the clinical vitality of pulp is still, one of the foremost dilemmas. Histology can confirm the viability of dental pulp, but is not realistic for clinicians, who rely on clinical and radiographic examinations, which do not give a precise evaluation of pulp vitality. It is by and large approved that vital pulp therapy is clinically efficacious if the tooth is symptom less, responds satisfactorily to sensitivity tests and appears normal radiographically. Verification of the clinical vitality of pulp is still, one of the foremost dilemmas. Histology can confirm the viability of dental pulp, but is not realistic for clinicians, who rely on clinical and radiographic examinations, which do not give a precise evaluation of pulp vitality. It is by and large approved that vital pulp therapy is clinically efficacious if the tooth is symptom less, responds satisfactorily to sensitivity tests and appears normal radiographically.

The diagnosis of failure was mainly based upon clinical judgment; it included pre- and intra-operative assessment of pulp status. The texture and colour of the pulp tissue as well as cessation of bleeding after coronal amputation have were as indicators of the status of the radicular pulp. Because more precise diagnostic tools are not available in the clinical situations, some pulpotomies performed on teeth could be histologically contra-indicated. This may be the reason attributed for the pulpotomy failure.
The lower success rate for FC observed in this study is consistent with previous studies that showed decreased success rate of FC with time. Olatosi OO\textsuperscript{10}.

WHO has estimated the use of Formocresol through air, water and food at 1.5- to 14-mg/ day (mean 7.8 mg/day). The estimated dose of formaldehyde associated with one pulpotomy procedure, assuming a 1:5 dilution of Formocresol placed on a number 4 cotton pellets that has been squeezed dry, is 0.02 - 0.1 mg. Thus, there is no inconsequential risk of carcinogenesis associated with the use of formaldehyde in pediatric pulp therapy. The 1-min application of Formocresol is found to be as effective as 5-min application Godoy FG\textsuperscript{13} and have found that 1:5 dilution (20% concentration) achieves desired cellular response and faster recovery of the affected cells.

Histological findings by this study confirm that Formocresol has no reparative ability and its action is limited as a fixative agent only. In formocresol group, increased inflammatory cells could be found in pulp. Odontoblastic layer was not intact throughout the dentine pulp complex. Pulp stones were isolated and scattered. Initiation of dentine bridge was not seen at 60 days interval. A zone of atrophy was noted in radicular portion of pulp. In vitro investigation has demonstrated the ability of Honey to stimulate cytokine release from bone cells, indicating that it actively promotes hard tissue formation rather than being inert. In Honey group, odontoblastic layer integrity was well maintained. Isolated calcific masses were found. The amounts of pulp stones were more than formocresol group. The pulp was hyperemic, yet less inflammatory cells could be seen compared with formocresol group. Reversal line/resting line were noted. An amorphous eosinophilic layer of new dentine formation with less dentinal tubules could be seen in the coronal portion of pulp. This could be considered as dentine bridge, which represents the pulpotomized regenerating site.

Honey maintains the integrity of the pulp. Dentin bridges formed could be a result of pulp irritation and/or inflammation, or alternatively due to a stimulus from the material placed directly over the exposed pulp. Discrete calcification seen suggest a close relation between nerve fibers and odontoblastic cell differentiation suggesting repair of pulpotomized site.

Honey has biological characteristics to be used as a pulpotomy medicament in deciduous teeth. These results are in accordance with study done by Srinivasan D\textsuperscript{12}.

Through this study we have seen that the success rate is almost equal but FC contains formaldehyde which is an established carcinogen, however honey is a natural product with no side effects and has wound healing capabilities. Furthermore, it is a natural, cheap and harmless material. Despite that FC is still being used in dentistry and as yet there is no known study comparing Honey and Formocresol in Dentistry. Hence through this study we have evidence that honey is effective in healing and recommend its use in partial pulpotomy in deciduous molars in future.

CONCLUSION

Honey is more effective in a long term therapy. Results prove that Formocresol gave instant relief but was effective more only in short term treatments.

There is prospective of honey as an active biologic pulp dressing agent without affecting the normal function. It is a natural harmless material with a long shelf-life that can replace formocresol.

Honey when applied as a dressing material onto amputated exposed pulp tissue of deciduous molars shall encourage accelerated tissue healing.

Author’s Contribution:

Concept & Design of Study: Babra Marium Anwari
Drafting: Mubashir Rasheed, Shazia Naz
Data Analysis: Rabia Ijaz Yousaf, Ayesha Bashir, Nadia Khan
Revisiting Critically: Babra Marium Anwari, Mubashir Rasheed
Final Approval of version: Babra Marium Anwari

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

REFERENCES

Evaluation of Lipid Profile in Patients with Anemia in Mirpur AJK

Rashad Mahmood¹, Khuram Shahzad Khan¹, Zara Shaukat⁴, Faisal Bashir² and Asnad³

ABSTRACT

Objective: The objective of this study to evaluate saliva biochemical composition of pregnant women and nonpregnant women in Mirpur AJK.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the department Physiology and Biochemistry Department of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK from March 2018 to August 2019.

Materials and Methods: Total 200 anemic patients were selected male and female and 100 control healthy people were selected for the study. Lipid profile (Total cholesterol, HDL, VLDL and triglycerides) was estimated in both groups in anemic patient and control healthy people. Blood samples were collected from both groups anemic and healthy people. Samples were analyzed by Micro lab 300 for lipid profile for both groups anemic and control. Merck kits were used for analysis of lipid profile in both groups. Hematology study was conduct by used hematology analyzer. Kits of Merk Company were used for analysis.

Results: The total mean cholesterol (mg/dl) in anemic patients was 182.6 ± 29.5 while in healthy control was 193.6 ± 30.5. The mean LDL (mg/dl) in anemic patients was 105.8 ± 15.5 while in healthy control was 118.7± 19.3. The mean HDL (mg/dl) in anemic patients was 42.77± 8.4 while in healthy control was 59.3 ± 8.1. The mean Triglycerides (mg/dl) in anemic patients was 120.2 ± 29 while in healthy control was 133.3 ± 31.2. Result showed that lipid profile is lower in anemic patient as compare to healthy control subjects. The mean Hb (g/dl) in anemic patients was 8.88 ± 1.32 while in healthy control subjects was 12.79 ± 1.43. The mean Serum iron (µg/dl) in anemic patients was 38.32 ± 6.35 while in healthy control subjects was 96.15 ± 18.68. The mean TIBC (µg/dl) in anemic patients was 399.03 ± 41.48 while in healthy control subjects was 282.72 ± 27.04. The mean Serum ferritin (µg/dl) in anemic patients was 9.93 ± 3.8 while in healthy control subjects was 49.4 ± 31.00.

Conclusion: The result showed that in anemia and lipoprotein relationship exist but the type of anemia is not affect the relationship. The lipoprotein level is decreased in anemic patient as compare to control.

Key Words: Lipid profile, Anemic patients

INTRODUCTION

Iron Deficiency (ID) is widespread nutritional disorder developing countries regardless of age, gender and socioeconomic status. Due to its complications, iron deficiency anemia becomes a big public health problem.

One of the risk factor of coronary artery disease (CAD) is Dyslipidemia and another public health issue is anemia.

Anemia is more common in low socioeconomic status.⁴ Anemia have role as protective on lipid profile and reduced the risk of CAD. In upper socioeconomic class more prevalence of CAD as compare to lower socioeconomic class. Nutritional Anemia is high prevalence in lower socioeconomic class.⁵ some studies showed contradictory result regarding lipid profile and anemia relationship. In some studies observed that VLDL levels and triglycerides are high in anemia due to iron deficiency as compare to non-anemic patients.⁴ Lipoprotein (LDL) cholesterol were found lower in anemic patients. Where in other study found that high-density lipoprotein (HDL), LDL, VLDL, and triglyceride levels are decreased in anemic patients as compare to control and health people. ⁵ Different study studies showed that deficiency of iron in animal caused alteration in the lipid profile.⁶,⁷ That when the concentration of the iron is low in animal IDA iron deficiency anemia it changed the high-density lipoprotein (HDL), LDL, VLDL, and triglyceride levels in animal. In other study of human, Iron deficiency anemia lipid profile is lower with respect iron deficiency.⁸,⁹ In severe IDA, Low levels of triglycerides and total cholesterol (TC), in young
Korean girls are decreased and returned normal after therapy of iron. These results and observations showed that there is variation in both findings. So we conducted this study to evaluate the lipid profile (high-density lipoprotein (HDL), LDL, VLDL, and triglyceride) in anemic patients and non anemic control healthy people.

**MATERIALS AND METHODS**

This study was conducted in the department Physiology and Biochemistry Department of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK from March 2018 to August 2019. It was cross section – control study. Total 200 anemic patients were selected male and female and 100 control health people are selected for the study. Lipid profile (Total cholesterol, HDL, VLDL and triglycerides) was estimated in both groups in anemic patient and control healthy people. Blood samples were collected from both groups anemic and healthy people. Samples were analyzed by Micro lab 300 for lipid profile for both groups anemic and control. Merck kits were used for analysis of lipid profile in both groups. Hematology study was conducted by used hematology analyzer. Kits of Merck Company are used for analysis.

**Statistical Analysis:** SPSS for Windows version 20 (SPSS, Inc., Chicago, IL, USA) was employed for all statistical analyses.

**RESULTS**

The total mean cholesterol (mg/dl) in anemic patients was 182.6 ± 29.5 while in healthy control was 193.6 ± 30.5. The mean LDL (mg/dl) in anemic patients was 105.8 ± 15.5 while in healthy control was 118.7 ± 19.3. The mean HDL (mg/dl) in anemic patients was 42.77 ± 8.4 while in healthy control was 59.3 ± 8.1. The mean Triglycerides (mg/dl) in anemic patients was 120.2 ± 29.5 while in healthy control was 133.3 ± 31.2. Result showed that lipid profile is lower in anemic patient as compare to healthy control subjects. The mean Hb (g/dl) in anemic patients was 8.88 ± 1.32 while in healthy control subjects was 12.79 ± 1.43.

**DISCUSSION**

Iron Deficiency (ID) is widespread nutritional disorder developing countries regardless of age, gender and socioeconomic status. Due to its complications, big public health problem is IDA iron deficiency anemia. The major risk factor in the development of CAD is Dyslipidemia. This study was conducted in the department Physiology and Biochemistry Department of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK from March 2018 to August 2019. It was cross section – control study. Total 200 anemic patients were selected male and female and 100 control health people are selected for the study. Lipid profile (Total cholesterol, HDL, VLDL and triglycerides) was estimated in both groups in anemic patient and control healthy people. Blood samples were collected from both groups anemic and healthy people. Samples were analyzed by Micro lab 300 for lipid profile for both groups anemic and control. Merck kits were used for analysis of lipid profile in both groups. Hematology study was conducted by used hematology analyzer. Kits of Merck Company are used for analysis. Iron and cholesterol are important for human body any deficiency of both caused serious effect on human body. The level of iron and cholesterol are important.

**Table No.1: Participant Characteristics**

<table>
<thead>
<tr>
<th>(n=200)</th>
<th>Control (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.4 ± 10.2</td>
</tr>
<tr>
<td>Male /Female (%)</td>
<td>100/100</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>68.9 ± 10.8</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>24.7 ± 2.6</td>
</tr>
</tbody>
</table>

The mean Serum iron (μg/dl) in anemic patients was 8.88 ± 1.32 while in healthy control subjects was 9.93 ± 3.8. The mean TIBC (μg/dl) in anemic patients was 399.03 ± 41.48 while in healthy control subjects was 282.72 ± 27.04. The mean Serum ferritin (μg/dl) in anemic patients was 9.93 ± 3.8 while in healthy control subjects was 49.4 ± 31.00.

**Table No.2: Lipid Profile of Anemic Patients and Control Health People**

<table>
<thead>
<tr>
<th></th>
<th>Anemic (n=200)</th>
<th>Control (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose (mg/dl)</td>
<td>97.8 ± 4.3</td>
<td>99.4 ± 4.6</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>182.6 ± 29.5</td>
<td>193.6 ± 30.5</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>105.8 ± 15.5</td>
<td>118.7 ± 19.3</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>42.77 ± 8.4</td>
<td>59.3 ± 8.1</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>120.2 ± 29.5</td>
<td>133.3 ± 31.2</td>
</tr>
</tbody>
</table>

**Table No.3: Hematological profile of anemic Patients and Control Health People**

<table>
<thead>
<tr>
<th></th>
<th>Anemic (n=200)</th>
<th>Control (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dl)</td>
<td>8.88 ± 1.32</td>
<td>12.79 ± 1.43</td>
</tr>
<tr>
<td>Serum iron (μg/dl)</td>
<td>38.32 ± 6.35</td>
<td>96.15 ± 18.68</td>
</tr>
<tr>
<td>TIBC (μg/dl)</td>
<td>399.03 ± 41.48</td>
<td>282.72 ± 27.04</td>
</tr>
<tr>
<td>Serum ferritin (μg/dl)</td>
<td>9.93 ± 3.8</td>
<td>49.4 ± 31.00</td>
</tr>
</tbody>
</table>
One of the risk factors of coronary artery disease (CAD) is dyslipidemia and another public health issue is anemia. Anemia is more common in low socioeconomic status. Anemia have role as protective on lipid profile and reduced the risk of CAD. In upper socioeconomic class more prevalence of CAD as compared to lower socioeconomic class. Nutritional Anemia is high prevalence in lower socioeconomic class. Some studies showed contradictory result regarding lipid profile and anemia relationship. In some studies observed that VLDL levels and triglycerides are high in anemia due to iron deficiency as compared to non-anemic patients. Lipoprotein (LDL) cholesterol were found lower in anemic patients. Where in other study found that high-density lipoprotein (HDL), LDL, VL DL, and triglyceride levels are decreased in anemic patients as compared to control and health people. Different studies showed that deficiency of iron in animal caused alteration in the lipid profile. That when the concentration of the iron is low in animal IDA iron deficiency anemia it changed the high-density lipoprotein (HDL), LDL, VLDL, and triglyceride levels in animal. In other study of human, Iron deficiency anemia lipid profile is lower with respect iron deficiency in severe IDA, Low levels of triglycerides and total cholesterol (TC), in young Korean girls are decreased and returned normal after therapy of iron. These results and observations showed that there is variation in both findings. Our result showed that anemic and non-anemic both groups plasma cholesterol and lipoprotein are significant lower that in anemic patient the lipoprotein is lower as compare to non-anemic control. The total mean cholesterol (mg/dl) in anemic patients was 182.6 ± 29.5 while in healthy control was 193.6 ± 30.5. The mean LDL (mg/dl) in anemic patients was 105.8 ± 15.5 while in healthy control was 118.7± 19.3. The mean HDL (mg/dl) in anemic patients was 42.77± 8.4 while in healthy control was 59.3 ± 8.1. The mean Triglycerides (mg/dl) in anemic patients was 120.2 ± 29.9 while in healthy control was 133.3 ± 31.2. Result showed that lipid profile is lower in anemic patient as compared to healthy control subjects. The mean Hb (g/dl) in anemic patients was 8.88 ± 1.32 while in healthy control subjects was 12.79 ± 1.43. The mean Serum iron (μg/dl) in anemic patients was 38.32 ± 6.35 while in healthy control subjects was 96.15 ± 18.68. The mean TIBC (μg/dl) in anemic patients was 399.03 ± 41.48 while in healthy control subjects was 282.72 ± 27.04. The mean Serum ferritin (μg/dl) in anemic patients was 9.93 ± 3.8 while in healthy control subjects was 49.4 ± 31.00. In the study of Choi et al. that there is no significant difference both groups anemic patient and control health people at moderate iron deficiency while in severe iron deficiency anemia patient serum total cholesterol and triglyceride level are significantly reduced. Ece et al. result showed that tat serum hemoglobin have linked with cholesterol and triglyceride concentrations. Higher levels of triglyceride and lower HDL-cholesterol levels were found in anemic patient as compared to control and healthy people. Increased erythropoiesis lead increased demand and ultimately lead hypercholesterolemia in anemic patients. Iron used as cofactor in many biochemical reaction which caused lipid metabolism abnormality in patients. In the study of Graham et al. showed that iron increased in hepatic storage, which caused up regulation of HMG-CoA reductase of cholesterol biosynthesis, rate-limiting enzyme. The result showed that in anemia and lipoprotein relationship exist but the type of anemia is not affect the relationship.

CONCLUSION

The result showed that in anemia and lipoprotein relationship exist but the type of anemia is not affect the relationship. The lipoprotein level is decreased in anemic patient as compared to control.

Author’s Contribution:

Concept & Design of Study: Rashad Mahmood
Drafting: Khuram Shahzad Khan, Zara Shaukat
Data Analysis: Faisal Bashir, Asnad
Revisiting Critically: Rashad Mahmood, Khuram Shahzad Khan
Final Approval of version: Rashad Mahmood

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

REFERENCES

6. Au YP, Schilling RF. Relationship between anemia and cholesterol metabolism in ‘sex-linked anemia’


Knowledge, Attitude and Practice of Emergency Contraception in Women Attending Outpatient Department of Shahida Islam Teaching Hospital (SITH) Lodhran

Joveria Sadaf, Tanzila Rafiq, Aslam Mahmood Malik, Saba Nadeeem and Sana Ara

ABSTRACT

Objective: The aim of this study was to assess the knowledge, attitude and practice of emergency contraceptive among women who attended Shahida Islam Teaching Hospital Obstetrics and Gynaecology Department in Out Patient department.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Shahida Islam Teaching Hospital, Lodhran from April to June, 2018.

Materials and Methods: All women of reproductive age, presenting in the gynaecology and obstetrics outpatient department in Shahida Islam Teaching Hospital Lodhran were included in the study. Unmarried, mentally retarded and those who were not willing to participate in survey were excluded. Face to face interview through structured questionnaire was done. Data was collected using structured questionnaire and analyzed using SPSS version 17.0. Descriptive statistics chi-square tests were done and significance of tests was decided at p-value 0.05.

Results: In this study 548 women were interviewed. Less than half of them 262(47.8%) were from urban area and 286(52.2%) were from rural area. All of them were married. Of all the respondents 92(16.8%) women had awareness about emergency contraceptive. 82(15%) of the women mentioned pills as emergency contraception and only 26(4.7%) of them mentioned intrauterine device as emergency contraception. 265(48.4%) of them have positive attitude towards emergency contraception but only 64(11.1%) of them have ever used emergency contraceptives.

Conclusion: The knowledge and practice of emergency contraception is very low. But there is high positive attitude towards emergency contraceptives. Since there is much deficit on knowledge of women on emergency contraceptives, in addition to making them accessible; programs targeted at promotion and education of emergency contraceptives is helpful to prevent unwanted pregnancy.

Key Words: Emergency contraception, IUD, Morning after pill


INTRODUCTION

Approximately, one third of pregnancies are not planned and one fifth of all pregnancies end in abortion. More than 170,000 legal abortions are performed in the United Kingdom annually.¹

Emergency contraception is effective and safe method to avoid an unwanted pregnancy happening after an unprotected sexual intercourse. History of emergency contraceptive dates back to the 1960’s when physicians in the Netherlands gave estrogen extracts to 13 years old girl who had been raped. Several methods for emergency contraception (EC) are now registered in many countries to be used in an emergency to avoid a pregnancy following an unprotected, possibly fertile intercourse or after a contraceptive accident like condom leak or condom rupture.²³⁴

There have been many attempts to control pregnancy after unprotected sexual intercourse (UPSI). So far, hormonal methods preventing or delaying ovulation have proved to be the most popular method starting with the combination of ethinyl estradiol and levonorgestrel (LNG), the Yuzpe regimen. The first dose had to be taken within three days of UPSI, a second one 12 hours later. Later on, LNG alone, at first in a regimen similar to the Yuzpe method (2 × 0.75 mg
12 hours apart) proved to be more successful, at last resulting in the development of a 1.5 mg LNG pill that combined good control of fertility with a high ease of use. Its limitations are the non-optimal efficacy which is decreasing the later the drug is taken and the fact that it is only approved for up to 72 hours after UPSI.\textsuperscript{3,5,6} It has become the standard method of emergency contraception used up to this day in most countries. Since the mid-1970s copper IUDs have been used for emergency contraceptive, which show a high efficacy. Their disadvantages are that emergency contraception is considered an off label use for most IUDs and that they sometimes not be acceptable for every patient. Moreover, IUD-insertion is an invasive procedure and it is required trained personals and sterilized facilities for insertion.\textsuperscript{3,7}

Mifepristone in the dosages of 10 or 25 mg is used with good results as an emergency contraceptive in China for up to 5 days after UPSI, but has never received any significant consideration in Western countries. It is not available in Pakistan.\textsuperscript{3,8}

The most recent development is the approval of the selective progesterone receptor modulator ulipristal acetate (UPA) in the dosage of 30 mg for EC up to 5 days after UPSI, combining the safe and easy application of the single dose LNG pill with an even higher efficacy. It has shown to be more efficacious than LNG and can be used for up to 120 hours after UPSI; the difference in efficacy is highest for 0-24 hours, followed by 0-72 hours following UPSI. It is also not available in Pakistan.

So, we are left with oral hormones and IUD devices and designed our questionnaire accordingly. Generally, the knowledge of contraception has increased in urban and rural population of Pakistan in recent years, so as the positive attitude towards contraception use. But still the knowledge about emergency contraception is poor even in educated females. Our study will not only help to show the level of knowledge and use as well as attitude of women toward emergency contraception it also provides useful information for the policy makers to control the rate of unintended pregnancy and unsafe abortions by overcoming the problems related to this neglected domain of family planning in Pakistan.

**MATERIALS AND METHODS**

Institution base cross-sectional study on knowledge, attitude and practice of emergency contraceptive was conducted at Shahida Islam Teaching Hospital, Lodhran from April to June, 2018. Total of 548 patients participated in the survey.

**Inclusion and Exclusion Criteria:** All women of reproductive age, presenting in the gynaecology and obstetrics outpatient department in Shahida Islam Teaching Hospital Lodhran were included in the study. Unmarried, mentally retarded and those who were not willing to participate in survey were excluded.

Data Collection: Face to face interview through structured questionnaire was done. The questionnaire was kept in the outpatient department and patients were interviewed on arrival.

Data Analysis and Presentation: The Data was analyzed by SPSS for windows version 17.0. Descriptive statistics chi-square tests were done and significance of tests was decided at p-value 0.05. Tables and graphs were used to depict results.

Operational Definitions: Knowledge-Awareness about the types and time limit to be taken after unprotected sex, of emergency contraceptives.

Attitude-The way to which clients are thinking or behaving towards emergency contraceptive. Practice - Trend of use of emergency contraceptives among women, in case of unprotected intercourse.

RESULTS

In this study 548 women were interviewed. Less than half of them 262(47.8%) were from urban area and 286(52.2%) were from rural area.

**Table No.1: Knowledge, Attitude and Practice n=548**

<table>
<thead>
<tr>
<th>Variable</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge of emergency contraception</td>
<td>92(16.8%)</td>
<td>456(83.2%)</td>
</tr>
<tr>
<td>Know the pill as emergency contraceptive</td>
<td>82(15%)</td>
<td>456(85%)</td>
</tr>
<tr>
<td>Know how to take the pill</td>
<td>47(8.6%)</td>
<td>501(91.4%)</td>
</tr>
<tr>
<td>Know the IUD as emergency contraceptive</td>
<td>26(4.7%)</td>
<td>522(95.3%)</td>
</tr>
<tr>
<td>Like to use emergency contraceptive if needed</td>
<td>265(48.4%)</td>
<td>283(51.6%)</td>
</tr>
<tr>
<td>Had ever practiced emergency contraception</td>
<td>64(11.7%)</td>
<td>484(88.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Practiced ever→ Knowledge ↓</th>
<th>Yes</th>
<th>No</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>64(11.7%)</td>
<td>28 (5.1%)</td>
<td>92(16.8%)</td>
</tr>
<tr>
<td>No</td>
<td>0(0%)</td>
<td>456(83.2%)</td>
<td>456(83.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>64(11.7%)</td>
<td>484(88.3%)</td>
<td>548(100%)</td>
</tr>
</tbody>
</table>

P value= 0.00

**Table No.3: Knowledge and Area of Origin n=548**

<table>
<thead>
<tr>
<th>Origin knowledge</th>
<th>Urban</th>
<th>Rural</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>71 (13%)</td>
<td>21 (3.8%)</td>
<td>92 (16.8%)</td>
</tr>
<tr>
<td>No</td>
<td>191 (34.8%)</td>
<td>265 (48.4%)</td>
<td>456 (83.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>262 (47.8%)</td>
<td>286 (52.2%)</td>
<td>548 (100%)</td>
</tr>
</tbody>
</table>

P value= 0.00

All of them were married. Of all the respondents 92(16.8%) women had awareness about emergency contraceptive. 82(15%) of the women mentioned pills as emergency contraception and only 26(4.7%) of them mentioned intrauterine device as emergency contraception. 265(48.4%) of them have positive
attitude towards emergency contraception but only 64(11.1%) of them have ever used emergency contraceptives. Results are shown in tables 1,2,3.

DISCUSSION

Unwanted pregnancy is a major challenge to reproductive health of young women in developing countries. Some women, who had unwanted pregnancies, obtain abortion. Many of which are performed in unsafe and unsterilized conditions by untrained and unauthorized personals and others carry their pregnancies to term. Emergency contraceptive can prevent pregnancy when taken shortly after unprotected sex.

The result of our study shows that knowledge of emergency contraception is very low (16.8%) especially among the women of rural origin (3.8%) similar findings are there in many other studies. 8,9,10,11 Knowledge of the emergency contraception is directly proportional to the use of the method. It is evident that to increase the use of emergency contraception to prevent unwanted pregnancy, knowledge of the method should be spread among the women of reproductive age especially in rural population.

It is also clear from our study that there is high level of positive attitude towards emergency contraception 48.8% women told that they would use an emergency contraception method if needed. These results are similar to those found in studies conducted by Hobbs M, Ball DE, Harper CC 12, 13, 14 Some women also commented that they would have definitely used a method if they could have known and found any emergency contraception earlier. It means that giving them the knowledge of emergency contraception is definitely going to reduce unwanted pregnancy rates.

George J et al, Silva FC et al, Siebert I et al conducted studies in developed countries, tertiary care centers. 15,16,17 They concluded that in developed countries the knowledge of emergency contraception is high but the use is less, though the attitude towards emergency contraception is highly positive. These results are contradictory to our study. They give the reason that in developed world the use of reliable regular contraception is so high that they have less incidences of unprotected sexual intercourse.

To conclude in our society giving awareness of emergency contraception is definitely a way to reduce unplanned unwanted pregnancies and will give women empowerment over decision of their family size.

CONCLUSION

The knowledge and practice of emergency contraception is very low. But there is high positive attitude towards emergency contraceptives. Since there is much deficit on knowledge of women on emergency contraceptives, in addition to making them accessible; programs targeted at promotion and education of emergency contraceptives is helpful to prevent unwanted pregnancy.

Author's Contribution:
Concept & Design of Study: Joveria Sadaf
Drafting: Tanzila Rafiq, Aslam Mahmood Malik
Data Analysis: Saba Nadeeem and Sana Ara
Revisiting Critically: Joveria Sadaf, Tanzila Rafiq
Final Approval of version: Joveria Sadaf

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

REFERENCES
11. MacDonald G, Amir L. Women’s knowledge and attitudes about emergency contraception: a survey
Immunohistochemical Expression of MMP-9 in Subtypes of Ameloblastoma

Farah Farhan¹, Maria Ilyas⁴, Misbah Ali⁴, Zainab Akbar² and Batool Zahra³

ABSTRACT

Objective: To assess the immune expression of MMP-9 in ameloblastoma and its association with different histological subtypes of ameloblastoma.

Study Design: Analytical / cross-sectional study

Place and Duration of Study: This study was conducted at the Armed Forces Institute of Pathology, Rawalpindi (AFIP) from June 2016 till June 2017.

Materials and Methods: In this study, total of 60 cases of ameloblastoma were included. Paraﬁnembedded blocks of patients of both genders, diagnosed with ameloblastoma were included as experimental samples while necrotic, scarce and autolized cases were not included. The tumor was sub-classiﬁed histologically on the basis of WHO classiﬁed and section were stained with H&E followed by (IHC) staining for MMP-9. SPSS version 20 was used to analyse the ﬁnal result analyzed using chi-square test.

Results: Out of 60 cases of ameloblastoma, 32 were males and 28 were females. Mean age was 35.6 years with maximum 25 cases(83.3%) from mandible. On histopathological sub classiﬁcation, 38 cases (63%) were diagnosed as follicular type, 14 cases(23.3%) were plexiform, 8 cases(13.3%) were acanthomatous type. All samples represent variable MMP-9 expression along with mild, moderate and strong intensity. Adjacent to the tumoral island invasive font was with highest reactivity. The strong immunoexpression, was seen in 75% acanthomatous and 57% plexiform, which was signiﬁcantly different from follicular type with only 5.26%. Statistical test on MMP-9(P<0.05) provide highest reactivity in acanthomatous type along with the presence of substantial differences within histological variant.

Conclusion: Our results proved the implication of MMP-9 in ameloblastoma growth and as a result their effectiveness in local aggressiveness monitoring in different subtypes of ameloblastoma.

Key Words: Ameloblastoma, MMP-9, odontogenic tumor.


INTRODUCTION

Ameloblastoma is a benign, slow growing odontogenic tumor of epithelial origin. It exhibits an invasive and aggressive behavior showing unlimited growth invading the surrounding cancellous bone beyond the tumor margin, if left untreated1,3. Recommended treatment to avoid massive destruction and recurrence is wide range radical resection extending 1-2cm from the tumor margin. It constitutes 11% of all odontogenic neoplasms.

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Most cases of ameloblastomas are observed in patients between 30 to 40 years of age1,2. World Health Organization in 2005 classiﬁed ameloblastoma on basis of anatomical location into 1) Multicystic/Conventional, 2) Peripheral/Extraosseous, 3) Unicystic types2,3. Multicystic is the most common type, exhibiting 91% of all cases. Histologically it is further subdivided into follicular, plexiform, acanthomatous, granular, basal cell and desmopo. Matrix Metalloproteinases (MMPs) belong to a family of structurally related zinc-dependent endopeptidases. They are collectively capable of degrading the basement membrane and nearly all other structural constituents of the Extracellular matrix (ECM) that appears to be critical in tumor cell invasion and metastasis4,6. It can control the tumor microenvironment by virtue of processing substrates, including growth factors and their receptors, chemokines, cell adhesion molecules, cytokines, angiogenic factors and apoptotic ligands7,8. The MMPs are formed as inactive precursors holding a propeptide and a secretory signal sequence. Proteolytic cleavage of this propeptide is essential for MMP activation. Carrying the label of enzyme, MMP-9 is encoded by MMP-9 gene in human9. It breaks down the type IV
collagen, a major component of the basement membrane in human tissues. This collagen allows the tumor cells to spread from the site of the primary tumor, resulting in invasion and metastasis\(^9\,10\).

The current study is designed to determine the immunohistochemical expression of Matrix Metalloproteinase-9 in histological subtypes of ameloblastoma for predicting the aggressiveness and behavior of this tumor in our population. Previous studies reveal that this marker directly degrades extracellular matrix(ECM) proteins and accelerates tissue.

The rationale of this study is the prevalence of lack of consensus on the most appropriate treatment modality for ameloblastomas. This indicates the absence of evidence based immunohistochemical studies on the diagnosis and management of ameloblastomas. The proposed study was able to measure the aggressiveness, behavior and resulting deformities of this epithelial odontogenic tumor, the outcome of the study may be used in improving and customizing the management of the tumor.

**MATERIALS AND METHODS**

In this descriptive study thirty(60) paraffin embedded blocks of freshly diagnosed ameloblastomas at AFIP, Rawalpindi were collected along with their demographic data and clinical/ radiographical information. After confirmation of diagnosis, classification according to the World Health Organization (WHO)\(^2\,3\) and histopathological subtyping was done on freshly prepared slides. MMP-9 was applied on the tissue according to standard protocol.

Necrosed, scarce and poorly oriented tissues were excluded. The intensity of the stain was measured using criteria described in Immunohistochemical Staining and Scoring section. Final results were analyzed. Immunoreactivity was evaluated and its association with histopathological subtypes was carried out. Immunoreactivity of MMP-9 was evaluated on the criteria described by Alves Pereira\(^4\) using a semi-quantitative analysis of immune stained cells using the following scores: 0 (without any reactivity in parenchymal component), 1 (<10% of positive cells), and 2 (>10% of positive cells). The cellular location of MMP-9 was determined in cytoplasm while for E-Cadherin, it was determined in cell membrane and cytoplasm.

Cases showing positive expression were labeled normal while those exhibiting negative and reduced patterns were considered as altered, for statistical analysis. Association between different histological subtypes and MMP-9 was evaluated by Chi-square test. P value value \(\geq 0.05\) was taken as significant. SPSS version 20.0 was used to inspect the data collected on specifically designed proforma. Parameters like age, gender, site and histological subtypes were narrated by descriptive statistics.

**RESULTS**

In the present study clinicopathologically out of 60 patients, 32 were male and 28 were female. The mean age ranges from 34.63 +/- 12.6 years. Most ameloblastomas were arising from right side of the jaw involving 34 cases (56.6%) while the left side was involved in 26 cases (43.3%). The frequency of the site involvement was recorded as 25 cases(83%) for mandible while maxilla was involved in 5 cases (17%). The most common histological type was follicular ameloblastoma 38 cases (63%), followed by plexiform 14 cases (24%) and 8 (13%) were of acanthomatous.

<table>
<thead>
<tr>
<th>Table No.1: MMP-9 Expression in Different Subtypes of Ameloblastoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histological Sub types of Ameloblastoma</strong></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>1 Acanthomatous Ameloblastoma</td>
</tr>
<tr>
<td>2 PlexiformAmeloblastoma</td>
</tr>
<tr>
<td>3 Follicular Ameloblastoma</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

\(P=0.0038\) (significant)

Immunostain reactivity was assessed by determination of percentage of positive stain cells under 40 x Objective Power with light microscope. The MMP-9 immuno reactivity was observed in a diffused pattern both in parenchymal and stromal cells, only parenchymal cells were observed. MMP-9 reactivity in these cells was found in the cytoplasm of stellate reticulum like angular cells and ameloblastic like columnus cells. Out of 60 cases of ameloblastoma, 38 cases were positively stained while 22 cases appeared negative. Amongst the positively stained, 22 cases scored 1 (36.7%) while 16 cases scored 2 (26.7%). Expression of MMP-9 was found variable in different subtypes of ameloblastoma (table-2). According to statistical analysis criteria proposed for MMP-9, amongst 8 cases of acanthomatous, 6 cases scored 2 (75%) as shown in fig-1 and only 2 case showed score 1 (25%).
Figure No.1: Acanthomatous ameloblastoma MMP-9 (100x magnification) (Showing strong positive expression in the squamous metaplasia area)

Figure No.2: Plexiform ameloblastoma MMP-9 (400x magnification) (Showing strong positive expression in stellate reticulum like cells and columnar cytoplasm)

Figure 3: Follicular ameloblastoma MMP-9 stain (400x magnification) (Showing mild positive expression in columnar cells cytoplasm)

The plexiform was diagnosed in 14 cases out of which 2 case showed score 0 (14.28%), 4 cases scored 1 (28.5%) and 8 cases appeared with score 2 (57%) with MMP-9 immunostain as shown in fig-2. The follicular ameloblastomas was diagnosed in maximum cases that is 38 in all out of which 20 cases appeared with score 0 (52%), 16 cases exhibited score 1 (42%) as shown in fig-3 and 2 case showed score 2 (5.2%) with MMP-9 immunostain.

DISCUSSION

Ameloblastomas are one of the benign epithelial odontogenic tumors arising of jaw bones. More commonly seen in mandible than in maxilla, these have the tendency to appear in the posterior part of the mandible. Clinically, ameloblastomas are divided into many subtypes which are multicystic, unicystic, peripheral ameloblastomas, malignant ameloblastomas and ameloblastic carcinoma represent unlike clinical behavior and prognosis. MMP-9 also called as gelatinase B, a class of enzyme that belongs to zinc-metalloproteinases family and are proficient degrading basement membrane and nearly entire the structural constituents of ECM. Therefore they are a subject of attention in research field regarding tumor invasion and metastasis. MMP-9 is thought to be found in activated and greater amount in and around the malignant tissue as compared to the benign or normal tissue with maximum expression found in areas of active invasion at the tumor stoma interface. Researches in different parts of world have provided evidences of intrication of MMP-9 involved in tumor cell invasion and bone metastasis suggested MMP-9 involvement in angiogenesis and tumor growth. According to Stankovic et al. (2010), there was a significant positive association between the tumor size in relation to breast cancer and MMP-9 expression. Jordan et al. (2004) correlated the expression of aggressiveness MMP-9 with head and neck tumors. Osteodestructive pathologies are also proved by MMP-9 as it plays a vital role in bone resorption.

Several studies conducted to analyze expression of MMP-9 on ameloblastoma. Kumamoto et al. (2003) has shown correlation between MMP-9 expression and ameloblastoma tumor growth. Pinheiro et al. (2004) proved role of MMP-9 in tumor cell proliferation through the release of mitogens. Qian and Huang (2010) suggested correlation between MMP-9 with osteoclastogenesis caused by ameloblastoma. Anne et al. (2014) and Florescu et al. (2012) published detailed studies showing correlation between different histological subtypes of ameloblastoma with their aggressiveness and metastatic potentials.

Our study detected MMP-9 expression in 19 cases (63.3%) out of 30 cases while 11 cases (36.6%) exhibited negative expression. Furthermore, our study reveal presence of MMP-9 in both stromal neoplastic and epithelial compartments of the solid ameloblastoma. Neoplastic epithelium signifies presence of MMP-9 reactivity in both stellate-reticulum like cells and peripheral columnar cells. However, at level of squamous metaplasia areas peak expression...
was noticed. Overall small rate and intensity of the MMP-9 positive neoplastic cells in the solid ameloblastomas were seen. This reactivity was detected far more prominent in stromal compartment, being highest expression registered around islands from the invasion front, especially in those cases which extended into the surrounding tissues.

This indicates harmonious result of Florescu et al. (2012)\(^2\) that found 76.5\% ameloblastoma with positive MMP-9 immunoreaction. Henriques et al. (2011)\(^2\) also showed 95\% positivity in ameloblastoma with MMP-9. However, the research study of Anne et al. (2014)\(^3\) showed all specimen of ameloblastoma showing positive immunoreaction to MMP-9.

Our research study of MMP-9 analysis proved score 1(36.6\%) in majority of cases indicating mild positivity, followed by score 2 (26.7\%) showing strong positivity. Yoon et al. (2005)\(^1\) also showed that ameloblastoma has mild to strong intensity of MMP-9 expression. The study outcome of Florescu et al. (2012)\(^2\) proved majority cases of ameloblastoma with score 1 (47\%), followed by the cases with score 2 (29.5\%). Thus detection of constant expression in all specimens may lead to a presumption that MMP-9 plays an indispensable role in development and further progression of ameloblastoma and therefore, can be associated with bone resorption caused by this tumor as well.

Amongst the three variants in our study, lowest reactivity was found in follicular ameloblastoma had the, with score 2 in only 1 cases of follicular type. Highest reactivity in this study was noticed in acanthomatous type. Out of 4 cases, 3 cases (75\%) showed score 2 with highest expression at the area of squamous metaplasia followed by plexiform type in which 4 cases (57\%) out of 7 cases had score 2. Florescu et al. (2012)\(^2\) observed Acanthomatous type with highest reactivity of MMP-9 at level of squamous metaplasia whereas Anne et al. (2014)\(^3\) noted plexiform with high immune score than follicular type. Maxillary ameloblastomasbeing thought as more aggressive and at times life threatening\(^15,16\) as compared to mandibular ones. They also show high recurrence rate as compared to mandibular ameloblastoma\(^1,11\). Our study included 5 cases in maxilla and 25 cases in mandible. While evaluating the MMP-9 expression it was noticed that tumors in maxilla showed more positive MMP9K9 expression as compared to mandibular ameloblastomas. In case of mandible only 7cases were strong positive (28\%) while in maxilla 3 out of 5 cases were strong positive (60\%). Therefore this may indicate aggressive behavior of maxillary ameloblastomas requiring need of more extensive surgery a and long term follow up.

In summary MMP-9 expression was assessed in three different histological subtypes of ameloblastoma i.e. follicular ameloblastoma, plexiform ameloblastoma and acanthomatous ameloblastoma. A varied immune reactivity of MMP-9 protein was observed in these subtypes displaying negative, mild positive and strong positive expressions. Higher MMP-9 expression is evaluated in Acanthomatous and plexiform type than follicular type. Therefore more energetic expression of MMP-9 related to Acanthomatous and plexiform type as well as maxillary ameloblastoma suggests that this protein may participate in proliferation of cell, along with explanation of bone resorption with prognosis marked as underprivileged and greater invasion potential.

Statistical analysis also highlighted significant difference between MMP-9 scores of immune reactivity and the three histological subtypes (p<0.05).

CONCLUSION

Expression of MMP-9 by ameloblastoma cells with subtypes variation. Higher MMP-9 expression in acanthomatous and plexiform ameloblastoma than follicular types, thus being more invasive than follicular ameloblastoma. Hence it may be used in future as a potential marker to serve as an indicator and utilized in monitoring degree of local aggressiveness of ameloblastoma.

REFERENCES


Author’s Contribution:

Concept & Design of Study: Farah Farhan
Drafting: Maria Ilyas, Misbah Ali
Data Analysis: Zainab Akbar, Batool Zahra
Revisiting Critically: Farah Farhan, Maria Ilyas
Final Approval of version: Farah Farhan

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


Outcome of Open Fractures of Tibia Treated with Interlocking & Intermedullary Nail in Terms of Infection and Union

Umair Ahmed¹, Mudassar Hassan², Ubaid Ullah Khan³ and Zubair Khalid¹

ABSTRACT

Objective: To find out the outcome of Gustilo Anderson Type I,II,III, A open fractures of tibia treated with intramedullary nail.

Study Design: A case series study

Place and Duration of the Study: This study was conducted at the Department of Orthopaedic Surgery, Ghurki Trust Teaching Hospital, Lahore from January 2019 to December 2019.

Materials and Methods: This case series study was done evaluating 60 patients presenting to us with Gustilo-Anderson I, II and III A open tibial fractures (OTFs). All patients were aged 18-70 years and had open diaphyseal tibial fractures. All included patients had a minimum follow up period of 6 months. All patients were managed adopting pre-op antibiotics, prompt debridement, fixation and primary closure. Demographic data of all cases along with mechanism of injury, time of fixation, flap coverage, rate of union and infection rates were noted.

Results: Overall, mean age was noted to be 37.17±13.5 years. Majority of the patients, 55 (91.7%) were male. Left side was turned to be involved in majority of the cases, 32 (53.3%). Road traffic accidents (RTA) were found to be commonest mechanism of injury. Overall, mean time to union was noted to be 35.8±8.17 weeks. Union was observed in 46 (76.7%). Comparatively, older age and smoking were also found to be significantly associated with delayed union (p<0.05). Infections were recorded among 14 (23.3%) cases. Infection was found to be significantly more common among older age and smokers (p<0.05).

Conclusion: Rates of delayed union and infections are high among Gustilo Anderson Type IIIA open tibial fracture cases treated with intramedullary nailing. Comparatively younger age and no history of smoking were found to have significant relation with union and no infection post-surgery.

Key Words: Open tibial fractures, intramedullary nailing, union, infection.


INTRODUCTION

Tibia is known to be the commonest long bone involved in fractures among humans. Treating open tibial fractures (OTFs) is not easy and controversies surround views about best approach to treatment. “Gustilo-Anderson” OTF injuries require debridement, appropriate fixation. Tibial fractures commonly occur due to high-velocity injuries, like falling from height or crush trauma injuries.

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Accepted: August, 2020
Printed: December, 2020
MATERIALS AND METHODS

This case series study was done evaluating 60 patients presenting to us with Gustilo-Anderson I, II, IIIAOTFs during January 2019 to December 2019 at The Department of Orthopaedic Surgery, Ghurki Trust Teaching Hospital, Lahore. All patients were aged 18-70 years and had open diaphyseal tibial fractures. All included patients had a minimum follow up period of 6 months. Patients who were skeletally immature or had tibial fractures other than Gustilo-Anderson III, IIA were not enrolled. All patients with preexisting external fixator that got changed to an intramedullary nail were also excluded. All cases who were referred from other settings were also not enrolled in this study as they were suspected to have delayed presentations. The study was approved by Institutional Ethical Committee. Written consent was sought from all study participants. All patients were managed adopting prompt debridement, fixation and primary closure as feasible. Demographic data of all cases along with mechanism of injury, time of fixation, union and infection rates were noted. Union was confirmed with radiographic evidence of callus bridging at least 3 cortices. Evaluation of radiological union was done by an FCPS orthopedic surgeon having at least 3 year post-fellowship experience. Details about infections, existence of microbes along with bacterial cultures were recorded. Deep infection as labeled as infection needing surgical debridement with positive tissue microbes along with bacterial cultures were recorded. For data entry and analysis, SPSS version 26.0 was employed. Age was presented as mean and standard deviation while qualitative data like gender, sides involved, mechanism of injury, presence of infection, union/non-union, and factors related to delayed union were shown as frequency and percentages. Chi square test was used to compare qualitative variables while quantitative data (age) was compared using independent sample t-test. P value below 0.05 was taken as significant.

RESULTS

At total of 60 patients were included. All cases were given intravenous antibiotics and managed surgically adopting thorough wound debridement and temporary fracture stabilization at the initial surgery. Overall, mean age was noted to be 37.17±13.5 years. Majority of the patients, 55 (91.7%) were male. Left side was turned to be involved in majority of the cases, 32 (53.3%). Road-traffic accidents (RTA) were found to be commonest mechanism of injury. Table number 1 shows characteristics of study participants. Table number 2 is showing significant relationship of Gustilo-Anderson types open fractures with respect to union and revision or delayed union (p<0.001). Type-III A open fractures were noticed to have significant relationship with revision or delayed-union.

### Table No.1: Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>55 (91.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (8.3%)</td>
</tr>
<tr>
<td>Side Involved</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>32 (53.3%)</td>
</tr>
<tr>
<td>Right</td>
<td>28 (46.7%)</td>
</tr>
<tr>
<td>Mechanism of Injury</td>
<td></td>
</tr>
<tr>
<td>Road-Traffic Accident</td>
<td>40 (66.7%)</td>
</tr>
<tr>
<td>Industrial Reasons</td>
<td>14 (23.3%)</td>
</tr>
<tr>
<td>Assault</td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Sports</td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Falling from Height</td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Gustilo-Anderson Types</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>30 (50.0%)</td>
</tr>
<tr>
<td>II</td>
<td>20 (33.3%)</td>
</tr>
<tr>
<td>III</td>
<td>10 (16.7%)</td>
</tr>
</tbody>
</table>

### Table No.2: Distribution of Gustilo-Anderson Types Open Fractures with respect to Union or Revision / Delayed Union

<table>
<thead>
<tr>
<th>Gustilo-Anderson Types</th>
<th>Union (n=46)</th>
<th>Revision or Delayed Union (n=14)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (n=30)</td>
<td>28 (60.9%)</td>
<td>2 (14.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>II (n=20)</td>
<td>16 (34.8%)</td>
<td>4 (28.6%)</td>
<td></td>
</tr>
<tr>
<td>III-A (n=10)</td>
<td>2 (4.3%)</td>
<td>8 (57.1%)</td>
<td></td>
</tr>
</tbody>
</table>

### Table No.3: Factors Linked with Revision or Delayed Union

<table>
<thead>
<tr>
<th>Factors</th>
<th>Revision or Delayed Union (n=14)</th>
<th>Union (n=46)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in Years (Mean±SD)</td>
<td>39.51±12.82</td>
<td>30.81±14.3</td>
<td>0.046</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12 (85.7%)</td>
<td>43 (93.5%)</td>
<td>0.357</td>
</tr>
<tr>
<td>Female</td>
<td>2 (14.3%)</td>
<td>3 (6.5%)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6 (42.9%)</td>
<td>8 (17.4%)</td>
<td>0.048</td>
</tr>
<tr>
<td>No</td>
<td>8 (57.1%)</td>
<td>38 (82.6%)</td>
<td></td>
</tr>
<tr>
<td>Time from injury to 1st Debridement (hours)</td>
<td>5 (35.7%)</td>
<td>15 (26.1%)</td>
<td>0.829</td>
</tr>
</tbody>
</table>

Overall, mean time to union was noted to be 35.8±8.17 weeks. Union was observed in 46 (76.7%) cases. Table number 3 is showing factors linked to delayed union or revision. Comparatively, older age was significantly linked to delayed union (p=0.0460). Smoking was also
found to be significantly associated with delayed union (42.9% vs. 17.4%, p=0.0485). Early surgical debridement was not noted to have significant effect on union. Infections were recorded among 14 (23.3%) cases. Out of these 14 cases, 9 were treated with antibiotics and wound wash while remaining 5 had removal of implant and ilizarov applied.

**DISCUSSION**

Treatment of OTFs is considered tricky and satisfactory outcomes depend upon multiple factors. Lots of work has been done describing various forms of treatment for OTFs but best treatment option is yet to be labeled. Intramedullary nailing is shown to have good success for the treatment of OTFs. This study is one of the biggest open tibial GustiloAnderson fractures series documented in the recent years in Pakistan. In the present study, 91.7% of the cases were male. Data from other parts of the world have reported male predominance ranging from 66-93.2% cases of OTFs.11,12 Data from Malaysia revealed 84.6% of OTF cases to be male.13 In a country like Pakistan where males are more exposed to outdoor and daily living activities, a clear predominance of male cases forming majority of OTF cases is not surprising.

RTAs were the commonest cause of OTFs in the present study, comparing 66.7% of total cases. Local study conducted by Haq SN et al also revealed that 78.5% cases of open diaphysal fractures of tibia were caused due to RTAs.14 Data from Nigeria revealed 71% cases due to RTAs while researchers from developed countries also noted RTAs to cause 58% of OTFs.11,15 In this study, 23.3% had non-union or delayed union and needed further treatment. A study done by Singh A et al reported that 41.1% of the treated GustiloAnderson OTF cases required further procedures following delayed union.12 Singh A et al revealed that intramedullary nailing in the treatment of OTFs is associated with high rates of non-union or delayed union and require revision and further treatment. In the present study, Infections were recorded among 23.3% cases. The infection rates seen among OTFs range between 9-52%.12,16-18 Appropriate debridement along with young age and no prior history of smoking can certainly aid minimizing chances of infection. Infection rate is considered to be directly linked to severity of injuries as described by “Gustilo-Anderson Classification” and host comorbidities. Superficial infections commonly resolve and need minimal interventions while deep infections require multiple additional surgeries and form major chuck of morbidities. In the present work, out of a total of 14 patients who experienced infections, 9 were treated with antibiotics and wound wash while remaining 5 had removal of implant and ilizarov applied.

In the present study, smoking was linked to delayed union and infection. Similar findings have been reported by Singh A et al where history of smoking was significantly associated with non-union and presence of infections following treatment of OTFs.12 Schmitz MA et al also reported prolonged time of healing among smokers with OTFs while Patel RA et al in their systemic review evaluating “effect of smoking on bone healing” revealed very similar findings.19,20 Our study had some limitations as well. Being a single center study, the findings cannot be generalized. We also did not have any comparator group so cannot conclude intramedullary nailing as the best possible choice handling Gustilo Anderson OTFs. We were also unable to record functional outcome, patient’s preference and cost issues in the present research.

**CONCLUSION**

Rates of delayed union and infections are high among GustiloAnderson TYPE IIIA open tibial fracture cases treated with intramedullary nailing. Comparatively younger age and no history of smoking were found to have significant relation with union and no infection post-surgery.

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**Author’s Contribution:**

**Concept & Design of Study:** Umair Ahmed

**Drafting:** Mudassar Hassan

**Data Analysis:** Zubair Khalid

**Revisiting Critically:** Umair Ahmed, Mudassar Hassan

**Final Approval of version:** Umair Ahmed

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

**REFERENCES**


Analysis of Various Histopathological Lesions in Routine Cholecystectomy Specimens
Abeer¹, Farah Kalsoom², Kanwal Babar³, Rozina Jaffar¹, Ghazia Fatima⁴ and Hamna Salahuddin⁵

ABSTRACT

Objective: The purpose of this study is to see the spectrum of diverse changes in cholecystectomy specimens. Study Design: Descriptive, Cross sectional study. Place and Duration of Study: This study was conducted at the Department of Pathology, tertiary care hospital, Lahore from January 2018 to January 2020 (after Institutional Review Board approval). Material and Methods: Total 183 gall bladder specimens of all ages and both sexes were taken. After receiving specimens in formalin grossing was done according to standard protocols. Sections from neck, body and fundus were taken in grossly unremarkable specimens and subjected for routine histopathological processing. The morphological changes in the gallbladders were examined. Data was entered and analyzed statistically. Results: Total of 183 patients were studied after cholecystectomy procedure. Majority of the cases were female i.e 136 (74.31%) and 47 (25.68%) were males. 102 number of patients were more than 40 years (55.73 %) and 81 were less than 40 years (44.26%). Conclusion: The study provides an insight into the variety of morphological features on microscopy ranging from non-neoplastic to neoplastic lesions. Detection of malignancy in clinically benign gallbladder is much lower but early diagnosis in initial stage tumor is the rationale to examine all cholecystectomy specimens. Key Words: Cholecystectomy, Cholecystitis, Cholelithiasis, Gall bladder.


INTRODUCTION

Histopathological examination is the gold standard for the absolute diagnosis in majority of the surgically removed specimens. This helps not only in making diagnosis but also take part in taking important decisions regarding patient’s management¹. Gall bladder is one of the most frequent surgically resected organ of the body but in order to decrease the burden on pathologist its routine histopathological examination especially of clinically and grossly benign gall bladders is still controversial.

Discarding of specimens without satisfactory histopathological assessment would be a disrespect in this era of evidence-based medicine. Despite of this, in majority of patient’s routine gall bladder histopathology is less likely contributing in clinical management². Diseases of gall bladder is one of the common health problems that causes morbidity and mortality worldwide³. Gall stones also called cholelithiasis are of two types, namely pigment stone and cholesterol stone. They are formed when secretions of gall bladder get solid due to metabolic or hormonal changes and they can accumulate in any part of biliary tree. Cholecystitis with cholelithiasis is the common medical emergency that requires surgical intervention. Simple cholecystectomy is the common procedure for majority of gall bladder diseases. Numerous risk factors are responsible for developing gall bladder diseases, precisely; race, age, sex, pregnancy, oral contraceptives, obesity, dietary habits, disturbance in cholesterol and glucose metabolism and hemolytic anemias. Multiple complications are associated with gall stone disease like cholangitis, pancreatitis and rarely squamous cell carcinoma⁴. In Pakistan the incidence of gall bladder disease followed by cholecystectomy is rising mainly in females due to hormonal irregularities⁵. Diseases of gall bladder with or without gall stone is associated with various morphological features ranging from benign conditions
which include acute & chronic cholecystitis, cholelithiasis, pyloric metaplasia, hyperplasia, xanthogranulomatous inflammation to advanced stage malignant tumors\(^6\). Although the frequency of carcinoma in gall bladder is much lower but overall prognosis is very poor\(^7\). In early gall bladder cancer, patient remains asymptomatic and no sign of malignancy is evident during or before surgery. Most of the cases are diagnosed at advanced stage that are detected incidentally on microscopy\(^7\). Malignancy in clinically benign gallbladder is much lower but early diagnosis in initial stage tumor is the rationale to examine all cholecystectomy specimens\(^7\). The rationale behind conducting this research is to observe the spectrum of histopathological findings in routinely performed cholecystectomy specimens to quantify various abnormalities in gallbladder specimens.

**MATERIALS AND METHODS**

This was a retrospective study over a period of 2 years from January 2018 to January 2020. The present study includes all surgically removed gall bladder specimens received in Rahbar medical and dental college (RMDCC) from Punjab Rangers Teaching Hospital (PRTH). Informed consent was taken from all patients. Clinical and demographic data were noted from case files. All gall bladder specimens removed surgically (open & laparoscopic cholecystectomy) from both genders of all age groups were included in this study.

**Inclusion Criteria:** All gall bladder specimens removed surgically (open & laparoscopic cholecystectomy) from both genders of all age groups were included.

**Exclusion Criteria:** 1. Specimen with incomplete bio data and clinical history

2. Specimen sent without formalin/ improper preservation.

3. All the gall bladder specimens received from other laboratory were excluded from this study.

Gall bladder specimens received in 10% formalin as adequate fixation is necessary for proper diagnosis of lesions especially epithelial changes of gall bladder. Specimens received with attached patients bio-data, laboratory number and brief clinical history. Pathological examination was performed in pathology department of Rahbar medical and dental college. Grossing of the specimens were done with macroscopic details according to standard protocol. Sections from neck, body and fundus were taken in grossly unremarkable specimens. Lymph nodes that are grossly present in and around neck of gall bladder were also passed for processing. Additional sections were taken in grossly suspicious gall bladders. The sections were then subjected for routine histopathological processing. After processing next step of embedding was done in liquid paraffin. Thin sections through microtome were taken and routine hematoxylin and eosin staining was done. The sections then examined microscopically by classified histopathologist.

All data was recorded using Microsoft Excel 2010 and analyzed in SPSS 20 version software.

**RESULTS**

It was a retrospective analysis of the histomorphology of 183 cases of cholecystectomy procedure. The age of the patients ranged from 22 years to 54 years. Most of the patients were in fourth decade and sex ratio of male to female is 3:1 (Table 1).

Table 2 describes the histopathological findings seen microscopically on gall bladder specimens.

**Table No.1: Gender distribution of patients according to age (n=183).**

<table>
<thead>
<tr>
<th>Age/ Gender</th>
<th>Female (%age)</th>
<th>Male (%age)</th>
<th>Total (%age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 40 years</td>
<td>75 (54.64)</td>
<td>25 (18.24)</td>
<td>100 (54.64)</td>
</tr>
<tr>
<td>More than 40 years</td>
<td>61 (25.68)</td>
<td>22 (9.99)</td>
<td>83 (45.35)</td>
</tr>
<tr>
<td>Total</td>
<td>136 (74.31)</td>
<td>47 (25.68)</td>
<td>183 (99.99)</td>
</tr>
</tbody>
</table>

**Table No.2: The histopathological findings examined in gall bladder specimens**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Diagnosis</th>
<th>Frequency (%age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chronic cholecystitis with cholelithiasis</td>
<td>123 (67.21)</td>
</tr>
<tr>
<td>2</td>
<td>Chronic acalculous cholecystitis</td>
<td>41 (22.40)</td>
</tr>
<tr>
<td>3</td>
<td>Acute on chronic cholecystitis</td>
<td>11 (6.01)</td>
</tr>
<tr>
<td>4</td>
<td>Chronic cholecystitis with cholestrolosis</td>
<td>3 (1.63)</td>
</tr>
<tr>
<td>5</td>
<td>Acute gangrenous cholecystitis</td>
<td>2 (1.09)</td>
</tr>
<tr>
<td>6</td>
<td>Xanthogranulomatous cholecystitis</td>
<td>1 (0.54)</td>
</tr>
<tr>
<td>7</td>
<td>Chronic cholecystitis with polypoidal gastric metaplasia</td>
<td>1 (0.54)</td>
</tr>
<tr>
<td>8</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>1 (0.54)</td>
</tr>
</tbody>
</table>

In our study total 183 patients were taken after cholecystectomy procedure. Majority 74.31 % of patients were females 74.31 % (136/183) and 25.68% (47/183) were males. Patients less than 40 years of age affected more, shown in table 1.

In our study majority of patient’s histopathological report were consistent with chronic cholecystitis with cholelithiasis 123/183 (67.21%) and chronic cholecystitis without cholelithiasis 41/183 (22.40%) as shown in table 2. Carcinoma of gall bladder was found in one patient only 1/183 (0.54%).
DISCUSSION

The most common histopathological finding in our study was histopathological evaluation of specimens is the gold standard way of diagnosing most of the diseases. Gallstone disease is the most common cause that require surgical intervention worldwide\(^4\). In Pakistan, gall bladder diseases in which most common is the cholelithiasis is reported 10.2\(^{11}\). Similar to the study done in India, our study shows females (71.31\%) affected more than males (25.68\%) and truly reflects the factual pneumonic used for risk factors i.e., “four fs” female, forty, fertile and fatty\(^{12}\). The age range in our study was found to be in 21 to 73 years with mean age was 57 years. Most of the patients were more than 40 years of age consistent with the age group study done in Iran\(^5\). Out of 183 cases, 182 were non-neoplastic and chronic cholecystitis with cholelithiasis 67.21\% similar to study done by Vikash et al (78.42\%) (14). The second most common finding seen in our study was chronic acalculous cholecystitis (22.40\%) followed by acute on chronic cholecystitis seen in 11 cases (6.01\%), chronic cholecystitis with cholelithiasis seen in 3 cases (1.63\%), acute gangrenous cholecystitis in 2 cases (1.09\%), xanthogranulomatous cholecystitis in 1 case (0.54\%), chronic cholecystitis with polypoidal gastric metaplasia in 1 case (0.54\%) and poorly differentiated carcinoma in 1 patient (0.54\%). The incidence of gall bladder carcinoma was found to be very low in our study (0.54\%) similar to study done in India (0.5\%) (15) But dissimilar to the incidence seen in the study done by YongchelAhn et al in Korea (1.6\%) (16). Factors responsible for different morphological features could vary according to geographical, ethnic and dietary habits of population. Aging and obesity is one of the major factor of gallstone disease in western population in which the cholesterol stones are present in more than 70\% people while mixed stones are more common in Asian population\(^7\),\(^8\). Although incidence of gall bladder cancer is found to be very low in our study and according to Royal College of pathologists (RCPath) guidelines macroscopically normal gall bladder needs not to be examined microscopically in routine. The selective approach for histopathological examination can reduce the burden on medical profession and ultimately on pathologist without compromising patient health but the final conclusion on examining the routine gall bladder specimens is still debatable\(^{16,19}\). The data collected is an experience from a single tertiary care hospital located in Lahore. The statistics might not be an exact representation of the entire region.

CONCLUSION

Cholecystectomy is a routine procedure done in every hospital. Cholelithiasis is the main reason for this routine procedure. The microscopy shows variety of morphological features ranging benign to malignant lesions. The major histopathological feature found in this study was chronic cholecystitis with cholelithiasis. Detection of malignancy in clinically benign gallbladder is much lower but early diagnosis in initial stage tumor is the rationale to examine all cholecystectomy specimens.

The histopathological spectrum of gallbladder is extremely variable. Incidental diagnosis of carcinoma gall bladder is not rare; if the protocol of routine histopathology of all gallbladder specimens is not followed, subclinical malignancies would fail to be identified with disastrous results. We strongly recommend routine histopathology of all cholecystectomy specimens.

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Author’s Contribution:
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Drafting: Abeer, Farah Kalsoom, Kanwal Babar
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Revisiting Critically: Abeer, Farah Kalsoom
Final Approval of version: Abeer

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

REFERENCES

Dashboard Utilization for Improvement in Key Performance Indicators (KPI) in Clinical Laboratory of Tertiary Care Hospital, Lahore Pakistan

Nusrat Alavi, Aneela Khawaja, Malika Asif, Asma Ejaz, Abeer and Rozina Jaffar

ABSTRACT

Objective: To identify dashboard utilization for improvement in Key Performance Indicators in clinical laboratory of tertiary care hospital, Lahore.

Study Design: Descriptive observational study.

Place and Duration of Study: This study was conducted at the Pathology Laboratory of Tertiary Care setting for Four months from May to August 2020.

Materials and Methods: All the samples received were entered in Laboratory Information System, identified and analyzed for reasons documented for delayed turn-around time, total critical alert reported and total no. of rejected samples calculated.

Results: During 4 months of study period, 61696 samples were received, 51265 (83.09%) samples were included in the study, and 397 (0.77%) identified for documented reasons regarding key performance indicators. Out of these 397 identified samples, delayed Turnaround Time was noted in 146 (36.77), samples, total critical alerts were reported in 225 (56.6%) and 26 (6.54%) samples were analyzed as rejected. On an average, the frequency percentage of the samples analyzed was equal, but overall improvement was seen in July and August’ 2020 as compared to May and June 2020, after the introduction of dashboard laboratory information system on 1st April 2020.

Conclusion: Quantitative analysis of some of the key performance indicators provided a layout of recently developed laboratory information system. The graph of KPI monitoring can be improved significantly by following standard operating procedures, using laboratory information system dashboard, coordination between the lab workers, proper training of technicians and phlebotomists. This can ensure compliance of quality lab services for patient care and safety.

Key Words: dash board, Key Performance Indicators (KPI), outcome indicator, patient safety, turnaround time (TAT)


INTRODUCTION

A dashboard is a visual display of the most vital information needed to achieve one or more objectives, combined and organized on a single screen so that information can be monitored at a glance1. Design of dashboard begins with defining objectives and determining key performance indicators to monitor the success of dashboards2.

Laboratory Key Performance Indicators (KPIs) measure the functioning of laboratory activities in terms of projects, processes, products or services. They are also used to track the performance of the inventory, devices, environment, data and results. Evidence of progress towards achieving a desired result indicate good KPIs. It evaluates what is intended to be measured to help inform better decision making and offers a comparison that gauges the degree of performance change over time. According to the available resources in any healthcare setting, it is unlikely to regulate all performance indicators altogether. For this purpose, critical and significant indicators are being focused on so to improve them step by step 3.

Static nature of performance reporting systems in healthcare sector has resulted in inconsistent, incomparable, time consuming, and presented reports that are not able to transparently reflect a clear picture that effectively support healthcare managers’ decision makings 4. Today, laboratory Information System (LIS) operates as...
a tool for facilitating and safety assurance of the most of the “total testing process” (TTS) which includes pre-analytical, analytical and post-analytical phases. Well-designed laboratory information systems through embedded intelligent dashboard will have potential to reduce laboratory errors and specimen rejection rates in pre-analytical phase, which includes ordering, specimen collecting, identifying and labeling, handling transporting and turnaround time. However, laboratory information system has limited capabilities for the management decisions. The turnaround time (TAT) steps in performing a laboratory test were outlined by Lundberg, who described the brain to brain TAT or “total testing cycle” as a series of nine steps: ordering, collection, identification, transportation, preparation, analysis, reporting, interpretation and action. The term “therapeutic TAT” is sometimes used to describe the interval between when a test is requested to the time a treatment decision is made.

Nearly 80% of hospital-attached clinical laboratories receive complaints about delayed TAT. Reporting in time is a crucial indicator of quality services along with accurate, precise and reliable reports, thus each clinical laboratory should identify affecting factors to eliminate them for the enhancement of quality services inventory.

In our setup at the beginning of the year we shifted from the conventional old reporting system to LIS (laboratory information system) and HMS (hospital management system) through a third-party vendor. The transition was not easy to adopt by the end users and customers. The system had predesigned domains and dashboards which were rigid and did not accommodate for customer demands. Shift from paper to paperless process required a lot of brainstorming, gap analysis and innovative solutions for monitoring the KPIs. We used PDCA (Plan, Do, Check, Act) cycle as a standard tool on monthly basis for four months duration, to identify where improvements are needed, to set priority for quality improvement and create a local dashboard for KPI monitoring. This study was conducted to identify the challenges in clinical laboratory regarding order and application management; and dashboard utilization for improvement in key performance indicators.

MATERIALS AND METHODS

This observational descriptive study was conducted at Pathology Laboratory of a tertiary care setting from 1st May till 31st August’ 2020. Requested tests with test requisition form (TRF) received and entered on database of laboratory information system (LIS). TAT of chemistry and hematology samples was calculated according to laboratory SOP of TAT, total critical alerts and total number of rejected samples were carefully screened according to laboratory SOP, and analyzed for any possible error. Reports issue and results entered on dash board software was analyzed for indicator mapping.

For outpatients, phlebotomy is generally performed by experienced staff using a vacutainer system. On the other hand; for inpatients it is done by paramedics. The blood specimens transported to the laboratory by the hospital personnel, were assessed by experienced staff and either accepted or rejected depending on the rejection criteria of the laboratory SOP. The rejection criteria of the laboratory are hemolyzed, clotted specimens, insufficient volume, mislabeled, inappropriate/or empty tube, and damaged/or not received specimens.

All data was collected and analyzed statistically by SPSS 20.0. TAT, total critical alerts and rejected specimens of hematology and biochemistry were presented as frequency and percentage.

RESULTS

The study was conducted from 1st May to 31st August 2020, and total samples received in 4 months along their request forms were 8248, 11689, 19059, and 20434 respectively. In May 7369 (89.34%), June 10911 (93.34%), July 15901 (83.43%), and 17094 (83.65%) samples in August were analyzed for KPI (Table 1). Frequency distribution in 4 months was identified in 397 (0.77%) samples, as given in table 2.

Table No.1: Frequency Distribution of Study Samples in Four Months

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Sample Detail</th>
<th>May (%)</th>
<th>June (%)</th>
<th>July (%)</th>
<th>August (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Total received</td>
<td>8248 (13.87)</td>
<td>11689 (19.66)</td>
<td>19059 (30.89)</td>
<td>20,434 (33.12)</td>
<td>61,696</td>
</tr>
<tr>
<td>2.</td>
<td>Selected for study</td>
<td>7369 (89.34)</td>
<td>10911 (93.34)</td>
<td>15901 (83.43%)</td>
<td>17094 (83.65%)</td>
<td>51,265</td>
</tr>
<tr>
<td>3.</td>
<td>Samples identified for KPI</td>
<td>110 (1.49)</td>
<td>92 (0.84)</td>
<td>90 (0.56)</td>
<td>105 (0.61)</td>
<td>397 (0.77)</td>
</tr>
</tbody>
</table>

Chi-square= 63.54 p-value=0.00001 (p<0.05, significant)

Table No.2: Frequency distribution of indicators in 4 months (n=397)

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Indicators</th>
<th>May &amp; June</th>
<th>July &amp; August</th>
<th>Total frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Turnaround time for analysis</td>
<td>75 (18.89)</td>
<td>71 (17.88)</td>
<td>146 (36.77)</td>
</tr>
<tr>
<td>2.</td>
<td>Total critical alert reported</td>
<td>115 (28.96)</td>
<td>110 (27.70)</td>
<td>225 (56.67)</td>
</tr>
<tr>
<td>3.</td>
<td>Total no. of rejected samples</td>
<td>12 (3.02)</td>
<td>14 (3.52)</td>
<td>26 (6.54)</td>
</tr>
<tr>
<td>Total</td>
<td>202 (50.88)</td>
<td>195 (49.11)</td>
<td>397 (99.98)</td>
<td></td>
</tr>
</tbody>
</table>

Chi-square= 0.25, p-value= 0.88 (p>0.05) not significant

a: 1) Payment for test in cash, 2) Test repetition, 3) Reagent related, 4) Equipment breakdown,
5) Reporting software held up.  
   b: 1) Total Bilirubin > 257 ummol/L, 2) Glucose < 2.2- >25 mmol/L, 3) Potassium <2.5-6.9 mmol/L, 4) Calcium <1.6-3.2 mmol/L, 5) Hemoglobin <7-27 g/dL, 6) Platelet count <30-10^10/μL, 7) WBC <1-3.5x10^9/μL.  
   c: 1) Hemolyzed, 2) Insufficient, 3) Clotted, 4) Mislabeled, 5) Not received, 6) Wrong sample  

**DISCUSSION**  
Laboratory works well when quality management systems have outcome indicators that relate to patient safety and medical management of patient. The most important issues about the management of clinical laboratories in the hospital are sample rejection, delayed TAT and non-communication of critical results  

The results of our study are consistent with other studies that also indicated inadequate samples, clotted, hemolyzed, wrong samples, and or delayed sample transport affecting the preanalytical phase of TAT  

The design of this study is the result of number of meetings that took place from 1st Jan till end of April 2020 between physician’s end users of LIS and lab director and IT team to select KPI and improve dashboard of LIS. From the list of 10 KPI, initially three were shortlisted namely Turn-around-time (TAT), Total critical alert reported, total rejected samples. The aim was to monitor the data with PDCA cycle as a quality tool. QA officer and pathologists made few suggestions and collaborated closely with nurses, doctors, receptionist and technologists. Customized screens for rapid ordering were put in LIS which enabled the ordering electronically, patient location tracking was updated, moreover Automate lookup of information on volume, container, and special precautions for handling specimens was made part of dashboard. Barcodes and barcode readers were introduced at each station, Interface of instrument to computer was done on priority and automatic printing of results in different locations of hospital was facilitated. Tracking of samples, transport in the main lab and elimination of preanalytical errors was emphasized through staff training and in service  

Shift from old system of reporting to new LIS was challenging. Manual records were sketchy and haphazard. IT team collaborated in putting the indicators in the Dashboard. Data of May June was collected and analyzed for nonconformity, due to the covid 19 crisis, a lot of lapse in data was found at end of April first PDCA quality tool was used to put in place laboratory workflow monitors to gauge process of improvement in KPIs. Number of problems were highlighted, training sessions were organized to familiarize staff with working of LIS, protocols were made to follow SOPs, and experienced staff was tasked with more complex work stations and lack of coordination in preanalytical phase was addressed  

Orientation of newly hired paramedics was carried out regarding patient sampling, shifting of sample to the main reception and expedition of urgent samples were fast tracked within the lab. Rejection rate of samples was closely monitored and root cause analysis was done periodically and necessary action was taken in real time by informing about nonconformity of sample. Requesting a new sample, using dash board to document the whole process. Various studies have documented, preanalytical prolonged TAT of outpatient and inpatient samples is around 70% of overall delay. Increased preanalytical TAT was primarily due to delayed transportation and rejection of samples to the laboratory  

The frequency percentage of the total samples identified for analyses was 0.77, showing significant p-value. On the other hand, a decreasing frequency was noticed in later months i.e. July and August 2020 (17.88%), as compared to May and June 2020 (18.89%) for the studied indicators, indicating the difference was not significant. It illustrates that second PDCA cycle upgraded the laboratory functioning by monitoring KPIs through dashboard utilization  

**CONCLUSION**  
Continuous monitoring the development and progress of designed dashboard is of great importance and is an ongoing quality improvement process. Analysis of the healthcare management system is a contribution to quality assurance with integration of more KPIs to improve hospital clinical laboratory performance. It is necessary that hospital laboratories must ensure conformity regarding standard operating procedures, the laboratory information system, the cooperation of healthcare staff and training of paramedics, to promote evidence-based research with social impact.  

**Acknowledgement:** The data collection was done by Bilal Ahmed, Medical Technologist, Pathology lab, at PRTH, Lahore.  

**Author’s Contribution:**  
Concept & Design of Study: Nusrat Alavi  
Drafting: Aneela Khawaja, Maliha Asif  
Data Analysis: Asma Ejaz, Abeer, Rozina Jaffar  
Revisiting Critically: Nusrat Alavi, Aneela Khawaja  
Final Approval of version: Nusrat Alavi  

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

14. Chandradasa DH, Dalpadadu KS. A project to improve process of quality assurance system at the laboratory of District General Hospital Kalutara using adapted Lang’s framework model for change. DOI: 10.29322/IJSRP.10.10.2020.p10610
Evaluation of Morphological Prognostic Factors and Survival Rate in Colorectal Cancer Patients
Kamran¹, Mohibullah Khan² and Ilyas²

ABSTRACT

Objective: To evaluate Morphological Prognostic Factors and Survival Rate in Colorectal Cancer Patients of the recent five years.

Study Design: Retrospective cohort study

Place and Duration of Study: This study was conducted at the in Peshawar Institute of Medical Sciences from June 2014 till August 2019.

Materials and Methods: We collect demographic data in the form of age, sex, body mass index, last date of contact, history of consuming betel nut along with the history of smoking to check the association of cancer with these factors. We include primary site, histological type, grade/differentiation, size of treatment, regional lymph nodes as a general characteristic of tumor.

Results: Factors like age greater than 65, high grade of pathological differentiation, distant metastasis were highly associated with a 5-year risk of death among the colorectal cancer patients. Conclusion: Perineural nerve invasion and distant metastasis are considered as important in early detection. Early detection of these parameters will surely increase the survival rate.

Conclusion: There are a lot of prognosis factors that may affect the survival rate among CCR patients. Some independent variables perineural nerve invasion, distant metastasis, age, pathological differentiation grade, obstruction, and regional lymph node metastasis are independent predictors that highly influence the ratio. But some like perineural nerve invasion and distant metastasis are considered as important in early detection. Early detection of these parameters will surely increase the survival rate.

Key Words: Colorectal Cancer, Betal Nut, Smoking, Histopathology


INTRODUCTION

All around the world colorectal cancer is one of the third-higher cancer types with 17.3% morbidity and an 8.3% mortality rate. Its ratio is quite high among males as compared to females¹. This disorder usually arises from glandular, epithelial cells of the large intestine. It emerges as a result of mutation inside the epithelial cells². The colon is responsible for reabsorbing water, minerals, and nutrients in the chyme. Death cells during the process come out in the form of feces but sometimes abnormal growth of colon cells cause complexities and turn out in form of cancer³.

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The development of tumors through the traditional pathway where APC and KRAS mutation arises on the left colon takes more than 5-20 years interval⁴. According to the top-down morphological model, APC mutation arises in the upper crypt compartment⁵. On the other hand, BRAF mutations and epigenomic instability (CIMP-high) occur lower crypt compartment in the right corner and triggers the growth of the tumor⁶. In 2007, the World cancer research fund found a significant association of colorectal cancer with obesity, lack of exercise, high consumption of meat, and alcohol⁷⁸. Age factor, hereditary mutations, inflammatory bowel disease, abdominal radiation, cystic fibrosis, cholecystectomy, androgen deprivation therapy, and some medications contribute to the emergence and development of the disease⁹. History of neoplasms, Lynch syndrome boosts the growth of colorectal cancer in 2%-4% cases¹⁰.

In early diagnosis, surgery is considered as the best treatment¹¹. In contrast in advanced cases where cancer has 25% metastasized at the time of diagnosis, neoadjuvant, cytotoxic therapies with the rapid evolution of drug resistance are a major source of treatment¹².
In Pakistan, less screening availability, costly treatment, and less awareness of malignancy cause severe complications and enhance the morbidity rate. The public set a general view that there is a little chance of recovery among cancer patients. This research aims to explore the morphological prognostic factors in colorectal cancer and analyze the survival ratio of the recent five years.

MATERIALS AND METHODS

This single-center retrospective study was conducted in the Cancer department of Peshawar institute of medical sciences, from the June 2014 till August 2019. This study was conducted to estimate the survival outcomes in the patients who were diagnosed with colorectal cancer. All the data was extracted from the patient's electrical records. For this study, we include patients who were diagnosed with the international classification of disease oncology, 3rd Edition (ICD-O-3) topographical codes of C18.0 (excluding C18.1), and morphology codes of 8000-8152, 8154-8231, 8243-8245, 8247-8248, 8250-8576, 8940-8950, and 8980-8981. Patients who were diagnosed with more than one type of cancer, metastasis to the brain, and less than one type of cancer, metastasis to the brain, and one type of cancer and one were excluded from the research.

We analyzed our data by categorizing its stages according to the American Joint Committee on Cancer (AJCC) criteria. Further, we add site-specific factors included CEA, circumferential resection margin (CRM), tumor regression grade, perineural nerve invasion, KRAS mutation, obstruction, and perforation. Survival rate was noted on the behalf of the last date of contact or death (in some cases).

For the statistical analysis, we used SPSS version 23.0 to apply a t-test for the independent group. P< 0.05 was set as significant and two-tail tests were applied for all variables.

RESULTS

We conducted this research from 2014 to 2019. A total of 869 patients was diagnosed in this period. Out of 869, 454 (52.24%) were male and the rest were from the female group. Mostly the patients were from the 57 to 75 years of age group with a median age of 64 years. A total of 63.75% of patients was diagnosed with colon cancer and one-third of them belong to stage III with a high percentage of adenocarcinoma (91.71%). Parameters like regional lymph node metastasis, distal organ metastasis, cancer stage, pathological differentiation, histopathologic type, tumor size, CRM, perineural nerve invasion, KRAS mutation, obstruction, and perforation in Table 2 and 3.

Regression model analysis depicts the values of death and describes the probability of survival for 3 to 5 years in Table 4.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Number of patients (%)</th>
</tr>
</thead>
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<tr>
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<td>Female</td>
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</tr>
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<td>Age</td>
<td>Median (range, y)</td>
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</tr>
<tr>
<td></td>
<td>Mean ± SD, y</td>
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<td></td>
<td>≥65 yr old</td>
<td>434(49.94)</td>
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<tr>
<td></td>
<td>&lt; 65 yr old</td>
<td>435(50.06)</td>
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<td>Primary tumor site</td>
<td>Rectum</td>
<td>315(36.25)</td>
</tr>
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<td>Colon</td>
<td>554(63.75)</td>
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<td>Tumor status</td>
<td>T4</td>
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</tr>
<tr>
<td></td>
<td>T3</td>
<td>468(53.86)</td>
</tr>
<tr>
<td></td>
<td>T1/2</td>
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<td>Regional lymph node inv.</td>
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</tr>
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<td>476(54.78)</td>
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<td>N2</td>
<td>185(21.29)</td>
</tr>
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<td></td>
<td>N1</td>
<td>208(23.94)</td>
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<td>476(54.78)</td>
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<td>Stage IV</td>
<td>138(15.88)</td>
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<td>303(34.87)</td>
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<td>Stage I</td>
<td>190(21.86)</td>
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<td>747(85.96)</td>
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<td></td>
<td>carcinoma</td>
<td>64(7.36)</td>
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<td>Adenocarcinoma</td>
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<td>Mucinous carcinoma</td>
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<td>Tumor size</td>
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<td>281(34.73)</td>
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<td>647(74.45)</td>
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<td>&lt;12</td>
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<td>CEA</td>
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<td>&lt; 5.0 ng/ml</td>
<td>34(3.91)</td>
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<td>25(2.88)</td>
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<td>BMI</td>
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<td>18.5-24</td>
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<td>≥24</td>
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<td>Perforation</td>
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<td>853(98.16)</td>
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<td>357(41.08)</td>
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<td>512(58.92)</td>
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Table No. 2: Pathological findings of parameters

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<tr>
<th>Variable</th>
<th>Category</th>
<th>Wald</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
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<tbody>
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<td>Age</td>
<td>≥65 yr old</td>
<td>19.85</td>
<td>1.87</td>
<td>1.42–2.47</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>&lt; 65 yr old</td>
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<td></td>
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<tr>
<td>Tumor status</td>
<td>T4</td>
<td>68.61</td>
<td>8.74</td>
<td>5.23–14.60</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>25.03</td>
<td>3.54</td>
<td>2.16–5.82</td>
<td>&lt; 0.001</td>
</tr>
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<td></td>
<td>T1/2</td>
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<td></td>
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<tr>
<td>Regional lymph node involvement</td>
<td>Yes</td>
<td>58.54</td>
<td>3.05</td>
<td>2.29–4.05</td>
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<td>Stage</td>
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<td>18.96</td>
<td>10.28–34.96</td>
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<td>Stage III</td>
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<td>1.04–7.55</td>
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<td>Adenocarcinoma</td>
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<td>Mucinous carcinoma</td>
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Table No. 3: Univariate regression analysis

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<th>HR</th>
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<th>p-value</th>
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<td>Age</td>
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<td>19.85</td>
<td>1.87</td>
<td>1.42–2.47</td>
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<td>&lt; 65 yr old</td>
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<td>Tumor status</td>
<td>T4</td>
<td>68.61</td>
<td>8.74</td>
<td>5.23–14.60</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>25.03</td>
<td>3.54</td>
<td>2.16–5.82</td>
<td>&lt; 0.001</td>
</tr>
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<td>T1/2</td>
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<tr>
<td>Regional lymph node involvement</td>
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<td>3.05</td>
<td>2.29–4.05</td>
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<tr>
<td></td>
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<td>1.56–3.10</td>
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<td>1.53</td>
<td>1.15–2.03</td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CRM Positive | 13.29 | 2.18 | 1.43–3.31 | < 0.001
CRM Negative
KRAS mutation Yes | 7.22 | 3.90 | 1.45–10.51 | 0.007
KRAS mutation No
Perineural invasion Yes | 83.05 | 4.43 | 3.22–6.10 | < 0.001
Perineural invasion No
Perforation Yes | 4.58 | 2.28 | 1.07–4.84 | 0.032
Perforation No
Obstruction Yes | 21 | 1.87 | 1.43–2.44 | < 0.001
Obstruction No

Table No.4: Stepwise cox regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Wald</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>≥65 yr old</td>
<td>32.68</td>
<td>2.36</td>
<td>1.76–3.17</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>&lt; 65 yr old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional lymph node metastasis</td>
<td>Yes</td>
<td>11.22</td>
<td>1.81</td>
<td>1.28–2.57</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td>Ji</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>Yes</td>
<td>36.48</td>
<td>2.78</td>
<td>2.00–3.87</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathological differentiation</td>
<td>High grade</td>
<td>10.54</td>
<td>1.84</td>
<td>1.27–2.66</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Low grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>Yes</td>
<td>34.26</td>
<td>2.90</td>
<td>2.03–4.14</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstruction</td>
<td>Yes</td>
<td>4.94</td>
<td>1.38</td>
<td>1.04–1.84</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

In this cohort study, we observed different factors that are correlated with disease and have a huge impact on the survival rate. In this study, we specifically focus on the five-year survival in order to demonstrate the severity of disease in our region. In our selected population expected survival duration mean of I to IV tumor stage lies within 71.27±1.27 with a significant lifestyle nut we didn't find any significant relationship of these with the survival ratio of patients.

In our study, we demonstrate that men had high exposure to CRC as compared to females. This result is in correspondence to many previous studies. The age group with 64 median age was at high risk of CRC. These results are slightly different from the previously conducted study in Taiwan city 2013 where they found high threats among the above 66 year age group. We observed a high five-year survival rate among the patients as compared to the previous study which found only a 55.70% survival rate among the patients of CRC. This differentiation occurs due to the selection of age groups, as they only selected patients above the age of 65 years. By age group, we found the five-yr survival rate was 76.50% in patients younger than 65 and 60.90% in patients ≥ 65 yr old (P<0.001). We found that patients with greater than age 65 were associated with excess hazard for the death of 2.36. The patient's age at the time of diagnosis is an important prognostic factor for all CRC patients. During this time frame, we found 17% of patients age less than 50 years old with a minimum age of 17 years. This ratio predicts that the young population also has a high chance of CRC. We observed that less than 50 years of age group would not be count for screening at the initial stage and have a poor prognosis. We suggest that screening at the initial stage must be initiate among this age group in order to prevent this disorder. Fecal occult blood along with immunochemical methods could easily be implemented in a particular age group. We observed a 68.70 overall five-year survival rate. Our result is far better than the previous results of the health promotion administration of China, Fang et al, and the American cancer society in which they only found survival rate 63.0%, 55.69%, and 66%, respectively. In our study, we found a 91.20% five-year survival rate for stage I, for stage two 82.20%, for stage III 63.20%, and 21.70% for stage IV. There is an 80%-90% chance of survival with 2.55-5.01 risk of death among stage I and II patients whereas we found a 68% survival rate along with an 18.96 death rate among stage III and very limited (8%) survival chance with high expectation of death (34.95) among stage IV patients. This result is in accordance with Mathur et al study and higher than some other studies. Some other factors like tumor site, size, grade, histology, lymph node metastasis, perineural nerve invasion along with AJCC T, N, and M independent stage also influence the survival rate of CRC.

Most of the early cases didn't have clear symptoms like muscle infiltration or distant metastases and observed at the time of analysis. These features along with tumor
status, grade level, and regional lymph node influence the survival rate of patients. These results are in the consistency of Yuan et al\textsuperscript{19} and Khanjani et al\textsuperscript{20} study. Histotype of CRC were the risk factors, we found 1.77 risks of death in signet ring-cell and 2.80 in adenocarcinoma. Total 4.43 ratio of death associated with perineural nerve invasion. Coz regression analysis depicts that perineural nerve invasion helps in the prediction of CRC and this result is in accordance with the previous studies\textsuperscript{3,15}.

**CONCLUSION**

There are a lot of prognosis factors that may affect the survival rate among CCR patients. Some independent variables perineural nerve invasion, distant metastasis, age, pathological differentiation grade, obstruction, and regional lymph node metastasis are independent predictors that highly influence the ratio. But some like perineural nerve invasion and distant metastasis are considered as important in early detection. Early detection of these parameters will surely increase the survival rate.

**Author's Contribution:**
Concept & Design of Kamran
Study: 
Drafting: Mohibullah Khan
Data Analysis: Ilyas
Revisiting Critically: Kamran, Mohibullah Khan
Final Approval of version: Kamran

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

**REFERENCES**

7. Lund EK, Belshaw NJ, Elliott GO, Johnson IT. Recent advances in understanding the role of diet and obesity in the development of colorectal cancer. Proc Nutr Soc 2011;70:194-204.
**Paradigm and Pattern of Fabricated Injuries in the Sialkot (2018-2019)**

Sajid Hussain, Javed Mughal, Farhan Malik, Zainab Shamim and Saman Zahid

**ABSTRACT**

**Objective:** To determine the occurrence and pattern of fabricated injuries in respect to dimensions, direction, depth, timings, weapon used and site involved to uncover all internal motives.

**Study Design:** Descriptive / observational study

**Place and Duration of Study:** This study was conducted at the Department of Surgery, Allama Iqbal Memorial Teaching Hospital from 2018 to 2019.

**Materials and Methods:** The study included 206 cases which were challenged before the standing medical board where their police inquest report, first declared medico-legal certificate, investigation officer findings, reexamination findings made by all members of DSMB were examined in detailed, all data processed in SPSS 20.

**Results:** The cases confronted were 109 in 2018, 97 cases in 2019, occurrence was more in male (155, 75%) as compared to female (62, 30%), most of them were belonging to rural areas (85%), occurrence were common in evening/night (69%), came in month of June/July (109, 52%) as compared to Nov /Dec, mostly caused by blunt weapon (77%), area involved was upper limb followed by head lower limb, nasal injury, teeth, back.

**Conclusion:** There is a need of thorough examination of the medical experts in order to prove fabrication on solid grounds in order to decrease the burden on society, medical professional and on legal work.

**Key Words:** invented, Tier, DSMB, Circumstantial Evidences, Fabrication.


**INTRODUCTION**

Self-inflicted injuries usually considered to be non-fatal are manipulated, invented and factitious injuries which are created in order to implicate others in animosity, property matter or certain other unresolved conflicts, so to get up to that extent they modify the appearance of certain wounds, in various localities professionals of fabrications are present who just for few prices invent such injuries ignoring future consequences. For a new professional difficulty arise in determining whether injuries are self-inflicted or it is due to some trauma and put burdens on others to implicate them falsely, this has become a normal practice in remote district areas of our Punjab province where it has become a common practice for personal reasons. Injuries are created after offering money to the concerned, so a scientific and solid view is necessary to interpret manner of such injuries in order to help investigating officer, legal minds and to decide the fate of all such cases.

The government of province of Punjab has made three tiers for such cases; first tier of initial medico legal examiner, second tier The District Standing Medical Board (DSMB) and third tier provincial standing medical Board (PSMB) to decide any ambiguity in medico legal work.

Like other districts the Sialkot city is the city of millions having urban and rural populations connected to the Indian border and the villages which are near to the belt. Incidences of such fabrication injuries are very common but at the same time minimal literature is available to find out the authentic criteria to label such injuries as fabricated injuries so it has become a challenge for the forensic experts to assess such injuries after a thorough study, examination, investigation police inquest, radiological findings before to declare the fabrication.

**MATERIALS AND METHODS**

The present study was carried out in the surgical unit of Allama Iqbal memorial teaching hospital, the period of study was from Jan 2018 to Dec 2019 where data included 206 challenged medico legal cases before second tier on the instruction of the first class magistrate where accused or in some cases injured themselves challenged the decision of the first tier medico legal officer, where experts of medico legal team with vast experience like medical superintendent as chairman, District health officer, District medico legal officer and Consultant surgeon assess their application, FIR, Police inquest report first medico legal officer certificate declared copy, reexamine the injured
in the presence of applicant and investigation officer in order to relate it with circumstantial evidences.

RESULTS

Total number of patients which were confronted before second tier was 150 in 2018 and 120 in 2019, where 109 cases in 2018 and 97 cases in 2019 appeared and reexamined by DSMB, rest of the cases were not carried out because of the absence of the police, injured or complainant, whole data which was collected processed in SPSS 20. The occurrence of the incidence was more marked in males (78 in 2018, 77 in 2019) as compared to female with a ratio of (31 in 2018, 20 in 2019). Most of them were belonging to rural areas (92 in 2018, 85 in 2019) as compared to urban areas (17 in 2018, 12 in 2019). Most of the cases occurred in the evening /night (75 in 2018, 68 in 2019) as compared to morning /noon (34 in 2018, 29 in 2019) as shown in table 1.

There were more incidences in month of June/July (146, 70%) a lesser number of cases were reported in months of November /December (60, 29%). The commonest age groups were between 31-40 yrs., followed by 21-30yrs. The commonest weapon which were used were blunt (79 in 2018, 80 in 2019) followed by sharp (9 in 2018, 12 in 2019), both blunt and sharp (13 in 2018, 3 in 2019), firearm (4 in 2018, 1 in 2019), and no weapon (4 in 2018, 1 in 2019) mentioned in cases. The area of involvement was upper limb (40 in 2018, 35 in 2019), head (30 in 2018, 30 in 2019). Lower limb (20 in 2018, 12 in 2019), nasal injury (10 in 2018, 10 in 2019) teeth (5 in 2018, 7 in 2019), back (4 in 2018, 3 in 2019). DSMB after their reexamination declared injuries as fabricated (65 in 2018, 48 in 2019) non fabricated (24 in 2018, 39 in 2019) traumatic to be decided on circumstantial evidences (20 in 2018, 10 in 2019).

Table No.1: Detail of Occurrence of cases

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2019</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>78</td>
<td>77</td>
<td>155(75.2%)</td>
</tr>
<tr>
<td>Female</td>
<td>31</td>
<td>20</td>
<td>51(24.7%)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>92</td>
<td>85</td>
<td>177(86.2%)</td>
</tr>
<tr>
<td>Urban</td>
<td>17</td>
<td>12</td>
<td>29(14.06%)</td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evening/Night</td>
<td>75</td>
<td>68</td>
<td>143(69.4%)</td>
</tr>
<tr>
<td>Morning/noon</td>
<td>34</td>
<td>29</td>
<td>63(30.5%)</td>
</tr>
</tbody>
</table>

DISCUSSION

Fabrication to implicate someone in a false charge has become an art in developing countries and even in some developed countries. The reasons are jealousy, personal gains, property issues and above all is the ego reasons, they are usually associated with cut wounds on the accessible parts of the body as self-inflicted injuries or friendly hand injuries, they are crafted in such a fashion and apertures are made on clothes. Later blood is thrown on the clothes to mimic it as a true injury. Sometimes injury do occur but in order to increase the severity of the crime. These wounds are enhanced particularly in head area where this injury become a bone exposed injury to intensify the crime. These fabricated injuries are of equal depth incised wound as compared to lacerated or contused wounds which are very rarely fabricated injuries. The alleged accused therefore direct himself at the mercy of the courts which for more confirmation rely their decision based on the opinion of experienced medical board members. The incidence of fabricated injuries is common in other provinces areas like Larkana, Sukhor, Shakarpur, Abbottabad pasawar but also in neighboring countries like India. This study also agrees with the studies carried out in other province that crafter of these fabricated injuries is found in the same institute or reckoned crafter are present in remote health centers so time elapsed between injuries and medicolegal issuance has a considerable importance for investigating officer and the DSMB. The incidences are found to be more in male (155, 75%) as compared to female (51, 25%) with the ratio of 3:1 which is in accordance with the studies carried out in other areas of this country. The reasons best explained is that male is actively participating their life in earnings for the families so very easily vulnerable to be involved in conflicts. Some may expose their female family member in order to get sympathies of the community, the male occurrence has also been reported in other countries particularly in our neighboring countries. The vulnerable age group was between 31 to 40 years followed by age group 21 to 30 years which is also in similar situation in other countries. The incidences were more common in rural areas (206, 85%) as compared to urban areas (29, 14%) which has not been explored in studies carried out in our country but the results of our study are in accordance with the study done in Indian Punjab, the reasons which were mentioned were poverty, lack of education, personal animosities, cast differences. Similarly, the occurrences of incidences were mostly found in evening/night as compared to morning /noon which is in similar situation in our neighboring countries. The reasons explained in our study was were that most of the occupation of this city is belonging to industries as this area is an industrial hub of the country and they usually return back to their homes in the evening or early night. The weapon which was used most commonly was blunt (159, 76%) as matched to other weapons which is in accordance with the studies carried out in this country, in regard to neighboring countries and world wide. The commonest site of infliction was upper limb in the form of fractures of left-hand little finger, index finger or right hand. This study is not consistent with our previous studies where head with bone deep injuries were the commonest site.
of infliction of injuries. This present study is also not consistent with the studies carried out in other provinces areas like shakarpur and Jacobabad, where fracture of nose was the commonest site while when it was compared with our neighboring country, it was the fracture of the long bones of leg. The DSMB declared more fabricated injuries as compared to first medicolegal officer so the percentage of discrepancy was more as compared to studies carried out in other areas of this country.

CONCLUSION

Fabricated injuries need to be thoroughly examined after taking detailed history of events, police inquest report, characteristics of the wound, accessibility direction and clothes examination to be framed scientifically thereby decreasing the burden on investigating experts. Expertise in medico legal work can be achieved by attending regular training workshops and electronic technology. Further reduction in fabrication may be achieved by awareness among public, discouraging false reporting, and recruiting highly qualified and honest investigation authorities.

Author’s Contribution:

Concept & Design of Study: Sajid Hussain
Drafting: Javed Mughal
Data Analysis: Zainab Shamim, Saman Zahid
Revisiting Critically: Farhan Malik
Final Approval of version: Sajid Hussain

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

REFERENCES

9. Bhullar DS. Profile & pattern of fabricated injuries by mechanical violence. JIAFM 2006;28(1) ISSN; 0971-0973.
Serum Bilirubin and G-Glutamyl Transferase in Female Patients Suffering from Migraine
Akram Munir and Muhammad Akbar

ABSTRACT

Objective: To analyze serum bilirubin and liver aminotransferase in migraine female patients at a tertiary care hospital of Sindh.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Department of Medicine, Isra University Hospitals from February 2019 to January 2020.
Materials and Methods: A sample of 100 diagnosed cases of migraine and 100 controls was selected according criteria. Severity of migraine headache was defined according to the Visual Analogue Scale (VAS). 5 ml blood was drawn; 2 ml was put in EDTA bottles for blood parameters and 3 ml was centrifuged to get sera for detection of liver function tests. Data was analyzed on statistical software SPSS (ver 21.0) by Student t-test (at P ≤ 0.05) and correlation by Spearman’s rho testing.
Results: Total, Direct and Indirect bilirubin in control and migraine patients were noted as 1.24±0.09 and 1.07±0.08 mg/dl (P=0.0001), 0.86±0.09 and 0.71±0.04 mg/dl (P=0.0001), 0.27±0.08 and 0.23±0.09 mg/dl (P=0.001) respectively. GGT in control was 36.3±6.09IU compared to migraine patients as 44.9±8.3 IU. Total bilirubin, direct and indirect bilirubin reveals negative correlation with migraine severity, while gamma glutamyl transferase (GGT) reveals positive correlation.
Conclusion: The present prospective study found low serum bilirubin and raised gamma – glutamyl transferase levels in migraine patients.
Key Words: Bilirubin, Migraine, G-glutamyl transferase

Citation of article: Munir A, Akbar M. Serum Bilirubin and G-Glutamyl Transferase in Female Patients Suffering from Migraine. Med Forum 2020;31(12):110-114.

INTRODUCTION

Migraine is a common health problem particularly in the women. Migraine is a vascular type headache and most common neurological diseases in all age groups. Migraine causes frustration and sufferance in migraneurs. It affects 12 – 15% adults in Western countries. Migraine is characterized by throbbing headache, tearing eyes, vertigo, nausea, photophobia, phonophobia, and tinnitus and in hemiplegia in severe cases. Studies show the migraine patients are at increased risk of coronary artery disease. Clinical research has confirmed the increased cerebrovascular accident symptomatology in mignaneurs and a remarkable role in migraine infarction and hemiplegia. Migraineur should be given special clinical attention for preventing complications.

Recently, many biochemical markers have been suggested play role in migraine and clinical risk factors have been studied. Bilirubin is one of clinical risk factor that has got attention in clinical research. Bilirubin is a toxic metabolite of heme catabolism. Bilirubin has demonstrated anti – oxidant and cytoprotective potential in recent studies. It has been reported the bilirubin influences the Fc receptor expression in phagocytic cells that indicates its immunomodulatory role in migrains. Bilirubin is reported reduce the produce of Interleukin – 2 (IL – 2) in lymphocytes. Obviously, the bilirubin is a vital anti – oxidant and anti – inflammatory substance. Serum bilirubin has been used to stratify the arterial – stiffness in coronary artery disease patients. Serum has been associated with GFR (glomerular filtration rate) and is correlated with decreasing renal functioning general populations. Research has proved correlation of serum bilirubin with systemic hypertension and multiple sclerosis patients positively. However, the association of serum bilirubin and migraine are not discussed well in medical literature. The present study was conducted to analyze the serum bilirubin in female patients suffering from migraine and its correlation with visual analogue scale presenting at our tertiary care.
hospital. The objective of study was to analyze serum bilirubin levels in migraine patients in comparison to controls and correlation with bilirubin subtypes in migraineurs.

MATERIALS AND METHODS

The present cross sectional study was conducted at Department of Medicine, Isra University Hospitals from February 2019 to January 2020. Study was approved by ethical review committee for research purpose. Sample was calculated by “sampling-proportions” using online Rao software. A sample of 100 diagnosed cases of migraine and 100 controls was selected. Inclusion criteria were; female diagnosed migraine and age 20-40 years. Migraine was defined as per international criteria.16 Severity of migraine headache was defined according to the Visual Analogue Scale (VAS).17 VAS 0 – 10 numeric pain rating scale was used. 0 – no pain, 1-5 moderate pain and 6 – 10 was severe pain. Controls were taken from the attendants of patients. Control were age and demography matched. Female patients suffering from concomitant morbidities were excluded. Systemic hypertension, anxiety tensions, depression, diabetes mellitus, chronic inflammatory lung and kidney diseases, viral hepatitis, and metabolic syndrome were excluded from study protocol. Volunteers were asked inclusion in study protocol voluntarily and abide by the protocol. Cases and control clinical history was taken to reach to the inclusion criteria. Data was entered in a protocol. Cases and control clinical history was taken to reach to the inclusion criteria. Data was entered in a protocol.

RESULTS

Demography, physical and laboratory findings are summarized in table 1. All comparisons in table – 1 are non- significant that shows the study subject groups were matched. Table – 2 shows the liver function tests that shows significant differences between control and migraine patients for the total bilirubin, direct and indirect bilirubin and the gamma glutamyl transferase (GGT) (P≤0.001).

Table No.1: Demography and Laboratory finds (n=200)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Migraine</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.5±3.5</td>
<td>32.7±7.5</td>
<td>0.71</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>77.4±12.2</td>
<td>78.45±13.9</td>
<td>0.56</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>131.3±5.2</td>
<td>130.58±8.54</td>
<td>0.46</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>80.4±14.8</td>
<td>70.8±8.5</td>
<td>0.34</td>
</tr>
<tr>
<td>PCV (Hct.) (%)</td>
<td>41.3±3.3</td>
<td>41.5±3.7</td>
<td>0.79</td>
</tr>
<tr>
<td>Hemoglobin (grams)</td>
<td>11.3 ±1.3</td>
<td>11.5±1.5</td>
<td>0.91</td>
</tr>
<tr>
<td>Red Blood Cells (x10^6)</td>
<td>3.7 ±0.2</td>
<td>3.6±0.5</td>
<td>0.91</td>
</tr>
<tr>
<td>White Blood Cells (x10^3)</td>
<td>4.7 ±0.3</td>
<td>5.0±0.3</td>
<td>0.71</td>
</tr>
<tr>
<td>Platelet counts (x10^3)</td>
<td>151.3±5.1</td>
<td>149.5±9.1</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Table No.2: Liver function test (n=200)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Migraine</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin</td>
<td>1.24±0.09</td>
<td>1.07±0.08</td>
<td>0.0001</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>0.86±0.09</td>
<td>0.71±0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Indirect bilirubin</td>
<td>0.27±0.08</td>
<td>0.23±0.09</td>
<td>0.001</td>
</tr>
<tr>
<td>ALT</td>
<td>33.7±5.6</td>
<td>33.9±5.7</td>
<td>0.39</td>
</tr>
<tr>
<td>ALP</td>
<td>80.6±14.9</td>
<td>82.4±14.3</td>
<td>0.94</td>
</tr>
<tr>
<td>GGT</td>
<td>36.3±6.09</td>
<td>44.9±8.3</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table 3. Migraine Pain Severity – Correlation of Liver function tests and Visual Analogue Scale

<table>
<thead>
<tr>
<th></th>
<th>Total Bilirubin</th>
<th>Direct Bilirubin</th>
<th>Indirect Bilirubin</th>
<th>ALT</th>
<th>ALP</th>
<th>GGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>r-value</td>
<td>-0.663</td>
<td>-0.751</td>
<td>-0.433</td>
<td>0.012</td>
<td>0.075</td>
<td>0.631</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.085</td>
<td>0.029</td>
<td>0.0001</td>
</tr>
<tr>
<td>N</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
</tbody>
</table>

Figure No.1: Scatter plot showing negative correlation of total bilirubin and migraine pain severity (Visual Analogue Scale - VSA)
The present cross sectional case – control study analyzed the total, direct and indirect bilirubins and liver aminotransferases in female diagnosed migraine cases compared to control. We found low levels of total, direct and indirect bilirubin in migraine cases compared to controls (P<0.001) and gamma glutamyl transferase (GGT) was high. The findings are consistent with previous studies. However, raised GGT is a new finding being reported for the first time. In present study the total, direct and indirect bilirubin in control and migraine patients were noted 1.24±0.09 and 1.07±0.08 mg/dl (P=0.0001), 0.86±0.09 and 0.71±0.04 mg/dl (P=0.0001), 0.27±0.08 and 0.23±0.09 mg/dl (P=0.001) respectively. GGT in control was 36.3±6.09 IU compared to migraine patients as 44.9±8.3 IU. Serum bilirubin has been associated with different diseases such as cigarette smokers, systemic hypertension, cardiovascular diseases, etc. A previous study concluded, the serum bilirubin significantly protects against the atherosclerosis. Various studies had attested the serum bilirubin is negative correlated with coronary artery disease in patients suffering from obesity, diabetes mellitus, metabolic syndrome, and cigarette smokers. A recent study reported evidence of low serum bilirubin in migraine patients and it may be used as a biomarker of neurogenic inflammation in this particular patient group. This is a consistent finding to the present study. A previous study conducted large study with sample of 2784 individuals reported low serum bilirubin in chronic kidney patients and may be used as a potential risk factor of declining renal function. This is in support to the present study that the serum bilirubin is a potential biomarker in migraine patients. The low serum bilirubin in particular disease has been attributed to its anti – oxidant properties. Bilirubin inhibits oxidative stress, is used up hence levels are low. Bilirubin helps as anti – oxidant in neutralizing the reactive oxygen species (ROS). Previous studies had reported association of bilirubin in migraine, brain stroke, coronary artery disease and atherosclerosis, etc. Neurogenic inflammation of migraine increases the oxidative stress and this is removed by bilirubin hence used up and its concentrations fall that has been noted in the present study too. Many studies have witnessed significant inflammation in migraine patients where large pro – inflammatory cytokines are secreted; stimulate nerve endings resulting in severe pain. Anti – inflammatory drugs have been considered effective in alleviating migraine pain. Neurogenic inflammation and oxidative stress in migraine patients lowers the serum bilirubin concentrations. GGT was found elevated in migraine patient that is a new finding and needs further elaboration of underlying mechanism. Present study is worth report on low serum bilirubin in migraine patients. Only limitation of present study is the small
CONCLUSION

The present prospective study found low serum bilirubin concentration in migraine patients. However, gamma – glutamyl transferase activity was found elevated. Low serum bilirubin indicates increased oxidative stress in migraine patients due to the neurogenic inflammation.

REFERENCES

16. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res 2011;63(S11);S240-S252.


The Outcome Combined Pars Plana Vitrectomy and Scleral Buckling (Vit-Buck) in Pediatric Retinal Detachment

Asim Ateeq¹, Saima Majid¹, Nausheen Hayat², Ali Zia¹, Nazia Qidwai¹ and Attiya Zehra Rizvi¹

ABSTRACT

Objective: To assess the visual and anatomical outcome of combined parsplana vitrectomy and Scleral Buckling procedure in pediatric retinal detachment patients.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Al-Ibrahim Eye hospital, Karachi for six months from April 2019 to March 2020.

Materials and Methods: A retrospective study was carried out on 57 patients with pediatric retinal detachment aged 3-14. Patients who underwent a combined surgical procedure of SB and PPV were included and had a follow-up for six months minimum. Medical records were studied thoroughly. Pre and post-operative visual acuity were assessed on follow-up, along with complications. Data were analyzed using SPSS Version 21.0 with P-value set at ≤0.05.

Results: Significant difference (P-value ≤0.05) in Pre and Post-Operative visual acuity upon follow-up and a reduction in complications upon follow-ups.

Conclusion: SB is a strong surgical procedure in paediatric retinal detachments and combined with parsplana vitrectomy improves visual acuity and shows a strong anatomic success outcome.

Key Words: Scleral Buckling, Retinal Detachment, Visual Acuity, Anatomic Success

INTRODUCTION

Estimates show that 43 million people blind worldwide, with 90% of these cases arising from developing nations in Asia, Latin America, and Africa. There are many causes of blindness, such as glaucoma, cataract, and trachoma. One of the causes of blindness is the detachment of the retina, which leads to complete blindness (¹). Retinal detachment (RD) is prevalent in developing countries due to poor health care provision (²). The number of RD in children is fairly low when comparing to the prevalence of RD in adults. Its occurrence is said to only be 3.2-5.6% in children. The main factors for RD in children include myopia, retinopathy of prematurity, associated conditions, and trauma (³,⁴).

Furthermore, retinal detachment can also be idiopathic. Pediatric RD in other studies indicates the frequency to be much higher, going on effect 12.6% of all patients suffering from retinal detachment (⁵). However, pediatric RD is often diagnosed at a later course of the disease, and the visual loss is less acute than the typical RD associated with acute posterior vitreous detachment. Combined with the fact that children possess an immature cognitive function means that they are far less likely to report and recognized any visual symptoms of acute RD (⁶). Therefore, children present later with RD clinical features, such as macular involvement and proliferative vitreoretinopathy (PVR) (⁷). The treatment of pediatric RD is surgical and is carried out on the same surgical principles as adult detachment. The majority of pediatric patients need to be treated using the surgical procedure called Scleral Buckling (SB). Since it was introduced way back in the 1950s, SB has proven to be a successful surgical technique in repairing RD. Although many innovations have developed since the inception of SB, the procedure still requires an intra-operative examination of the retina and the treatment of retinal breaks via indirect ophthalmoscopy (⁸). SB is a challenging procedure and requires good surgical skills and prolonged duration of surgery. It is associated with low risk of ocular complications, cost-effectiveness, and similar outcomes compared with other surgical techniques such as Pars Plana Vitrectomy (PPV) (⁹,¹⁰). Combination of both

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surgical procedures contributes significantly towards better outcome. Pakistan is another developing country where there is a poor provision of health care and improper eye facilities to diagnose and treat eye conditions. Therefore, a retrospective study was carried out to assess the outcome of scleral buckling combined with Pars Plana Vitrectomy in pediatric retinal detachment.

MATERIALS AND METHODS

After gaining proper approval from the ethical review board, a retrospective study was carried out at Al-Ibrahim eye hospital, Karachi. Fifty-seven medical files of patients between the ages of 3 and 14 with primary rhegmatogenous retinal detachment were selected. These patients have been treated with both pars plana vitrectomy and scleral buckling. Patients that had a follow-up course of at least six months were included in this study. 60 eyes of 57 patients were then studied. Medical records were thoroughly reviewed to obtain data related to name, age, gender, duration of symptoms. Status of the lens, location, and quadrants of retinal detachment, the number of retinal breaks, the status of the macula, the type of sclera buckle used (circumferential or segmental), intraoperative injection of temporary vitreous adjunct, anatomy after surgery, and if further surgery was needed after the primary surgery. Pre and Post-operative best-corrected visual acuity was then measured on the 1st, 2nd, and 3rd follow-up. Pre- and post-operative intraocular pressure and post-operative refractive errors were also obtained. Data obtained from medical records were analyzed using the Statistical Package of social sciences (SPSS) version 21.0, and the paired "t" test was applied. The value of significance was kept at ≤0.05.

Surgical Technique: The surgery was carried out under general anesthesia. The ocular surface was washed using 5% povidone-iodine before the commencement of the surgery. A 360° conjunctival peritomy with dissection of the tenon capsule was done. Traction sutures were placed under the insertions of exposed rectus muscle exposure with a 4/0 silk. For circumferential buckling, a silicone band (silicone band 240) and the sleeve was used by passing it beneath the four rectus muscles and the sclera tunnels. The buckling materials, either for segmental or circumferential, were sutured to the sclera using a 5/0 ethibond sutures. Three port Pars Plana Vitrectomy was performed using a 23 G Alcon constellation. Induction of posterior vitreous detachment was done by staining it using triamcinolone. Breaks are located and identified to complete vitrectomy. Under heavy liquid, the laser is perfumed at 360° and on the breaks. Gas fluid was carried out, and silicone oil tamponade was instilled, which was removed after six months. Peritomy was closed with 6-0.

RESULTS

Sixty eyes were examined, in which 23 eyes were of female patients, whereas 37 were male patients. Table 1: shows frequency and percentage of Pre and Post-operative Visual Outcome on 1st follow up. A significant difference was seen (P-Value= 0.01) between Pre and Post-operative Visual Outcome.

Table 2: shows frequency and percentage of Pre and Post-operative Visual Outcome on 2nd follow up. A significant difference was seen (P-Value= 0.05) between Pre and Post-operative Visual Outcome.

Table 3: shows frequency and percentage of Pre and Post-operative Visual Outcome on 3rd follow up. A significant difference was seen (P-Value= 0.01) between Pre and Post-operative Visual Outcome.

Table 4: shows the Frequency and Percentage of Pre and Post-operative complications on different days of Follow-up. Primary anatomical success in single surgery was achieved in 82%. A significantly better anatomical outcome was observed in patients with better preoperative visual acuity.

Table No.1: Shows the Frequency and Percentage of Pre and Post-Operative Visual Outcome on 1st Follow-up

<table>
<thead>
<tr>
<th>Variables</th>
<th>Preoperative</th>
<th>Post-operative</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perception of light</td>
<td>12</td>
<td>20.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Hand Movement</td>
<td>19</td>
<td>32.2</td>
<td>0.00</td>
</tr>
<tr>
<td>Counting fingers</td>
<td>0</td>
<td>0.0</td>
<td>0.00</td>
</tr>
<tr>
<td>1/60</td>
<td>0</td>
<td>0.0</td>
<td>0.00</td>
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<tr>
<td>2/60</td>
<td>17</td>
<td>28.4</td>
<td>0.08</td>
</tr>
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<td>3/60</td>
<td>0</td>
<td>0.0</td>
<td>0.00</td>
</tr>
<tr>
<td>4/60</td>
<td>0</td>
<td>0.0</td>
<td>0.00</td>
</tr>
<tr>
<td>5/60</td>
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<td>0.0</td>
<td>0.00</td>
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<tr>
<td>6/60</td>
<td>12</td>
<td>19.3</td>
<td>0.32</td>
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<tr>
<td>6/36</td>
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<td>0.00</td>
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<tr>
<td>6/24</td>
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<td>6/12</td>
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<tr>
<td>6/9</td>
<td>0</td>
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</tr>
<tr>
<td>6/6</td>
<td>0</td>
<td>0.0</td>
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</tr>
</tbody>
</table>

Figure No.1: Days of follow up
DISCUSSION

There are arrays of different surgical procedures that can be used to treat RD. SB is being used to repair RD for more than six decades, having a vital role in repairing various categories of RD, including detachments in young phakic patients, detachments caused due to dialysis, and in conjunction with vitrectomy in patients who have suffered trauma. SB is proven to be an effective method in treating RD. Our study showed improvement in the best-corrected visual acuity on all follow-ups to be significantly different (P-value ≤0.05) compared to preoperative visual acuity in the 57 patients on which the study was conducted. An anatomic success rate of 82% was achieved in our study by carrying out a single surgical procedure; these rates are comparable to other previous studies. Our study showed an improvement in the final visual acuity. These findings are similar to another study, which showed that SB was a superior procedure in terms of visual acuity compared to PPV. Our study showed that SB is highly effective and with vitrectomy showed even better anatomical success. This was seen in another study in which SB alone had an initial success rate of 86%, whereas SB combined with vitrectomy showed a success rate of 94%. After successive follow-ups, the post-operative complications also went on the decrease, and eventually, there was no indications of buckle infection or vitreous hemorrhage on the 3rd follow-up. However, studies have found that SB, combined with vitrectomy, has a much higher complication rate than both procedures alone. However, these complications can be easily managed and do not necessitate shifting towards other surgical procedures to treat RD. Both PPV and SB are two procedures that are widely used in ophthalmology to treat RD. However, no one is superior to the other and combining both surgical techniques gives a better anatomic success than if both of them are used separately.

CONCLUSION

Scleral buckling is a strong option for patients with pediatric retinal detachment as it improves visual acuity and shows a strong anatomic success rate.

Author’s Contribution:
Concept & Design of Study: Asim Ateeq
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Data Analysis: Ali Zia, Nazia Qidwai and Attiya Zehra Rizvi
Revisiting Critically: Asim Ateeq, Saima Majid
Final Approval of version: Asim Ateeq

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

Alcohol-Induced Hepatotoxicity: Evaluation of Protective Effects of Vitamin C and Naproxen Based on Hematological and Histopathological Parameters in Rats

Raja Faisal\(^1\), Nazia Qamar\(^3\), Jamil Ahmed Siddiqui\(^4\), Ghazala Panhwar\(^2\), Syed Liaquat Ali\(^2\) and Shahid Korai\(^1\)

ABSTRACT

Objective: To evaluate the protective effect of Vitamin C and Naproxen in Alcohol-induced Hepatotoxicity based on Hematological and Histological Parameters.

Study Design: Experimental Interventional Study

Place and Duration of Study: This study was conducted at the Anatomy Department of Al-Tibri Medical College and Hospital, Isra University Karachi from November 2018 to April 2019.

Materials and Methods: 60 albino rats were selected with an equal gender ratio and placed in three groups. Group A (Control Group) was given purified Ethanol for ten days, Group B (Prophylactic Group) was given Vitamin C and Naproxen prophylactically for seven days after which they were intoxicated with Ethanol for ten days, and Group C was simultaneously given Vitamin C, Naproxen, and Ethanol for ten days. Hematological and Histological parameters were then recorded, whereas data was analyzed using SPSS Version 24.0, and P-Value of ≤0.05 was considered statistically significant.

Results: Group A experienced a severe rise in hematological biomarkers, and a grossly damaged hepatic architectural change was also evidently observed histologically. Group B had also elevated hematological markers above the normal range but lower than Group A. Furthermore, they also had milder cellular damage compared to Group A. Group C produced excellent results by showing within standard range biomarkers and a remarkably near-normal hepatic architecture.

Conclusion: Hepatoprotective effects were observed in the rats’ liver due to the antioxidant and anti-inflammatory effects of Vitamin C and Naproxen.

Key Words: Hepatocytes, Alcohol, Vitamin C

INTRODUCTION

The use of alcohol is customary in many cultures, consumed as to enhance social well-being, relationships, and even health, however, alcohol abuse is common worldwide\(^1\). More than 50% of American consumes alcohol, with about 23.1% Americans taking part in heavy and binge drinking.

Chronic alcoholism is said to be associated with 60 major types of diseases. This makes alcohol the third leading cause of disease and disability worldwide. Chronic alcohol use is associated with a spectrum of liver diseases ranging from steatosis, steatohepatitis to cirrhosis and hepatocellular carcinoma. The pathogenesis of acute and chronic alcohol consumption has various consequences in different cell types. This occurs because the production of reactive oxygen species (ROS) increases; simultaneously antioxidants productions are reduced\(^2\). ROS has always had substantial implications in many diseases, and one of them is acute and chronic alcohol treatment\(^3,4\). Alcohol represents the most common cause of chronic liver disease in most industrialized countries after hepatitis\(^5\). Ultimately this results in 2.5 million deaths worldwide due to alcohol, mostly due to alcohol liver disease (ALD). There is no definitive treatment available to treat the hepatotoxic effects of alcohol. However, studies have been conducted to see if certain substances can elicit a hepatotoxic effect.
Vitamin C is the redox form of Ascorbate and a physiological antioxidant that is various functions such as enhancing immune function, facilitating enteral uptake of iron, synthesis of collagen, catecholamine, carnitine, and improving tissue perfusion and oxygen, thereby mitigating organ dysfunction\textsuperscript{6,7}. WHO lists it as an essential medicine, and studies suggest that its antioxidant effects can have a beneficial impact by protecting the liver from oxidative stresses\textsuperscript{8,9}. Similarly, another commonly used therapeutic worldwide belong to the class of Nonsteroidal anti-inflammatory drugs (NSAIDs) called Naproxen. NSAIDs are the most commonly used class of analgesic agents, with 30 million users worldwide and over 100 million prescriptions being written out in the USA\textsuperscript{10,11}. Naproxen was first introduced in 1976, and Naproxen sodium is approved in many countries for over the counter use. Naproxen, a member of the NSAIDs family, also inhibits prostaglandin synthesis by inhibiting the cyclooxygenase enzyme. Vitamin C and Naproxen are both essential medications used globally to treat various conditions; they both have well-documented safety profile. With alcoholic intake also increasing in Pakistan and causing hepatotoxicity among chronic users, leading to alcohol liver disease, a study was conducted to assess Naproxen and sodium's protective effects on alcohol-induced hepatotoxicity.

**MATERIALS AND METHODS**

After seeking ethical approval from the concerned ethical committee, an experimental interventional study was carried out in the anatomy department of Al-Tibri Medical College and Hospital, Isra University Karachi Campus. Our study aimed to evaluate if there are protective effects of Naproxen and Vitamin C on alcohol-induced hepatotoxicity based on hematological and histological parameters. Animals were taken from the animal house of Al-Tibri medical college. Sixty health albino rats that weigh between 150-200 grams were selected, and all aged between 8-12 weeks. All of the albino rats were selected through a random sampling technique. The gender ratio of the albino rats was then kept at equal, after which we separated both of the genders during the study to prevent mating. The rats were all kept in plastic cages. All of the cages containing rats were kept in the anatomy department under controlled temperature (30°C) with an equal light-dark interval (12/12 hour). The rats were all given a standard diet and water ad libitum. We purchased purified Ethanol 99.7%\%, 500 mg Naproxen Tablet, and 500mg Vitamin C tablet from the local pharmacy located near the hospital for the experiment. Sixty albino rats were then divided into three groups, with each group consisting of 20 rats with an equal gender ratio. The following intervention was then carried out on each group:

**Group A**: Served as our positive control group and received purified Ethanol at 8ml/kg body weight for 10 days

**Group B**: we prophylactically gave vitamin C and Naproxen Sodium to this group at a dose of 100mg/kg and 5mg/kg, respectively, for 7 days, after which they were intoxicated with Ethanol for 10 days.

**Group C**: was simultaneously given Vitamin C, Naproxen, and purified Ethanol at doses 100mg/kg, 5mg/kg, and 8ml/kg, respectively, for 10 days.

All the rats were administered Vitamin C, and Naproxen Sodium between 9 am, and 11 am, while not being provided with any food during the night. Ethanol was given regularly after a one-hour interval through gastric gavage. After the completion of the dosing, all the rats were given anesthesia in a glass dissection. They were then euthanized, and the thoracoabdominal organs were exposed. Blood samples were then taken by carrying out an intracardiac puncture with 5CC syringes into tubes already labeled and having antisera present within them to detect serum levels of hepatic enzymes (ALT, AST, and GGT). The liver tissue was fixed using 10% formalin solution and cut into small pieces to create blocks. Fixed liver pieces were then processed in ascending alcohol concentration, cleared and stained using paraffin to make blocks. Rotatory microtome was used to cut thick sections floated in a water bath at 37°C for one minute. Tissues were then placed on a glass slide and fixed in the oven. Finally, the sections were then stained using hematoxylin and eosin for morphological and morphometric observation using a light microscope. Data were analyzed using the Statistical Package for social sciences (SPSS) Version 24. All variables and means were calculated, and results were expressed as mean ± standard error (Mean ± SE). Assessment of significant differences among groups was done using one-way ANOVA with post-hoc tukey's test and secondly student's t-test. The P-value was set at ≤0.05 to be statistically significant.

**RESULTS**

Figure 1: shows the Mean serum level of Alanine transaminase (ALT), Aspartate transaminase (AST), Gamma Glutamyl transferase (GGT) in IU/L of rats in different groups.

Table 1: shows statistical analysis shows the Level of Significance between the different therapeutic groups

Figure 2: Shows Histopathological section of Liver taken from Group A

Figure 3: Shows Histopathological section of Liver taken from Group B

Figure 4: Shows Histopathological section of Liver taken from Group C.
Figure No. 1: Shows the Mean values of Serum ALT (Alanine transaminase), AST (Aspartate transaminase) and Serum GGT (Gamma Glutamyl transferase) IU/L among different therapeutic groups

Table No.1: shows the Level of Significance between the different therapeutic groups

<table>
<thead>
<tr>
<th>Comparison Between the Groups</th>
<th>Serum ALT</th>
<th>Serum AST</th>
<th>Serum GGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A vs B</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>A vs C</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>B vs C</td>
<td>&lt;0.001</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

One-Way ANOVA was applied followed by Post-hoc tukey’s test
P=<0.05

Figure No. 2: Shows Histopathological section of Liver taken from Group A
Liver section of group (A) showing damaged hepatocytes. Markedly dilated sinusoids, highly increased number of inflammatory cells (Thick arrows), and necrotic debris. Congested portal vein (PV) and hepatic artery (HA). Abundant clear cytoplasmic vacuoles (Arrowheads) present. Hepatocytes plates were damaged.

Figure No. 3: Shows Histopathological section of Liver taken from Group B
Liver section of group (B) showing the mildly distorted hepatic architecture of lobule. Hepatocytes damaged and mild infiltration of immune cells (Thick arrows). Dilated sinusoids (Thin arrows) and portal vein (PV). Considerable numbers of clear cytoplasmic vacuoles (Arrowheads) are visible. Compared to group (A) figure is histologically better but in comparison to (C), it shows marked pathological changes.

Figure No. 4: Shows Histopathological section of Liver taken from Group C
Liver section of group (C) showing intact histologic arrangement. The hepatocytes (Thin arrows) are arranged as single-cell thick radiating plates surrounding the central vein (CV) with narrow sinusoids (Thick arrows) placed in between. Portal vein (Arrowheads) normal in diameter. No congestion and rare inflammatory cells are present. Almost absent cytoplasmic vacuoles. Much better histology in comparison to (B) and excellent in comparison to (A).

DISCUSSION

Alcoholic hepatitis is a prevailing complication not just in the west but all around the world and within our society. The liver becomes severely damaged, causes severe morbid complications. Consequently, 40% of individuals aren't even eligible for a liver transplant due to their chronic alcohol use. With its ability to neutralize free radicals and the potent anti-inflammatory effects of Naproxen sodium, Vitamin C was studied to see if it may have a hepato-protective effect.

We assessed the hepato-protective effects based on two parameters, Hematological and Histological. ALT, AST, and GGP are commonly used hepatobiliary markers; an increase in these enzymes indicates a hepatocellular injury or bile obstruction. There was a remarkable rise in all of the hepatobiliary markers in group A, which also corresponds with the cells' histology. The rise is due to degeneration and necrosis of hepatocytes resulting in leakage of these enzymes into the blood; these findings are similar to another study of Zaidi et al. (2005), who also showed an increased level of transaminases after hepatocellular damage. Compared to group B, the levels were significantly better than what was in group A but still above the normal ranges. This was because of the reduction in oxidative stress that was accomplished by the antioxidant effects of Vitamin C, thereby protecting the cells' vitality and minimizing cellular leakage. Similar results were also reported in another study. However, the best results were produced by group C in which simultaneous infusion of both vitamin C and Naproxen lead to transaminase levels being marginally above the normal upper limits but within limits of normal values. Both therapeutic agents had a significant impact on keeping the levels of ALT in normal ranges.

Hepatocellular degeneration caused directly by Ethanol was observed in the liver of rats treated with alcohol for ten days. Vacuolar degeneration was also observed, along with changes in the generalized architecture of the hepatic lobules. These histopathological findings were also seen in other previous studies. Necrosis in the pericentral region was also visible along with an increased number of mononuclear inflammatory cells is also seen under the microscope. All these points towards severely damaged hepatic tissue seen in group A rats. Group B rats, on the contrary, showed milder damage as compared to group A. This probably has to do with the anti-inflammatory effect of Naproxen along with the antioxidant effect of Vitamin C halt severe hepatotoxicity caused by Ethanol. These findings are in line with other previous studies carried out by researchers. Remarkably, the nearly standard architecture of hepatic lobule was observed in group C. Our results thus prove that there are hepa-protective effects of Naproxen and Vitamin C. However, further studies need to be carried out to see if other antioxidants (such as Vitamin A and E) or anti-inflammatory agents such as other members of the NSAIDs family or Steroids can replicate the same effects that were seen in our study.

CONCLUSION

Group B and C both had positive results and showed a significant difference when it came to hematological and histological parameters compared to group A. This was mainly down to the protective affection by Vitamin C and Naproxen. Due to their particular antioxidant and anti-inflammatory actions, these two agents synergistically produced a positive effect on the liver of rats, even in the presence of alcohol intoxication. Further studies on other agents can be carried out to see if they can deliver the same hepatoprotective effect as these two agents managed to do.

Author’s Contribution:
Concept & Design of Study: Raja Faisal
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Data Analysis: Ghazala Panhwar, Syed Liaquat Ali and Shahid Korai
Revisiting Critically: Raja Faisal, Nazia Qamar
Final Approval of version: Raja Faisal

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

REFERENCES

15. Kaplan MM; Serum alkaline phosphatase-another piece is added to the puzzle. Hepatol 1986;6: 526-528.
Probiotics Accelerate the Process of Neovascularization in Wound Healing: A Comparative Study in Rats

Hina Khan1, Shagufa Memon4, Shahid Korai1, Ahmed Mujtaba Memon5, Farheen Hameed3 and Shahid Kamran3

ABSTRACT

Objective: To assess the role of probiotics in accelerating the process of Neovascularization in wound healing.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted at the Al-Tibri Medical College and Hospital, during May 2018 to December 2018.

Materials and Methods: Total 18 male albino rats were selected through randomized sampling and divided into three groups; Group A was given topical normal saline, Group B was given topical probiotic (Lactobacillus Acidophilus), and Group C was given topical antibiotic. The interventional agent was given once for 21 days. Samples were taken on the 3rd, 7th, 14th, and 21st day to observe under the microscope at 400x. Data were analyzed using SPSS Version 20.0, and the mean between the groups was compared using ANOVA and post hoc Tukey's test. A P-value of ≤0.05 was considered statistically significant.

Results: Neovascularization was seen most among the group B candidates that were given topical probiotics. A significant difference (P-value ≤0.05) existed when comparing Group B with Group A and comparing Group B with Group C.

Conclusion: The results revealed the effective role of topical probiotic in accelerating the process of neovascularization, and due to their potent anti-inflammatory effects the probiotic accelerates the early availability of immune cells at site of healing and faster the process of repairing.

Key Words: Wound, Probiotic, Neovascularization, Healing

INTRODUCTION

Wound damage to the epithelial barrier in the superficial or deep layer of skin requires repairing through the generalized process of healing. There are so many factors that can accelerate or delay the healing process. The healing process comprises extracellular interactions, acceleration of chemical mediators, and availability of inflammatory cells at the site of healing. Repairing of the wound can be assessed through biological, chemical, or histological parameters. The healing process mainly depends on the balance between the host and the microbes.

Naturally, the body with different compositions and distributions of the host microorganisms may help in healing and maintain immunity like microbes from intestinal flora. Currently, there are so many therapeutic agents available for wound repair, and surgeons or physicians can adopt different strategies to fasten the healing process, either topically and orally like topical antibiotics, anti-inflammatory, and probiotics. The probiotics are the organisms that ferment energy substrates that can be resistant to multiple pathogens. By WHO, probiotics are a live organism that can administer in an adequate amount, providing healthy and beneficial effects. Commerically different compositions of probiotics, probiotics, and symbiotics can be isolated for the various resources in the form of different species. The most common species used by the clinicians are Lactobacillus, and can modulate the healing process. The study's objective is to evaluate the role of topical probiotics in the acceleration of the neovascularization process of wound repair compared with topical antibiotics and steroids. Due to unhealthy environmental conditions, the requirement of early wound closure is an essential part of therapy, and prevention from late complications can be hold by taken such benefits from this research.
MATERIALS AND METHODS

An experimental study was designed at Al-Tibri Medical College and Hospital, Isra University. Karachi campus. A total of 18 male albino rats were selected through randomized sampling, and they were subdivided into three groups based on topical treatment. Each group comprises of 6 animals and weight between 150 to 250mg. After taking ethical approval from the concerned ethical committee, the study was conducted from May 2018 to December 2018. Group A was given topical normal saline once daily (control group), Group B was given probiotic topically containing $10^{10}$ or $10^{11}$ CFU/ml, and Group C was given topical antibiotic (neomycin cream) once daily for 21 days. The probiotic (Lactobacillus Acidophilus) were isolated from yogurt, and for that purpose, the fresh yogurt was purchased from the market, and organisms were isolated by the department of Microbiology (PCSIR) Karachi. The organisms were grown on MRS agar plates and incubated at 34°C for the next 48 hours. For the confirmation of the bacterial species, a catalase test was performed because the lactobacilli are catalase-negative. The fresh culture was taken after every 48 hours, and liquid form was given as a topical application in Group B. Wound was formed at the dorsal surface of the rat with the area of 2x2cm{sup 2}, after given anesthesia with ether and then the animals were kept in separate cages with tagging of groups. During the study, the different samples were taken on various days, like day 3, 7, 14, and 21. The sample of the dermis was taken from the site of the wound to observe the healing process. The microscopic slides were prepared to assess the skin’s microscopic features through a light microscope at 400x. In this study, we observed the numbers of blood vessels as a process of Neovascularization among different therapeutic groups. The data were analyzed through SPSS version 20.0. To compare the mean between the groups, the ANOVA was applied along with post hoc Tukey’s test. The level of significance was considered P=<0.05.

RESULTS

Figure: 1.1 shows the Mean numbers of blood vessels among different therapeutic groups on Day 3, 7, 14, and 21.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 14</th>
<th>Day 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>B vs A</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>B vs C</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 1: Shows level of significance between the different therapeutic groups

One Way ANOVA Post hoc Tuckey’s test applied

Figure No.2: Photomicrographs of histological slides of skin x400 on day 7 among the different groups.

DISCUSSION

Microbial colonization can occur immediately after the development of a wound. The bacterial load can have a significant impact on wound healing. Potential new talk about therapeutic agents is ongoing, regulating the microbes, pathogens, and the body's immune system, thereby accelerating wound healing{sup 11}. Lactobacillus treat wounds resulted in reduction of wound size at favorable time period when compared with the group treated with normal saline. Our study successfully showed that probiotics resulted in efficient contraction of wound area when compared with the other groups in our study. The results showed that Lactobacillus successfully helped in speeding up angiogenesis and repair. One of the researchers used different species of Lactobacilli (Lactobacillus Plantarum and Lactobacillus Brevis) but showed similar results to our study in which the interventional groups experienced reduced in the number of neutrophils and acceleration of wound healing{sup 12}. Productions of white blood cells such as macrophages were stimulated by Lactobacillus. New fibroblast cells proliferation and abundance were also increased. These two cells synergistically helped in neovascularization. New blood vessel formation contributes in the healing process of the wound along with the formation of granulation tissue in a process called hemostasis. Hemostasis is necessary for proper healing and provides access to inflammatory cells at the repair site. The probiotics treated groups showed the best hemostasis action amongst all the groups. Lactobacilli have shown to suppress the inflammation in animal models of experimental colitis, and this can also be seen...
in our study as the inflammatory phase of wound healing subsides more quickly. The proliferative phase, which results in granulation tissue formation and angiogenesis, took place much earlier, thereby accelerating wound healing.13-14 Per Tamawski et al. 2005, probiotics may even help in stimulating growth factors and cytokines. Due to this, increased migration of fibroblast cells can occur at the site of injury. Lactobacillus treated wounds had a higher quantity of fibroblast cells compare to the rest of the groups. Fibroblast is important and helps in the synthesis of collagen as well as areolar tissues. Fibroblast and macrophages help in angiogenesis at the site of damage. Fibroblasts favor the formation of new collagen fibers, as well as new vessel formation. These factors are critical in helping earlier re-epithelialization of tissue. 15. This re-epithelialization process was also shown by Mehrabani et al.: 2010, who used Rhus Coriaria extracts and showed an acceleration in wound healing with its effects due to an increase in re-epithelialization, collagen deposition and a decrease in MPO activity.16. This treatment can also be beneficial in individuals who suffer from systemic complications from wound healing such as diabetes, as shown in the study by Mohseni et al. 2017. Furthermore, Campos et al. 2020 also showed in diabetic rats that perioperative supplementation with probiotics resulted in better skin wound healing.18. This can once again be related to a reduction in the inflammatory phase of wound healing and increased Neovascularization and type I collagen deposition, this is in accordance with our study. This strongly suggests that probiotics can be used in diabetic patients with impaired wound healing due to persistent inflammatory cytokines being developed. Probiotics should strongly be considered as a strong contender as a therapeutic agent in wound healing. Our previous studies have also shown that its Neovascularization, anti-inflammatory ability, and wound healing acceleration make it a robust therapeutic agent for people with wounds.19. However, it must be noted that although it is a very viable agent in wound healing, there are other treatment options available such as Low-level laser therapy, which has been proven to be more effective than probiotics.20-21 More studies are required to assess probiotics with other agents used in wound healing and test them in individuals with local and systemic complications that may delay wound healing and see what effect probiotics may have in these parameters.

CONCLUSION

The results revealed the effective role of topical probiotic in accelerating the process of neovascularization, and due to their potent anti-inflammatory effects the probiotic accelerate the early availability of immune cells at site of healing and faster the process of repairing.

REFERENCES

Awareness and Compliance of Paramedics Towards Airborne Infection Control in Sindh

Ajmaal Jami1, Umer Kazi2, Bushra Zulfiqar3, Ahmed Mujtaba Memon5, Israr Ahmed Bhutto6 and Hina Khan4

ABSTRACT

Objective: To evaluate the knowledge and compliance of paramedics regarding preventive measures in Sindh.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Naz Memorial Hospital, Karachi from January 2020 to May 2020.

Materials and Methods: 100 numbers of paramedics from different medical institutes through snow ball sampling selected. The valid questionnaire was filled by the paramedics and received via email with the ethical approval from concerned ethical bodies. Both gender with 18 years and above age were included, no medical professional other than paramedics were included in present study. Both questionnaires were filled by the participant, who voluntarily participates in the study. The data was expressed in the form of frequency and percentage through SPSS version 21.0

Results: 100% of paramedic’s well response the knowledge at higher level of appreciation regarding preventive measures and their application at their work places. They are well trained and excellent skills in their field of health care, the deficit area if the availability of resources for both the workers and patients.

Conclusion: In fighting a battle against the corona virus team of paramedics are generally highly equipped with knowledge, skills and attitude. The only barriers at their work place are the availability of resources that can make hazards in management of illness and meanwhile cure the patients and self-protection are at high risk. If the ministry involved and make sure the proper accessibility of all protective maneuvers at the site of health management, the outcomes will be more than the thought.

Key Words: Cough etiquettes, Corona virus, air born disease, preventive measures

INTRODUCTION

The Coronavirus pandemic has been an issued faced by the entire medical world since the start of the year 2020. This has led to the hospitals being overwhelmed due to the high infection rate of this diseases also affecting surveillance of further outbreaks systems and response measures to other diseases.

Previously, just like the current pandemic of the SARS-COV2, we also saw epidemic of SARS in china in 2003, and MERS in the middle east all having the commonality of being from the same family of RNA positive Viruses, spreading mainly by airborne droplets from, which are generated through coughing and sneezing eventually leading to transmission from person to person. If proper washing of hands and respiratory hygiene isn’t followed, they can become a source of infection for other either directly or indirectly. The people working in this pandemic, such as the doctors and most importantly the paramedical staff are at the highest risk of contracting the infection from infected people they are treating. The awareness and knowledge concerning with the transmission of people working in HealthCare setting is very important, in order to stop the further spread of these types of virus which have a high transmission rate. Hence it is very important that during outbreaks like these doctors, nurses, and paramedical staff follow the correct infection guidelines issued by various health agencies and administration in order to prevent further spread of the diseases. On 26th February 2020, the first case of SARA-COV2 was also reported in Pakistan and it became necessary for all workers in hospital settings to be prepared for the worse possible outcome by following proper infection control guidelines and PPE...
in order to contain the spread of the virus. Hence a study was conducted in order to assess the awareness and compliance of paramedics towards airborne infection control in Sindh. The basic concept of the study to highlight the barriers, that were creating hurdles while serving to the community, and also impact on their health. Community based health departments can establish the new policies and SOPs for the hospital and higher authorities.

MATERIALS AND METHODS

The cross sectional study was designed at Naz Memorial Hospital, and conducted from January to May 2020. Total 100 numbers of paramedics were included from different medical institutes through snow ball sampling. The valid questionnaire was filled by the paramedics and received via email with the ethical approval from concerned ethical committee. Both gender with 18 years and above age were included, no medical professional other than paramedics were included in present study. Both questionnaires were filled by the participant, who voluntarily participates in the study. The data was expressed in the form of frequency and percentage through SPSS version 21.0.

RESULTS

Table No.1: Shows the Frequency and Percentage of Knowledge regarding preventive maneuvers among the paramedics

<table>
<thead>
<tr>
<th>Knowledge regarding cough Etiquettes</th>
<th>Reactions</th>
<th>Frequency &amp; %age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of transmission</td>
<td>Through coughing, spitting &amp; sneezing</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>Direct contact</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>Through blood</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Preventive methods used to avoid transmission</td>
<td>Cover the month during coughing</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>Face mask</td>
<td>78(78%)</td>
</tr>
<tr>
<td></td>
<td>Don’t come in contact with others</td>
<td>68(68%)</td>
</tr>
<tr>
<td></td>
<td>Avoid spitting &amp; generally used dustbin</td>
<td>76(76%)</td>
</tr>
<tr>
<td></td>
<td>others</td>
<td>17(17%)</td>
</tr>
<tr>
<td>Do you have any idea about cough etiquettes?</td>
<td>Yes</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0(0%)</td>
</tr>
<tr>
<td>What is your main source of information?</td>
<td>Physicians</td>
<td>53(53%)</td>
</tr>
<tr>
<td></td>
<td>paramedics</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>Friends &amp; family</td>
<td>24(24%)</td>
</tr>
<tr>
<td></td>
<td>Television, social media &amp; internet</td>
<td>95(95%)</td>
</tr>
<tr>
<td></td>
<td>others</td>
<td>11(5.5%)</td>
</tr>
<tr>
<td>Can you explain respiratory hygiene?</td>
<td>Correctly reply</td>
<td>94(94%)</td>
</tr>
<tr>
<td></td>
<td>Incorrectly reply</td>
<td>6(6%)</td>
</tr>
<tr>
<td>Can you explain hand hygiene?</td>
<td>Correctly reply</td>
<td>92(92%)</td>
</tr>
<tr>
<td></td>
<td>Incorrectly reply</td>
<td>8(8%)</td>
</tr>
<tr>
<td>In your opinion cough etiquettes can help to prevent the transmission of infection?</td>
<td>Correctly reply</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>Incorrectly reply</td>
<td>0(0%)</td>
</tr>
</tbody>
</table>

Table No.2: Shows the Frequency and Percentage of Application of preventive maneuvers among the paramedics

<table>
<thead>
<tr>
<th>Application of cough etiquettes</th>
<th>Reactions</th>
<th>Frequency &amp; %age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you practicing the cough etiquettes during daily life?</td>
<td>Yes</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Which one of the following Preventive methods you are using to avoid the transmission?</td>
<td>Cover the month during coughing with hand</td>
<td>71(71%)</td>
</tr>
<tr>
<td></td>
<td>Cover the month during coughing with handkerchief/tissue</td>
<td>14(14%)</td>
</tr>
<tr>
<td></td>
<td>Face mask</td>
<td>92(92%)</td>
</tr>
<tr>
<td></td>
<td>Avoid spitting &amp; generally used dustbin</td>
<td>78(78%)</td>
</tr>
<tr>
<td></td>
<td>others</td>
<td>0(0%)</td>
</tr>
<tr>
<td>How often you practice these measures while coughing?</td>
<td>Constantly</td>
<td>57(57%)</td>
</tr>
<tr>
<td></td>
<td>Infrequently</td>
<td>43(43%)</td>
</tr>
<tr>
<td>What are the reasons behind the non-compliance</td>
<td>Lack of knowledge</td>
<td>0(0%)</td>
</tr>
<tr>
<td></td>
<td>Severity of symptoms</td>
<td>37(37%)</td>
</tr>
<tr>
<td></td>
<td>Unavailability of tissues/ handkerchief</td>
<td>65(65%)</td>
</tr>
<tr>
<td></td>
<td>No such benefit</td>
<td>0(0%)</td>
</tr>
<tr>
<td></td>
<td>others</td>
<td>10(10%)</td>
</tr>
<tr>
<td>Are you habitual for hand washing after an episode of coughing and sneezing?</td>
<td>Constantly</td>
<td>31(31%)</td>
</tr>
<tr>
<td></td>
<td>Infrequently</td>
<td>69(69%)</td>
</tr>
<tr>
<td>How frequent you are used to for such measures?</td>
<td>Constantly</td>
<td>68(68%)</td>
</tr>
<tr>
<td></td>
<td>Infrequently</td>
<td>32(32%)</td>
</tr>
<tr>
<td>Which one of the following are used to for hand hygiene?</td>
<td>water</td>
<td>39(19.5%)</td>
</tr>
<tr>
<td></td>
<td>water and soap</td>
<td>17(17%)</td>
</tr>
<tr>
<td></td>
<td>Sanitizers</td>
<td>83(83%)</td>
</tr>
<tr>
<td>What the reasons behind the non-compliance of preventive measures</td>
<td>Lack of knowledge</td>
<td>100(100%)</td>
</tr>
<tr>
<td></td>
<td>Unreachability of water, soap or sanitizers</td>
<td>83(83%)</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>17(17%)</td>
</tr>
</tbody>
</table>

Out of 100 numbers of respondent 44(44.0%) were male and 56(56.0%) were female
Mean age of male participants was 29.3 ± 0.23 and Mean age of female was 31.4 ± 1.45
Figure: 1 shows Percentage of Paramedics Working at different Departments of Hospitals
Table 1: shows Frequency and percentage of awareness of paramedics regarding preventive measures
Table 2: shows Frequency and Percentage of Compliance of paramedics regarding preventive measure.
the etiology and its complication of the concerned disease, while below 50% of the participants showed low level of awareness about the main source of infection spread and basic epidemiology of the respective disease. In comparison with the level at our domain, 100% of the paramedics were well aware about the etiological factors, source of spread, preventive measures and maneuvers. The only deficit corner is the resources that act as a barrier in compliance of the respiratory and hand hygiene (8). The study evidences about the perception of paramedics in controlling the respiratory illness at emergency department. The paramedics concluded the essential availability of resources for the prevention of other patients and health care providers, without these safety measures the life of all in danger and not able to control the infectious diseases. Similar requirement was documented in our study the availability of required facilities for the application of preventive measures. This can affect the compliance of precautionary measures in daily work (9). In Japan the study was done regarding the preparedness of primary care centers for the precautionary measures towards the pandemic Influenza. The availability of N95 masks, gowns and eye protection devices at very low rate was stocked. That was below 50% of the total stocked. Similar at our country, the resources are limited and preparedness was at low level in accordance of resources while the knowledge and perception are at higher level (10-11). In Pakistan the study was done about the infection control of tuberculosis, the similar factors were mentioned, availability of recourses for both patients and health care professionals. In comparative to the recent study the education level is higher than the mentioned study, in previous results further retraining was the requirement of the field workers. They need advance level of knowledge to deal with the situation as in this study the paramedics are highly prepared and well aware the epidemiology of the current disease with low level of facilitation form the higher authorities(12, 13, 14).

CONCLUSION
In fighting a battle against the airborne diseases, team of paramedics are generally highly equipped with knowledge, skills and attitude. The only barriers at their work place are the availability of recourses that can make hazards in management of illness and meanwhile cure the patients and self-protection are at high risk. If the ministry involved and make sure the proper accessibility of all protective maneuvers at the site of health management, the outcomes will be more than the thought.

Author’s Contribution:
Concept & Design of Study: Ajmaal Jami
Drafting: Umer Kazi, Bushra Zulfiquar
Data Analysis: Ahmed Mujtaba Memon, Israr Ahmed Bhutto and
REFERENCES


7. Bar-Dayan Y, Manor SN, Boldor N, Kremer I, Barak MI, Bar-Dayan Y. Relationship Between Sources of Information and the Willingness of Healthcare Workers to Risk their Lives for a Patient During the Peak of A/H1N1 Pandemic in Israel. The Open Epidemiology J 2010 9;3(1).


Does Orthoptic Exercise Improve Convergence Insufficiency? A Prospective Study at Al-Ibrahim Eye Hospital

Israr Ahmed Bhutto¹, Asif Mashood Qazi², Saima Majid², Attiya Zehra Rizvi² and Munawwar Hussain²

ABSTRACT

Objective: To see if orthoptic exercise improves convergence insufficiency (CI).

Study Design: A Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Al-Ibrahim Eye Hospital, Karachi for 08 months Jan.2020 to Aug. 2020.

Materials and Methods: 60 numbers of patients suffering from CI were taken in the study after taking consent from them. The near point of convergence (NPC) and the fusional range of all the patients were measured. All patients were prescribed pencil push-up tests for one month after which all variables were reassessed. To assess the difference that orthoptic exercise had on CI patients, one-way ANOVA chi-square test was applied keeping the P-value≤0.05 as statistically significant.

Results: Significant difference (P-value≤0.05) in all measured variables after patients carried out pencil push-up tests for one month. NPC improved in all patients along with improvement in fusional amplitude.

Conclusion: It can be concluded that Orthoptic exercises had a beneficial effect on patients with CI. It is still the primary treatment option when it comes to reducing the symptoms of CI.

Key Words: Convergence insufficiency, Orthoptic Exercise, Near Point of Convergence, Pencil push-up test

INTRODUCTION

Convergence insufficiency, often denoted only as CI, is a condition of binocular vision dysfunction, characterized by patient unable to accurately converge, or sustain accurate convergence while focusing on objects nearby. CI is associated with many ocular symptoms such as eyestrain, blurred vision, and double vision, along with other symptoms such as headaches, having to re-read, reading slowing, troubling in remembering what was read, and sleepiness.¹,² CI affects levels of achievement and is attributed to negative factors such as health and quality of life.³ The causality for CI is typically unknown; however, the intraocular muscles are involved in the misalignment of the eye.⁴ The prevalence of Convergence Insufficiency is said to be about 4%.⁵,⁶ Convergence insufficiency generally presents in age sets of less than 9 years, although increase burden of near vision work and longer working hours can cause it to appear ahead of time.⁷ CI can be clinically diagnosed as an exodeviation that is greater at near than at distance, a diminished near point of convergence (NPC), and redundant positive fusional vergence at near (PFV).⁸ Convergence insufficiency however common is treatable. The treatment of choice for patients with CI is intensive Orthoptic therapy.⁹ Pencil push-ups and use of accommodative targets have a strong role in treatment of CI. Orthoptic exercises have been deemed as an effective means of reducing symptoms of CI and decompensating exophoria.¹⁰ Pencil push-ups and base-in prism reading glasses are one of the most commonly prescribed treatments, with 87% optometrists and ophthalmologists prescribing these two treatment methods fairly consistently to patients.¹¹ Due to a lack of quality of information to eye care to providers regarding CI and its improvement through Orthoptic exercises in Pakistan. A cross-sectional study was conducted at Al-Ibrahim Eye Hospital to assess the outcome of Orthoptic Exercise in patients suffering from Convergence Insufficiency.

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MATERIALS AND METHODS
After taking approval from ethical review board, an observational longitudinal study was conducted at the squint clinic of Al-Ibrahim Eye Hospital Karachi. The duration of the study was for 8 months in which 60 patients were selected based on non-probability convenience sampling technique. All the patients that were taken in this study were those patients which had a confirmed diagnosis of convergence insufficiency and were aged between 15-30 years. All patients were consented before being included in the study. For all the patients, we measured the near point of convergence (NPC) using the Royal Air Force Rule (RAF). Furthermore, the fusional range was checked with the help of prism fusional range (PFR), with the help of prisms. After measuring both of these variables, the patient was prescribing pencil push-up tests for one month after which both variables were checked once again on follow up. Data was analyzed using statistical package of social science (SPSS) Version 21.0. The entire data was continuous and presented as Mean and Standard deviation. To assess the difference of orthoptic exercise on convergence insufficiency (CI), we applied one-way ANOVA and CHI square test while keeping the P-Value <0.05 as statistically significant.

RESULTS
In this research total numbers of patients are 60, from which the most number of patients were between the age group of 15 to 20 years 28(46.7%). And the minimum number of patients is 6(1%) and their age 26 to 30 years. Out of the 60 patients, the maximum frequency of patients was females, the number of female patients is 32 (53.3%). And minimum patients are male number of patients 28(46.7%) patients.

Table 1: In this research the number of patient 60. The maximum near point of convergence in 10cm improve the number of patients was 35(58.3%) and the minimum 15cm improve the number of patients was 8(13.3%). no change in convergence after orthoptic exercise in 6 patients (10.0%).

Table No.1: Frequency and Percentage of outcome related with Orthoptic exercise pre and post Near point of convergence

<table>
<thead>
<tr>
<th>Near point of convergence</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>same</td>
<td>6</td>
<td>10.0%</td>
</tr>
<tr>
<td>5cm improve</td>
<td>11</td>
<td>18.3%</td>
</tr>
<tr>
<td>10cm improve</td>
<td>35</td>
<td>58.3%</td>
</tr>
<tr>
<td>15cm improve</td>
<td>8</td>
<td>13.3%</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table No.2: Frequency and Percentage of Outcome related with Orthoptic exercise pre and post Near point of convergence with glasses

<table>
<thead>
<tr>
<th>Near point of convergence with glasses</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>same</td>
<td>2</td>
<td>3.3%</td>
</tr>
<tr>
<td>5cm improve</td>
<td>3</td>
<td>5.0%</td>
</tr>
<tr>
<td>10cm improve</td>
<td>20</td>
<td>33.3%</td>
</tr>
<tr>
<td>15cm improve</td>
<td>2</td>
<td>3.3%</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>45.0%</td>
</tr>
</tbody>
</table>

DISCUSSION
Convergence insufficiency is an issue that affects the quality of life of individuals suffering from it. We conducted this study to see if orthoptic exercises have a positive impact on convergence insufficiency or not. Since the first description of CI in 1855, orthoptic exercises have been the mainstay of treating CI. It works by improving the fusional convergence in patients with CI (12). In our study 35 (58.3%) patients had an improvement in near point of convergence at 10cm, whereas 8 (13.3%) had an improvement of 15cm. Near point of convergence with glasses improved in 20 (33.3%) patients at 10cm, and 2 (3.3%)
patients exhibited improvement at 15 cm. Westman et al. in his study also showed that effective treatment for children and adults with CI and asthenopic symptoms is orthoptic exercises. It was also suggested that orthoptic exercises can relieve longstanding symptoms of CI (13). In our study, we used pencil push-up tests as a form of orthoptic exercise and see if it can improve the NPC and symptoms of CI patients. We saw significant improvement (P-value ≤ 0.05) in NPC. Similarly, another study conducted to assess if pencil push-up tests are beneficial in patients with CI also saw improvement in NPC prime fusion vergence (PFV) and reduction in the symptoms of the patients (14). We only used pencil pushup tests to see if there is an improvement in CI, in future studies, other methods can also be used to see if it has an improvement in CI. Studies have been done on other types of orthoptic exercises to assess their effectiveness. For instance, a study was conducted to see the outcome of home-based computer orthoptic exercise program. The study concluded by stating that home-based computer orthoptic exercise program reduced symptoms of CI and had an improvement on NPC and fusional amplitudes, thus making it an effective option for treating symptoms of CI (15). Improvements in the fusional reserve negative, fusional reserve positive, fusional reserve negative at near, and fusional reserve positive were also seen in our study showing the beneficial effects of orthoptic exercise. Another study also showed that Positive fusional vergence improved in patients undergoing orthoptic exercises, aligning with our study (16). Overall we can conclude that orthoptic exercise is highly beneficial in improving convergence insufficiency. However, more studies can be conducted targeting different age groups and evaluating other methods besides pencil pushup tests.

CONCLUSION

The study concluded that orthoptic exercises are a strong tool in treating convergence insufficiency. Orthoptic exercises should remain the mainstay treatment in treating and reducing symptoms of CI.

Author’s Contribution:
Concept & Design of Study: Israr Ahmed Bhutto
Drafting: Asif Mashood Qazi
Data Analysis: Saima Majid, Attiya Zehra Rizvi, Munawwar Hussain
Revisiting Critically: Israr Ahmed Bhutto, Asif Mashood Qazi
Final Approval of version: Israr Ahmed Bhutto

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

REFERENCES

Exercise Electrocardiogram Testing in Asymptomatic Patient with Type-II Diabetes and Left Ventricular Diastolic Dysfunction

Zeeshan Hassan¹, Aamir Siddique² and Zaheer ud Din Babar³

ABSTRACT

Objective: To find the exercise electrocardiogram testing in asymptomatic patient with Type-II diabetes and left ventricular diastolic dysfunction.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Allama Iqbal Memorial Teaching Hospital, Sialkot during January 2019 to November 2019.

Materials and Methods: The data was collected from 50 patients of type II DM. These all patients has normal electrocardiogram (ECG) and normal systolic function.

Results: The data was collected from 50 patients of both genders. The mean age of the patients was 47.83±5.61 years. After getting data the results were divided into two parts. There were 25 patients in group A and 25 patients group B. The mean duration of diabetes is 2.5±5.61 years. There were 20 males and 30 females in this data. There were no significant difference of fasting blood sugar in both groups. There was no statically significant difference between two groups regarding left atrial dimension, aortic root dimension, LV end-diastolic dimension, ejection and LV mass.

Conclusion: It is concluded that It is concluded that coronary supply route sicknesses is a typical issue in DM, with diastolic brokenness and increment uniquely in patients with positive pressure practice electrocardiography.

Key Words: Electrocardiogram Testing, Asymptomatic Patient, Type-II Diabetes, Left Ventricular Diastolic Dysfunction


INTRODUCTION

Patients with type 2 diabetes often complain of fatigue and reduced exercise capacity which might be related to other illness conditions, for example, hypertensive left ventricular hypertrophy as well as coronary supply route sickness, and the resulting improvement of cardiovascular breakdown, however the presence of diabetes may freely add to the hindered practice limit. A few examinations have uncovered that activity limit diminishes in patients with type 2 diabetes and is related with cardiovascular mortality¹.

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Doppler echocardiography is one of the most valuable clinical apparatuses for the appraisal of LV diastolic capacity. Doppler lists of LV filling are utilized for analytic purposes as well as for building up guess and assessing the impact of treatment. LV diastolic brokenness may speak to the primary phase of diabetic cardiomyopathy strengthening the significance of the early assessment of diastolic capacity in individual with diabetes.

Diabetes is related with expanded cardiovascular confusions, the most widely recognized of which are ischemic cardiomyopathy and LV brokenness. Diabetes is likewise connected with HF, basically through its association with hypertension and coronary vein disease. Diabetes mellitus (DM) speeds up the cycle of coronary atherosclerosis and practical and basic heart disabilities.

DM isn't just a huge autonomous danger factor for the improvement of atherosclerotic ischemic coronary illness or ventricular hypertrophy, yet it is likewise ready to trigger a diabetic cardiomyopathy because of some metabolic cycles: restraint of exchanging inside the cardiomyocyte from free unsaturated fat (FFA) to glucose digestion, dysregulation of FFA digestion with expanded take-up, diminished FFA oxidation, decrease of peroxisome proliferator-activated receptor (PAPAR), increment of PAPAR-g and insulin-obstruction, and expanded intracellular lipogenesis which prompts cardiomyocyte lipotoxicity.

MATERIALS AND METHODS

This descriptive study was conducted in Allama Iqbal Memorial Teaching Hospital, Sialkot during January 2019 to November 2019. The data was collected from 50 patients of type II DM. These all patients has normal electrocardiogram (ECG) and normal systolic function.

Exclusion criteria: Patients suffering from hypertension, ECG abnormalities and muscular disorder were excluded from this study.

Inclusion criteria: All the patients who have type II DM, and ready to participate in the study.

Data collection: The data was collected from 50 patients. All patients went through complete reverberation Doppler study utilizing an industrially accessible echocardiography machine. LV measurements, left atrial measurements, divider thickness and launch part were estimated. Besides, transmitral stream was finished by beat wave Doppler between the tips of mitral valve flyers from four-chamber see measure top E wave speed, top A wave speed, E/A proportion, E wave deceleration time, and isovolumic unwinding time (IVRT). Exercise ECG was done to all patients to identify ischemic coronary illness and those with positive exercise ECG will inclined to coronary angiography. The data was collected and analysed by using excel 2010.

RESULTS

The data was collected from 50 patients of both genders. The mean age of the patients was 47.83±5.61 years. After getting data the results were divided into two parts. There were 25 patients in group A and 25 patients group B.

Group A: diabetic patients with LV diastolic dysfunction with negative stress ECG

Group B: patients with LV diastolic dysfunction with positive stress ECG.

The mean duration of diabetes is 2.5±5.61 years. There were 20 males and 30 females in this data. There were no significant difference of fasting blood sugar in both groups. There was no statically huge contrast between two gatherings with respect to left atrial measurement, aortic root measurement, LV end-diastolic measurement, launch and LV mass. The exhibition of activity stress test has appeared in diabetics, a lower increment of E' speed (12.02±1.6 cm/sec versus 16.7±1.3 cm/s, p<0.01), slight increment of A' speed (p=0.01) contrasted and control subjects.

Table No.1: Tissue Doppler Echocardiography characteristics of both groups after the stress test

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>E' (cm/sec)</td>
<td>12.02±1.6</td>
<td>16.7±1.3</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>A' (cm/sec)</td>
<td>12.35±1.8</td>
<td>13.1±1.2</td>
<td>P=0.02</td>
</tr>
<tr>
<td>E'/A'</td>
<td>0.89±0.1</td>
<td>1.8±1.2</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>S' (cm/sec)</td>
<td>10.22±0.95</td>
<td>12.92±1.2</td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>

In group A there were 25 patients who were negative stress ECG in group A and 54% in group B. The statistical analysis showed a significant increase in the number of stress exercise ECG-positive patients among diabetic patients with diastolic dysfunction than diabetic patients without diastolic dysfunction (P<0.001).

Table No.2: Stress exercise ECG in group A and group B

<table>
<thead>
<tr>
<th>Exercise ECG</th>
<th>Group A</th>
<th>Group B</th>
<th>X²</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ve</td>
<td>0</td>
<td>46</td>
<td>37</td>
<td>0.001</td>
</tr>
<tr>
<td>-ve</td>
<td>100</td>
<td>54</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table No.3: Functional Capacity

<table>
<thead>
<tr>
<th>Functional Capacity</th>
<th>Group A</th>
<th>Group B</th>
<th>X²</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>0.1</td>
<td>9.1</td>
<td>15.91</td>
<td>0.100</td>
</tr>
<tr>
<td>9.9</td>
<td>67.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>38.9</td>
<td>12.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>61.1</td>
<td>11.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Diabetes is notable to altogether expand CVD hazard, yet can't be viewed as a CHD same, because of extraordinary heterogeneity of the patients. All things considered, life-time danger of CHD is by all accounts....
very high in practically all individuals with the infection, which calls for individualized methodology and assessment for the presence and conceivable treatment of an incredible assortment of other as often as possible coinciding danger factors that can expand this danger [8].

Aside from hazard factor treatment, be that as it may, the estimation of obstructive treatment of coronary atherosclerosis (with the exception of the instance of intense coronary conditions) stays disrupted, on the grounds that all earlier randomized preliminaries have restrictions and are pointing towards equipoise, and accordingly, routine screening for quiet CHD in asymptomatic people with DM isn’t right now suggested, as long as cardiovascular danger factors are dealt with [9].

Conversely, old style measures dependent on CE don't appear to have a similar capacity. Moreover, this irregularity is by all accounts related to the diabetic cardiomyopathy. Almost certainly, metabolic variations from the norm may assume a significant job [10]. Exploratory data from creature models of diabetes unequivocally uphold a causal part of insulin obstruction in the advancement of diastolic brokenness. Treatment with metformin forestalled the improvement of cardiomyocyte brokenness [11]. In an insulin-safe pre-diabetic rodent model, Mizushige et al. seen that the variations from the norm of diastolic filling happened before the advancement of straight to the point hyperglycaemia [12].

Histopathology contemplates proved expanded myocyte fibrosis and collagen statement, recommending that these auxiliary adjustments assume a significant function in the advancement of diastolic brokenness [13]. Another factor that may weaken diastolic capacity is hyperglycaemia. There is trial proof that momentary hyperglycaemia can modify cardiomyocyte contraction and unwinding. Moreover, high glucose focus causes the arrangement of cutting edge glycation end products (AGE) that change collagen structure and meddle with the arrangement and unwinding. Moreover, high glucose focus causes the arrangement of cutting edge glycation end products (AGE) that change collagen structure and meddle with the arrangement and unwinding. Moreover, high glucose focus causes the arrangement of cutting edge glycation end products (AGE) that change collagen structure and meddle with the arrangement and unwinding.

CONCLUSION

It is concluded that coronary supply route sicknesses is a typical issue in DM, with diastolic brokenness and increment uniquely in patients with positive pressure practice electrophysiology. Patients with positive pressure practice electrophysiology and coronary corridor infection apparent by coronary angiography had a practically identical diastolic capacity record to those with negative pressure practice electrophysiology. Doppler imaging application may legitimize routine screening for diastolic brokenness in diabetic patients dared to have healthy hearts.

REFERENCES


Rathod MI, Sharma SK, Jain RK, Joshi RS, Mangudkar SS. A Study of Left Ventricular Diastolic Dysfunction in Patients with Diabetes Mellitus; 2010.


Response of Neoadjuvant Chemotherapy in Triple Negative Breast Cancer and the impact of Pathologic Complete Response on Survival

Susheel Kumar1, Iqtedar Ahmed Moazzam1, Waqas Ishtiaq Ali1 and Naveed Lodhi2

ABSTRACT

Objective: To evaluate response of neoadjuvant chemotherapy (NACT) in stage I-III triple negative breast cancer (TNBC) and impact of pathologic complete response (pCR) on survival.

Study Design: Descriptive / Cross-sectional study

Place and Duration of Study: This study was conducted at the Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore, Pakistan between January 2010 to July 2016.

Materials and Methods: All patients with TNBC who received NACT were included and data was abstracted from cancer registry of hospital. The patients received NACT followed by surgery. Radiotherapy was given wherever clinically indicated. Kaplan-Meier and log-rank test was used to calculate survival.

Results: Out of 1113 TNBC patients, 150 received NACT. Mean age was 43 ± 7 years. Fifty-two patients (34.7%) achieved pCR (defined as complete eradication of invasive or in situ carcinoma in breast and axilla (ypT0/is/ypN0) in surgical specimen). Over a median follow up of 61 months, 52 patients (34.7%) had disease progression. In pCR group, only 5 patients (9.6%) had disease progression whereas in non-pCR group, 47 patients (48%) experienced disease progression. Patients who achieved pCR had significantly better 5-years disease-free survival (DFS) (p-value0.001) and 5-years overall survival (OS) (p-value0.002) in comparison to non-pCR group. The 5-years DFS was 90% in pCR group compared to 55% in non-pCR group. Similarly, 5-years OS was 94% in pCR group compared to 70% non-pCR group.

Conclusion: NACT is an effective treatment modality in management of TNBC. Achievement of pCR is a potential surrogate endpoint as it is associated with significantly better DFS and OS.

Key Words: Disease free survival (DFS), Overall survival (OS), Pathologic complete response (pCR), Triple negative breast cancer (TNBC).

INTRODUCTION

Breast cancer is the most common type of cancer in women worldwide1. It is a heterogeneous disease with variable clinical behavior, response to treatment and prognosis depending on its molecular subtype. Approximately 20% of all breast cancer patients have an aggressive subtype called ‘triple negative breast cancer’.

Triple negative breast cancer (TNBC) lacks the expression of estrogen receptor (ER), progesterone receptor (PR) and there is neither expression nor the amplification of human epidermal growth factor receptor 2 (Her-2)2. It is more common among younger premenopausal women, African-American or non-Hispanic black race and is associated with high BMI and BRCA Mutations3. In comparison with other breast cancer subtypes, TNBCs are predominantly high grade invasive ductal carcinomas and usually presents with larger palpable masses4. They are associated with early disease recurrence within the first 2-3 years after treatment and propensity to metastasize to viscera, mainly lungs and brain5,6. Cytotoxic chemotherapy is the mainstay of systemic treatment in TNBC and has more sensitivity to neoadjuvant chemotherapy regimens than other breast cancer subtypes6,7. Despite overall poor prognosis, survival is comparable to other breast cancer subtypes, if pathologic complete response (pCR) is achieved6. A number of studies have demonstrated that TNBC patients who achieve pCR, experience better DFS and OS than the patients with residual disease8,9,10.
Considering the outstanding prognostic importance of pCR, it is considered to be an important surrogate endpoint in clinical trials assessing the efficacy of neoadjuvant chemotherapy.6,8,9

MATERIALS AND METHODS

This was a cross sectional study done at Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH & RC) Lahore, and was approved by the institutional review board. Hospital’s electronic database was queried from Jan 2010 to July 2016 to identify all patients with a diagnosis of stage I–III TNBC who received neoadjuvant chemotherapy. All women were greater than 18 years of age with biopsy proven TNBC. Patients were excluded from the study if they had received treatment previously for breast cancer, had non-invasive breast cancer or any malignancy other than breast cancer. Medical records of 1113 TNBC patients were reviewed and 150 patients with complete information on clinical stage and receptor status were identified who received NACT. Data was collected for clinical stage according to TNM staging AJCC 8th edition, tumor grade, NACT regimen, type of surgery, date of surgery, pCR, use of radiation therapy, date of recurrence, date of last follow up and date of death. ER and PR status was assessed by immunohistochemistry (IHC) and tumors with less than 1% stained cells were considered to have negative receptor status. HER-2 status was assessed by either IHC or fluorescent in situ hybridization (FISH). HER-2 negativity was defined as either lack of HER2 gene amplification (FISH) or a score of 0 or 1+ (IHC). The pCR was defined as the lack of invasive or in situ carcinoma in breast and axilla (ypT0/is/ypN0) in surgical specimen at definitive surgery.11

Statistical analysis: SPSS software (version 20.0; SPSS, Chicago, IL, USA) was used for statistical analysis of the data. Mean ± standard deviation was used for continuous variables while frequencies and percentages was reported for categorical variables. The DFS was defined as time from date of definitive surgery to date of first relapse. The OS was defined as time from date of definitive surgery to time of death of any cause or last follow-up. The Kaplan-Meier method was used to estimate survival as a function of time, and survival differences was analyzed by using log-rank test. Statistical significance will be defined as a two-tailed p-value less than 0.05.

RESULTS

We screened 1113 TNBC patients and identified 150 patients with stage I–III who were treated with neoadjuvant chemotherapy. The mean age of the study population was 43 years (standard deviation of ± 7) with 88 patients (58.6%) being < 45 years. Baseline characteristics of patients are shown in Table-1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Categories</th>
<th>Total = N* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± standard deviation</td>
<td>43. ± 7</td>
</tr>
<tr>
<td>Family History</td>
<td>No</td>
<td>114 (77.0)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>34 (23.0)</td>
</tr>
<tr>
<td>Grade</td>
<td>II</td>
<td>30 (20.0)</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>120 (80.0)</td>
</tr>
<tr>
<td>Histology</td>
<td>IDC</td>
<td>145 (96.7)</td>
</tr>
<tr>
<td></td>
<td>IDC + DCIS</td>
<td>5 (3.3)</td>
</tr>
<tr>
<td>Clinical stage</td>
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</tr>
<tr>
<td></td>
<td>IIA</td>
<td>63 (42.0)</td>
</tr>
<tr>
<td></td>
<td>IIB</td>
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<td>IIIB</td>
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</tr>
<tr>
<td></td>
<td>IIIC</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Clinical tumor size</td>
<td>T1</td>
<td>5 (3.3)</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>118 (78.7)</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>23 (15.3)</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>4 (2.7%)</td>
</tr>
<tr>
<td>Clinical nodal status</td>
<td>N0</td>
<td>78 (52.0%)</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>65 (43.3%)</td>
</tr>
<tr>
<td></td>
<td>N2</td>
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</tr>
<tr>
<td></td>
<td>N3</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Surgery type</td>
<td>Breast-conserving surgery</td>
<td>98 (65.3)</td>
</tr>
<tr>
<td></td>
<td>Mastectomy</td>
<td>52 (34.7)</td>
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<thead>
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<th>Variables</th>
<th>Categories</th>
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<tbody>
<tr>
<td>Sequential Anthracyclines + taxane</td>
<td></td>
<td>106 (70.7)</td>
</tr>
<tr>
<td></td>
<td>AC/Taxol</td>
<td>35 (33.0)</td>
</tr>
<tr>
<td></td>
<td>AC/DOC</td>
<td>48 (45.0)</td>
</tr>
<tr>
<td></td>
<td>FEC/DOC</td>
<td>23 (22.0)</td>
</tr>
<tr>
<td>Concomitant Anthracyclines + taxane</td>
<td></td>
<td>9 (6.0)</td>
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<tr>
<td></td>
<td>TAC</td>
<td>9 (100.0)</td>
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<tr>
<td>Miscellaneous</td>
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<td></td>
<td>AC</td>
<td>9 (26%)</td>
</tr>
<tr>
<td></td>
<td>FEC</td>
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</tr>
<tr>
<td></td>
<td>TC</td>
<td>2 (6%)</td>
</tr>
</tbody>
</table>

One hundred and twenty-five patients (82%) had tumor sizes ≤T2 and 27 (18%) had tumor sizes >T2. All patients had invasive ductal carcinoma and out of them 120 (80%) were grade III tumors. Seventy-two patients (48%) had clinically involved axillary nodes. Ninety-
eight (65%) patients underwent breast conservation surgery (BCS) whereas remaining had mastectomies. All patients received adjuvant radiotherapy, except one who had disease progression before radiotherapy. Different chemotherapy regimens were used, as reported in Table-2. One hundred and fifteen patients (77%) received anthracyclines-taxane based chemotherapy and out of them 106 patients (92%) received sequential therapy. Thirty-five patients (23%) received other different neoadjuvant regimens. Out of 150, fifty-two patients (34.7%) achieved pathologic complete response (pCR). With respect to chemotherapy regimens, sequential anthracyclines-taxane based regimens were associated with the higher pCR rate (34%) and among them adriamycin,cyclophosphamide plus paclitaxel (AC/Taxol) was the most effective one (pCR rate 41%). The clinical T and N stage were inversely related to pCR rate. The pCR rate for tumors ≤T2 was 36.6% compared to 26% for tumors >T2. However, the proportion of patients with tumor size >T3 were much less than ≤T2. Among node negative patients, pCR rate was 41% compared to only 28% in node positive patients. Over a median follow up of 61 months (range; 2-145 months), 52 patients (34.7%) among 150 experienced disease progression. In pCR group (n = 52), only 5 (9.6%) had disease progression whereas in non-pCR group (n = 98), 47 patients (48%) experienced disease progression. The 5-years DFS and OS were 63% and 80% respectively, as shown in Figure-1. In pCR group, survival outcomes were significantly better than patients with residual disease. The 5-years DFS was 90% in pCR group compared to 55% in non-pCR group. Similarly, 5-years OS was 94% in pCR group compared to 70% non-pCR group as shown in Figure-2. The baseline nodal involvement also affected survival outcomes with respect to achievement of pCR. In node negative patients, 5-years DFS and OS were 90% vs 60% and 95% vs 72% in pCR and non-pCR group respectively. Node positive patients who achieved pCR, experienced better 5-years DFS and OS compared to non-pCR group (95% vs 42% and 95% vs 65% respectively).

![Figure No.1](image1.png)

Figure No.1:(A) 5-years Disease-free survival (B) 5-years Overall survival

![Figure No.2](image2.png)

Figure No.2(A): Disease free survival with respect to pCR(B) Overall survival with respect to pCR
DISCUSSION

TNBC is an aggressive subtype of breast cancer that lacks targeted therapy and systemic treatment is limited to chemotherapy. TNBC is more chemosensitive than other breast cancer subtypes with higher pCR rates in neoadjuvant settings. Conventionally, anthracyclines-taxane based regimens have been the most optimal chemotherapy regimens\(^\text{12}\). With the development Next Generation Sequencing (NGS), molecular classification of TNBC has been done and novel targets are under investigation\(^\text{13-15}\). Cumulative evidence from review of large randomized clinical trials has shown that neoadjuvant and adjuvant chemotherapies have similar results in terms of disease free survival (DFS) and overall OS\(^\text{16,17}\). However, the role of neoadjuvant chemotherapy has much evolved in recent decades as it allows more breast conservations and enables prompt assessment of treatment response\(^\text{18-20}\). Several neoadjuvant trials have demonstrated that achievement of pCR is associated with improved DFS and OS. Therefore, it is considered a potential surrogate endpoint for long-term survival in TNBC.

Majority of our study population received sequential anthracyclines with taxane based chemotherapy regimens and 52 patients (34.7\%) achieved pCR. The highest pCR rate in our study was observed in AC/Taxol group (41\%). This is in accordance with international literature that has reported pCR rates ranging from 22-45\% in TNBC with use of anthracyclines-taxane based regimens\(^\text{6,9,11}\). Liedtke C et al in their prospective study at M.D. Anderson Cancer Centre published in 2008 reported that TNBC patients have higher pCR rates than other breast cancer subtypes (22\% vs 11\%; p value 0.034). The patients who achieved pCR had very good survival comparable to other breast cancer subtypes than those who have residual disease. The 3-years OS was 94\% in pCR group compared to 68\% in patients with residual disease\(^\text{6}\). Cortazar and colleagues in a large pooled analysis of 12 international randomized neoadjuvant chemotherapy trials in breast cancer (the CTNeoBC pooled analysis) studied association between pCR and long-term survival. TNBC and Her-2 positive patients who achieved pCR, experienced significantly better event free survival (EFS) and OS than with residual disease\(^\text{8}\).

Similarly, Symmans et al have reported that TNBC patients who achieve pCR after NACT, had significantly better 10-years relapse free survival compared to patients with residual disease (86\% vs 23\%)\(^\text{10}\). Fisher et al in their retrospective study comparing neoadjuvant and adjuvant chemotherapy in TNBC have reported OS of 92.3\% for patients achieving pCR after NACT and 67.2\% in patients with residual disease\(^\text{11}\). Although, survival outcomes were comparable in NACT and adjuvant treatment groups, important to note is tumors with high risk features were included in NACT group.

The findings in our study are consistent with international literature depicting the predictive value of pCR on long-term survival outcomes. Our study also demonstrated that the patients who achieved pCR, experienced significantly better 5-year DFS and 5-year OS (90\% vs 55\% and 94\% vs 70\% respectively) compared to patients with residual disease. The patients with positive axillary nodes experienced comparable survival to node negative tumors after achievement of pCR.

Although, the impact of addition of carboplatin on survival outcomes with achievement of pCR is still to be established, we suggest the use of additional carboplatin to standard chemotherapy regimens in selected patients. We think it would be a suitable practice in young fit patients with locally advanced disease to achieve better local control of disease in the form of pCR. As only conventional chemotherapy regimens were used in our study, the pCR rate was comparatively lower than demonstrated in recent clinical trials.

Selection bias was an important limitation of our study. We had a skewed population with young fit patients as per institutional acceptance criteria for treatment at SKMCH & RC. This might have affected the survival results demonstrated in our study. Further, BRCA testing was not available by that time in our institute so we lack the information and treatment response in possible BRCA positive patients.

CONCLUSION

Our study has shown the benefit of NACT in TNBC patients in terms of improved survival with achievement of pCR, in concordance with other neoadjuvant studies. Outcome is worse in patients with residual disease in breast and/or axilla in terms of significantly lower DFS and OS. So NACT is helpful to identify the chemoresistant patients (i.e. those who have not achieved pCR) and considering them for salvage treatments as residual disease. Further trials are needed to develop novel neoadjuvant approaches in TNBC patients to increase pCR rates.

Author’s Contribution:
Concept & Design of Study: Susheel Kumar
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Revisiting Critically: Susheel Kumar, Iqtedar Ahmed Moazzam
Final Approval of version: Susheel Kumar

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


Analysis of Role of Bowel Preparation in Colorectal Surgery

Liaqat Ali Zia, Muhammad Khalid, Mudassir Rasool, Imran Amin, Muhammad Ansar Aslam and Hafiz Muhammad Khizar Nawaz Cheema

ABSTRACT

Objective: An important goal of this study is analyzing bowel preparation’s role in process of colorectal surgery among local population of Pakistan.

Study Design:

Place and Duration of Study: This study was conducted at the DHQ Teaching Hospital Gujranwala during January 2019 till June 2019.

Materials and Methods: Incidental colorectal cancer with minimal BRBPR, can be taken as minute quantity of RBCs in post wiping conditions or small quantity of blood drops in the post defecation conditions. There were small quantities of blood over the stool and they are also considered as minimal BRBPR. The blood that was mixed in stool was not considered as minimal BRBPR. All patients were interviewed and examined by a gastroenterologist.

Results: No effected person was with zero symptoms when he went to seek medical assistance. About 60% of total 81 person were experiencing rectal bleeding. Apart from rectal bleeding, the most common symptoms were reported by 20% or more of the sample, they were some changes in habits of bowels (65%), stress and fatigue (47%), painful conditions (35%), loss of weight (21%), and general type of indisposition (20%). There were some rare symptoms that were reported including feeling dizziness (13.2%), appetite loss or nausea (11.8%) and Temperature or fever (5.2%).

Conclusion: It is concluded effected person who were experiencing the situation of rectal bleeding were seen to be longer patient intervals while in contrast to it patients who were not suffering from rectal bleeding while controlling for the influence regarding possible or feasible confounders as well as other most common symptoms that were reported.

Key Words: Cancer, Surgery, Colorectal, Examined, Symptoms

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INTRODUCTION

Colorectal malignancy is the second commonest disease emerging on the planet. Colorectal malignancy can give a variety of manifestations and about 35 to 48% of the patients determined to have colorectal disease were encountering deaths of rectals. Despite the fact that the positive prescient estimation of the rectal seeping for the colorectal malignant growth is less than 3%, it is viewed as a dangerous alert manifestation inside people beyond 40 years old years. Then, most of people who experience rectal draining don't report it to their overall professional (GP).

All the more shockingly, contemplates have indicated that particular colorectal disease effected persons, who were encountering deaths of rectal, postponed aid-chasingin more frequent manner as compared to effected patients who were not experiencing rectal draining. The conceivable relationship in between the rectal draining &suffering patient deferral separates colorectal malignancy from most diversified and different diseases at place where the draining seems, by all accounts, to be related with a minute patient stretch. Consequently, that can be the basic that the components adding in this are deeply inspected and perceived. It is verily accepted that uncovered relationship between the rectal draining and longer suffering patient spans can be a result of the patients crediting the rectal seeping for benevolent will cause, for example, hemorrhoids. Then, the after effects of investigation of nearly 93 suffering patients who gave rectal seeping to GP recommended that a connection between the rectal type draining and the suffering patient span gave off an impression of being changed by close to home encounters. Accordingly, that was discovered that those particular patients who were encountering rectal seeping previously and were
having experience that was known considerable rectal issues were lesser inclined for postponing help-chasing as compared to the individuals who never had the experience of rectal dying. An extent of suffering patients who were considering malignancy while encountering rectal draining isn't known⁵. The consequences of British populace based review have recommended that reaction to a potential disease side effect is controlled by an intricate transaction between level of malignancy mindfulness and passionate boundaries⁶. Consequently, around 94% of the members revealed that they would contact the specialist in under about fourteen days on the off chance that they encountered an unexplained dying, yet 37% of similar members detailed that stresses over what the specialist may discover would cause them to delay help-chasing⁷.

**MATERIALS AND METHODS**

This study took place in DHQ Teaching Hospital Gujranwala during January 2019 till June 2019. Coincidental colorectal malignancy with insignificant BRBPR, was characterized as modest quantities of red blood in the wake of cleaning or a couple of few blood drops of in the latrine bowl right after crap. Modest quantities of the blood that was on the outside of stool have been additionally viewed as negligible BRBPR, yet red blood that was mixed with stool was most probably not. All patients had been met and inspected by a gastroenterologist. As needs be, patients' educated through composed assent was gotten from every patient prior to setting meeting as per the systems of the nearby organizations. After clinical evaluation, all patients endured butt-centric assessment and computerized rectal end. Endoscopy had been carried out by a specialist endoscopist that was available in suffering patients’ right after the ingestion reached the quantity of 4-6 liters of the polyethylene glycol arrangement. Any of the unusual sore had been biopsied and was sent safety for the process of histology. IBD had been analyzed dependent on the colonoscopy highlights & histopathological discoveries. Every one of those patients who are endured with helpless inside planning were booked for rehash colonoscopy and the consequences of an appropriate investigation are accounted for. Colonoscopy was enhanced with twofold difference barium douche if a colon was to be inspected to and that too at any rate a hepatic type flexure, however the cecum couldn't be in reach.

**RESULTS**

None of the suffering patients were asymptomatic when they looked for clinical assistance, and a sum of 81 suffering patients out of them about 60 percent had encountered rectal seeping in between the patient stretch. Extra to rectal dying, the simply announced side effects, for example side effects detailed by 20% or a greater amount of an example, were the changes inside propensities (65 percent), weariness (47 percent), torment (35%), reduction of weight (21%), as well as a general incapacitation (20%). With the seldom detailed indications were unsteadiness (13.2%), absence of hunger/sickness 11.8 percent & temperature or fever (5.2 percent). A sum of 14 suffering patients that was 10 percent of all, had faced rectal seeping without co-event of any of the other five regularly detailed side effects. The middle patient spans in days are accounted for patients, who revealed changes in enthrall propensities, weakness, torment, weight reduction, and general incapacitation either in blend with rectal draining or not in mix with this indication.

| Table No.1: Median of the patient interval(days) for the 5 symptoms occurred in less than 20% of the sample |
|---------------------------------------------------|-----------------|----------------|-----------------|-----------------|-----------------|
| Changes in bowel habits                          | Pain            | Weight loss    | Fatigue         | General indisposition |
| Median (IQR) patient interval when the presented without rectal bleeding | 16 (5–31) | 14 (3–28) | 18 (4–29) | 17 (4–29) | 10 (0–29) |
| N=30 (22.1%)                                      | N=25 (18.4%)   | N=17 (12.5%)  | N=26 (19.1%)   | N=11 (8.1%)    |
| Median (IQR) patient interval when they were presented together with rectal bleeding | 61 (12–112) | 31 (13–119) | 38 (22–74) | 34 (5–96) | 31 (0–57) |
| N=58 (42.6%)                                      | N=22 (16.2%)  | N=12 (8.8%)   | N=38 (27.9%)   | N=16 (11.8%)   |

**DISCUSSION**

Patients having rectal draining revealed a long patient stretches than patients who were not having rectal dying. The distinction in between groups was seen perfectly with the suffering patients who had to face rectal draining revealing a suffering patient time frame days & fifteen (15) days in the present patients who were not experiencing rectal draining⁸. Considerations regarding malignancy weren’t related with the suffering patient stretch & didn’t go about as mediator on the connection between rectal draining and a longer patient spans, it is the relationship between the rectal draining and a longer patient stretches wasn’t subject to whether the suffering patients answered to have the musings regarding disease in the span from 1st side effect for
clinical assistance looking for\textsuperscript{9}. Be that as it may, more patients who were having rectal draining answered to have also been contemplating whether their symptom could had been because of disease during patient span than non-suffering patients who were without any rectal draining\textsuperscript{10}. Sensibly higher number of the members & use or utilization of a solid Danish register for ID of suffering patients are among the qualities of this investigation. The utilization of a dependable register made sure about that all episode colon malignancy and rectal type disease patients were seen welcome to take an interest. In any case, various impediments of the current investigation ought to likewise be noted\textsuperscript{11}. To start with, the moderately low cooperation rate on 42% may have impacted the generalizability of our outcomes. The relationship in between rectal draining and a long patient stretches has additionally been also reported in past examination\textsuperscript{12}. The relationship between the rectal draining and more contemplations about disease seems to repudiate the supposition that longer patient span in patients with rectal draining should had been caused exclusively by doling out the side effect to kindhearted causes\textsuperscript{13}. The aftereffects of the current examination may recommend that passionate obstructions, for example, humiliation about side effects and dread of symptoms that were reported. Controlling for the influence regarding possible or conceivable confounders as well as other most common factors was among the quantities of this investigation. The prevalence of hemorrhoids patients who were having rectal draining answered to clinical assistance looking for their symptom. It is concluded effected person who were experiencing the situation of rectal bleeding were seen to be longer patient intervals while in contrast to it patients who were not suffering from rectal bleeding while controlling for the influence regarding possible or feasible confounders as well as other most common symptoms that were reported.

**CONCLUSION**

It is concluded effected person who were experiencing the situation of rectal bleeding were seen to be longer patient intervals while in contrast to it patients who were not suffering from rectal bleeding while controlling for the influence regarding possible or feasible confounders as well as other most common symptoms that were reported.

**Author's Contribution:**
- Concept & Design of Study: Liaqat Ali Zia
- Drafting: Muhammad Khalid, Mudassir Rasool, Muhammad Ansar Aslam, Hafiz Muhammad Khizar Nawaz Cheema
- Data Analysis: Liaqat Ali Zia, Imran Amin
- Revisiting Critically: Liaqat Ali Zia
- Final Approval of version: Liaqat Ali Zia

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

**REFERENCES**

Comparison of Diathermy Haemorrhoidectomy and Scissor Dissection Milligan Morgan Procedure’s Operation

Mudassir Rasool, Muhammad Khalid, Liaquat Ali Zia, Imran Amin, Muhammad Ansar Aslam and Hafiz Muhammad Khizar Nawaz Cheema

ABSTRACT

Objective: The main goal of the whole study is comparison of the outcome of diathermy haemorrhoidectomy against scissor dissection Milligan Morgan operation.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Quarter Teaching Hosp. Gujranwala during August 2019 till December 2019.

Materials and Methods: Group A combines with Haemorrhoidectomy through diathermy and Group B consolidates Haemorrhoidectomy of Milligan Morgan by utilizing the subjective bit.

Results: The data were collected from 100 patients which can be divided into two groups. The mean age of both groups were 40 to 60 years. Out of 29 cases of group A 20 of them were with third degree haemorrhoids and out of 21 cases of group B 17 were suffering from this disease. The calculations have shown that group A was having a mean time operating near to 52.5 and standard deviation was 11.9. Group B had values of 36.6 and 9.8 simultaneously. The blood loss’ mean amount was 51.92ml in group A and standard deviation was 15.68. In B these values were 70.34 and 25.59 simultaneously.

Conclusion: It is concluded that diathermy haemorrhoidectomies are without sutures, a technique of haemorrhoidectomy that is closed and depending upon a modified electro-surgical type of unit to gain tissue sealing as well as a sealing of vessel.

Key Words: Hemorrhoidectomy, Surgical, Tissue, Hospitals, Milligan Morgan Operation

INTRODUCTION

The Hemorrhoids have been narrated as regular clinical conditions. A good populace portion tend to fall a prey to hemorrhoids nearing 50 years. Surveys showed that about 58% American people who are above 40 years are suffering from this disease. Close to 33% effected are brought to doctors for the cure. Hemorrhoids has ability to take place whatever stage throughout everyday life, and they impact the two people. Distinct rate in non-mechanical countries is dark, anyway the affliction is when in doubt even more occasionally experienced, possibly in view of westernized lifestyle.

Hemorrhoids have been considered as submucosal type of beds that contain venules, vein and smooth type muscle strands arranged over the butt-driven trench. Hemorrhoidal disorder is represented in generally 5% of everyone, especially following age of forty years. Since hemorrhoids have always been commonplace anatomical type portions regarding butt-driven channel, curing technique is appeared inside interesting and unique cases. Such appearances consolidate kicking the bucket, circulatory trouble, and hemorrhoidal type of prolapses. Diversified methods have been utilized while curing patients of hemorrhoids, which include clinical type cure, restorative band’s ligation, infrared orinted photocoagulation, techniques of sclerotherapy, opened hemorrhoidectomy, shut type hemorrhoidectomy, hemorrhoidectomy t.e whitehead, and stapler type of hemorrhoidectomy.

Hemorrhoids, the most common infections like varicose causes a per rectal biting the dust. The essential convincing and outrageous treatment for third or fourth degree hemorrhoids is Haemorrhoidectomy. Furthermore Different systems have been dealt with, fluctuating by open or shut sharp type extraction, laser based treatment, ultrasonic careful edge examination to stapled Hemorrhoidectomy. In spite of the way that Haemorrhoidectomy has been accepted as a little
method oriented technique anyway disarrays and postoperative type recovery have been pretty much hard for the effected persons and perhaps that can be the inspiration driving why the suffering persons take haemorrhoidectomy as a final option of cure⁵. Patients as well as experts don't like Haemorrhoidectomy and the reason is the pain it causes to the suffering person. Similarly it is seen as an irksome framework among various specialists⁶.

The essential suitable and outrageous treatment for third or fourth degree hemorrhoids is Haemorrhoidectomy⁷. Different various strategies have in like manner been chipped away at, fluctuating from open or shut sharp extraction, laser treatment, and ultrasonic careful device dissection to stapled Hemorrhoidectomy⁸. In spite of the way that Haemorrhoidectomy has been accepted as a little method oriented technique anyway disarrays and postoperative type recovery have been pretty much hard for the effected persons and perhaps that can be the inspiration driving why the suffering persons take haemorrhoidectomy as a final option of cure.⁹

Standard haemorrhoidectomy of Milligan Morgan that is an open medical process wherein haemorrhoid pedicle has been ligated through a spellbinding fastens that can incite some of the postoperative troubles by and large torture, depleting and wound sickness which finally reason postponed stay in clinic⁹.

The main goal of complete study revolves around comparison of the outcome of diathermy hemorrhoidectomy as compared the scissor dissection of Milligan Morgan operation.

**MATERIALS AND METHODS**

This cross sectional type of study took place in District Head Quarter Teaching Hosp. GRW during August 2019 till December 2019. There were total 100 patients which were included in this study. All effected persons were between eighteen to seventy years. 3rd and 4th degree Haemorrhoids were seen in the studies.

**Data collection:** Two groups of effected persons were made. Group-A fuses Haemorrhoidectomy through diathermy & Group-B consolidates Haemorrhoectomy of Milligan Morgan through utilizing the subjective bit. The whole process ended with an effected person inside the lithotomy position & a minor type inverse Trendelenberg’s point. Fundamental steps inside the two operations have been seen to be same and involved Examination that was under sedation, movement of the hemorrhoids through the conductor forceps, I used at the muco-cutaneous convergence of ‘hemorrhoid, at another pinnacle as well as ‘skin’s cut at hemorrhoids’ base. The hemorrhoid’s tissue separation from within present sphincter fibers through the monopolar diathermy or scissors.

**Statistical analysis:** SPSS software version 20 was used for statistical studies. An Independent sample T-test was utilized for comparing operative time, loss of blood and pain in post-operative conditions in the groups. After stratification an Independent Sample T-test happened to be utilized; value that is ≤ 0.05 will have to be taken as a significant one.

**RESULTS**

The data were collected from 100 patients which can be divided into two groups. The mean age of both groups were 40 to 60 years. Out of 29 cases of group A 20 of them were with third degree haemorrhoids and out of 21 cases of group B 17 were suffering from this disease. The calculations have shown that group A was having a mean time operating near to 52.5 and standard deviation was 11.9. Group B had values of 36.6 and 9.8 simultaneously. The blood loss mean amount was 51.92ml in group A and standard deviation was 15.68. In B these values were 70.34 and 25.59 simultaneously.

**Table No.1: Comparison of operative outcomes in patients undergoing diathermy hemorrhoidectomy and Milligan Morgan’s hemorrhoidectomy.**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Milligan-Morgan hemorrhoidectomy</th>
<th>Diathermy hemorrhoidectomy</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time</td>
<td>20 (6–40)</td>
<td>15 (4–30)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>No of packages</td>
<td>2 (1–4)</td>
<td>2 (1–4)</td>
<td>0.5</td>
</tr>
<tr>
<td>Analgesic requirement n (%)</td>
<td>182 (88.3)</td>
<td>107 (67.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thrombosed hemorrhoids</td>
<td>10 (4.9)</td>
<td>13 (8.2)</td>
<td>0.195</td>
</tr>
<tr>
<td>Time of Hospitalization (days)</td>
<td>1 (1–16)</td>
<td>1 (1–2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Re-operation n (%)</td>
<td>3 (1.6)</td>
<td>4 (2.7)</td>
<td>0.704</td>
</tr>
<tr>
<td>Return to normal daily activity [mean (range) days]</td>
<td>7 (1–30)</td>
<td>6 (1–15)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Prolonged pain n (%)</td>
<td>27 (14.7)</td>
<td>10 (6.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>28.3±15.7</td>
<td>25.9±15.6</td>
<td>0.176</td>
</tr>
</tbody>
</table>

**DISCUSSION**

For indicative evaluation three and four hemorrhoids, some type of a hemorrhoidectomy always remains as the acknowledged methodology of cure. Ordinary types of methods including Milligan Morgan system as well as the Ferguson's strategy are essential in the larger section century in need of the prevalent other choice. Continuous no of years are seen in the introduction regarding fresher techniques having relative advantages and bad marks⁷. Principle continuous introduction is the traffic circle that staples contraption for a prolapsed type hemorrhoids. That is investigated for not curing.
piece on external sides of hemorrhoids and the skin names. Moreover, stapler type cartridges are exorbitant & past extent of majority of patients². Around two years earlier we had picked up the Ligasure™ device. That’s an electro-cautious type of device and improved type of a bipolar diathermy. That is fruitful in gaining hemostasis that it should be portrayed as a 'vessel fixing structure'. An energy is passed on interestingly to a tissue understood inside the jaws that are on the hand piece along insignificant spreading of an electrical or warm energy to close by tissues¹⁰. Vessels’ complete coagulation and besides tissues are refined with irrelevant singing instead of normal diathermy¹¹. A PC controlled analysis circle normally stops the movement of energy when coagulation of the vessels and mucosa is refined. The vascularised type tissue got in between the jaws is converted into a thin seal, which could be cut across with help of scissors¹².

CONCLUSION

It is concluded that diathermy haemorrhoidectomies are without sutures, a technique of haemorrhoidectomy that is closed is depending upon a modified electro-surgical type of unit to gain tissue sealing as well as a sealing of vessel. It is considered as a safe as well as an effective method. It has a less loss of blood, postoperative pain as well as complications as compared to the conventional haemorrhoidectomy.

AUTHOR’S CONTRIBUTION:

Concept & Design of Study: Mudassir Rasool
Drafting: Muhammad Khalid, Liaqat Ali Zia
Data Analysis: Imran Amin, Muhammad Ansar Aslam, Hafiz Muhammad Khizar Nawaz Cheema
Revisiting Critically: Mudassir Rasool, Muhammad Khalid, Liaqat Ali Zia
Final Approval of version: Mudassir Rasool

CONFLICT OF INTEREST: The study has no conflict of interest to declare by any author.

REFERENCES

Study of Superior Thyroid Artery and its Relationship with the External Laryngeal Nerve
Sabahat Zulfiqar¹, Naveed Lodhi² and Sobia Ramzan¹

ABSTRACT

Objective: This study aims to study the origin of the superior thyroid artery and investigate the relationship of STA with the external laryngeal nerve.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Sharif Medical and Dental College Lahore from the year March 2018 till November 2019.

Materials and Methods: We take 44 preserved human cadavers. We assure that the common carotid arteries of the cadavers were not damaged. Those cadavers with complete information of internal carotid artery (ICA) and external carotid artery were included for this research. Before surgical incision we inspect superior thyroid artery and facial artery of cadavers. Bilateral dissection was conducted on the anterior region of the neck to investigate the origin of STA. Distance from the upper pole of thyroid gland and measurement STA was notified from the point of EBSLN rotation.

Results: Out of 41 cadavers, 26 were female and 18 were male. In 71% of specimens of our study, we found STA emerge out from the exterior carotid artery, 39% belongs to the right side whereas 32% emerges from the left side of the external carotid artery. We did not find any significant relationship between sex and age of specimen which affects the relationship of STA and ELN.

Conclusion: We conclude that a huge diversity of the population has a huge impact on the relationship between STA and ELN.

Key Words: Superior thyroid artery, external carotid artery, common carotid artery, high sound pitch, external branch of the superior laryngeal nerve (EBSLN)


INTRODUCTION

From upper part of thyroid gland muscles a connection between larynx and skin of neck region take place with the help of superior thyroid artery (STA)¹,³. Though it is a main artery to supply gland but its origin is still confusing. The Exterior carotid artery is considered as a branching point of STA which further spread at the low level of the hyoid motor to reach the superior pole of the thyroid gland, it further subdivides into the lateral border of thyrohyoid muscle anterolateral to the external branch of the superior laryngeal nerve (EBSLN)¹,³,⁷.

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Previous literature considers the common carotid artery and bifurcation of the common carotid artery (CCA) as a starting point of STA after deep observations²,³. Furthermore, branches of STA are named as infrahyoid, superior laryngeal, sternocleidomastoid, and cricothyroid⁴,³,⁸. Superior Thyroid Artery plays a tremendous role in the surgical procedure of the neck and head⁹. In case of thyroid embolization for head and neck tumor, emergency cricothyroidotomy, radical neck dissection, diagnostic and therapeutic catheterization, plastic surgery, reconstruction of the aneurysm, carotid endarterectomy, it acts as a recipient and helps in implantation of microvascular free tissue²,⁷,⁹. During thyroid surgery, STA also assists in the recognition of EBSLN¹⁰. Thyroid diseases require surgical intervention and become a common medical practice in recent years. On the other hand, it needs a complete knowledge of the blood supply of glands to prevent the chance of future hemorrhage³. For head and neck surgeons it is necessary to study the origin and variation patterns of STA because EBSLN and STA have a strong relationship⁸,¹¹. Usually, EBSLN runs parallel to the STA but sometimes STA crosses EBSLN from the lower and upper portion of the thyroid gland⁴,⁷. EBSLN provides the cricothyroid muscle. Cricothyroid muscle puts pressure on the vocal folds which result in
the production of high-frequency sound during phonation. This muscle is also responsible to build a shield in between airways that protect against aspiration during breathing and swallowing\textsuperscript{11,12}. EBSLN are generally responsible for the production of high pitch tone usually above 150 Hz and utilize mostly by professional singers\textsuperscript{13}. During thyroidectomy, hemostasis is maintained with the help of ligated STA\textsuperscript{14}. During the process of ligation, EBSLN is at high risk due to its close relationship with STA\textsuperscript{11,14}. Injury to the EBSLN cause weakness in ericothyroid muscle leads to the alteration of in airways protection and mechanism and results in dysphagia\textsuperscript{11}. Weakness, tightness, maximum effort during the speech, increased throat clearance, and vocal fatigue are the common clinical symptoms that cause during EBSLN injury\textsuperscript{15,16}.

**MATERIALS AND METHODS**

This descriptive cross sectional study was conducted in Sharif Medical and Dental College Lahore from the year March 2018 till November 2019. We take 44 preserved human cadavers. We assure that the common carotid arteries of the cadavers were not damaged. Those cadavers with complete information of internal carotid artery (ICA) and external carotid artery were included for this research. Before conducting research we checked that either lingual artery, vague nerve, superior laryngeal artery, EBSLN, and lobes of the thyroid gland of cadavers were present or not. In case of any damage to these structures, we withdraw that cadaver from research. All the macerated cadavers and which were hard for dissection were excluded from research. Cadavers were placed into a supine position and a longitudinal midline cut was made from the tip of the chin superriorly to the downward side of the sternal notch. We further performed two incisions on the lower margin of the mandible and each side of the superior margin of the clavicle. On the lower side of platysma sectioned, the skin was reflected and at the upper side of superficial fascia which was removed and cleaned from cadavers. We further retracted each side of the sternocleidomastoid which contains visceral, and thyroid gland deep Fascia with muscular parts and fats at the posterior belly of digastric, at the backside of omohyoid, and the front side of the sternocleidomastoid were laterally removed. Removed parts revealed information about the carotid sheath. We further incise the carotid sheath to study its contents e.g. common carotid artery, internal jugular vein, vagus. We further observed the origin of the superior thyroid artery its length and diameter and take notes from each cadaver. We further reflected the internal carotid artery to expose the external laryngeal nerve (ELN). We exposed the external laryngeal nerve after the dissection of the carotid artery. In the end, we investigate the relationship between the STA and ELN at the crossing points of the superior pole of the thyroid gland\textsuperscript{15}.

Bilateral dissection was conducted on the anterior region of the neck to investigate the origin of STA. Distance from the upper pole of thyroid gland and measurement STA was notified from the point of EBSLN rotation. Furthermore we measured the space between the CCA bifurcation and the origin of the STA by cm.

For taking accurate observations we fixed position with pins and compared the origin of STA with the lamina of the thyroid cartilage. Based on the cornea, we classified the relationship of EBSLN to the superior thyroid pole as follows. In the category of type 1, from the superior pole, more than 15 mm of nerve crosses the artery. Whereas in type 2, the external branch of the superior laryngeal nerve (EBSLN) crosses the artery in between 10-15 nm. At last in type 2b, below the superior pole EBSLN crosses the artery\textsuperscript{19}.

All the collected information was analyzed through the IBM SPSS version 21.0. Nominal variables were presented in the form of percentage whereas continuous variables were presented in the form of mean and standard deviations. Variables that are beyond the normal distribution were analyzed through the student t-test and Chi-square were used for normal distribution and nominal variables. p-value < 0.05 considered significant in all the analyses.

**RESULTS**

Out of 41 cadavers, 26 were female and 18 were male. In 71% of specimens of our study, we found STA emerge out from the exterior carotid artery, 39% belongs to the right side whereas 32% emerges from the left side of the external carotid artery. After applying the statistical test we did not find any statistically significant difference among males and females. The p-value was >0.05.

**Table No.1: Origin site and aspect of superior thyroid artery**

<table>
<thead>
<tr>
<th>Sight of origin</th>
<th>Overall (n=44)</th>
<th>Females (n=26)</th>
<th>Male (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common carotid artery</td>
<td>7 (16%)</td>
<td>4 (15%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>External carotid artery</td>
<td>14(32%)</td>
<td>8 (30.77)</td>
<td>6 (33.33)</td>
</tr>
<tr>
<td>Absent</td>
<td>1(2%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Anteromedial</td>
<td>1(2%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Posterior-medial</td>
<td>1(2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Medially</td>
<td>20(46%)</td>
<td>12(48%)</td>
<td>8</td>
</tr>
</tbody>
</table>

**Table No.2: Mean length and diameter of superior thyroid artery**

<table>
<thead>
<tr>
<th>Mean length (mm)</th>
<th>Mean diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Left side</td>
<td>50.1</td>
</tr>
<tr>
<td>Right side</td>
<td>53.3</td>
</tr>
</tbody>
</table>
On the other hand in one of our female specimen left STA was not present. The ratio of STA origination from the common carotid artery was comparatively less (27%). Meanwhile in our study medial region was a more reliable origin of STA. In our study, the mean length was between 50-53 mm whereas the mean length of both sides was between 6.5-7.4 mm.

Table No.3: Relationship between ELN and STA

<table>
<thead>
<tr>
<th>Un-cropped</th>
<th>Both sides</th>
<th>Female</th>
<th>Male</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>&lt; 10 mm</td>
<td>21 (48%)</td>
<td>6</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>10-15 mm</td>
<td>10 (23%)</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 15 mm</td>
<td>7 (16%)</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

In our study majority of the specimens were belongs to type 2 classification.

**DISCUSSION**

Generally, many anatomical books considered the external carotid artery (ECA) as the originating point of STA but many studies negate this point and observed variation among the genesis of STA. Researchers observed that infrequent cases, STA came out from ECA just above the carotid bifurcation. Some other studies claim that it can be originated from the common carotid artery and CCA bifurcation or sometimes it started from the common trunk which is associated with the lingual and facial branches of ECA. In our study, we confirm the claim of STA origination from the external carotid artery (70%). This observation is greater than the previous study of Gavrildou and Anitha. In contrast, other studies recorded the common carotid artery as an origin of STA. The variation in results found due to the selection of the population, in Toni studies they observed that majority of the Caucasians population STA begins from the ECA, and the majority of the Eastern population STA has an origin of the common carotid artery. In some cases, the superior thyroid artery was not present bilaterally and only found on one side. Among these cases, inferior thyroid glands are responsible for the supply of lobes of glands. In our studies, we also reported one case with the absence of STA on one side and inferior thyroid Artery supply the lobes. In a previous study, he observed the bilateral and unilateral anastomoses between the thyroid arteries. He further explores one case in which he found anastomoses between lingual through a suprhyoid branch whereas found STA from the cricothyroid branch.

**CONCLUSION**

We conclude that a huge diversity of the population has a huge impact on the relationship between STA and ELN. The close relationship between STA and ELN depicts that different surgical procedures and methods of fixation may also cause variation in the assessment of STA and ELN relationships. It also helps us to understand about anatomical variation among the nerve and artery.

**Acknowledgment:** We are thankful to the department of the Centre for Anatomy and Human Identification (CAHID) to allow us to perform our study. I express my gratitude towards my colleagues and professors who help me during my studies.

**Author’s Contribution:**
- Concept & Design of Study: Sabahat Zulfiqar
- Drafting: Naveed Lodhi
- Data Analysis: Sobia Ramzan
- Revisiting Critically: Sabahat Zulfiqar, Naveed Lodhi
- Final Approval of version: Sabahat Zulfiqar

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

**REFERENCES**

25. Gavrilidou P, Iliescu Dm, Rusali Lm, Bordei P. Anatomical peculiarities of the origin and trajec of the superior thyroid artery. ARS Medica Tomitana 2013;19:124-129.
Association of Inflammatory Biomarkers with the Severity of COVID-19 Patients
Naveed Lodhi¹, Kashif Aziz Ahmad², Usman Amin Hotiana³ and Hafiza Sobia Ramzan⁴

ABSTRACT

Objective: The main objective of the study is to find the association of inflammatory markers with the severity of COVID-19.

Study Design: Analytical Study

Place and Duration of Study: This study was conducted at the Al Aleem Medical College Lahore with the collaboration of LHG, Lahore during April 2020 to July 2020.

Materials and Methods: The data was collected from 200 patients, having confirm COVID-19 through real time PCR. Patients were divided into two categories, one was mild and second was severe. Those patients who have mild symptoms of COVID fall into the group A and those who was with severe condition, fall in Group B.

Results: The data was collected from 200 COVID-19 confirmed patients. The mean age of Mild group patients was 37.25±5.45 years and 50.0±6.75 years for sever group. There were 87 males and 43 females in mild group and 58 males and 12 females in severe group. There were 1.5% deaths occur due to mild symptoms of COVID-19 and 10% deaths were due to severe condition. There were 109 (83.8%) patients have fever in mild condition and 58 (82.8%) in sever condition.

Conclusion: It is concluded that most of the patients with confirmed COVID-19 has increased values of inflammatory markers.

Key Words: COVID-19, Acute, Inflammation, Mild, Markers

Citation of article: Lodhi N, Ahmad KA, Hotiana UA, Ramzan HS. Association of Inflammatory Biomarkers with the Severity of COVID-19 Patients. Med Forum 2020;31(12):154-156.

INTRODUCTION

COVID-19 is the infectious disease caused by the corona virus and directly effects on respiratory system of the human being. Results are particularly poor in patients needing progressed respiratory help, with ongoing UK data announcing a mortality of 54.4% in this gathering. Clinical disintegration frequently happens 7–10 days after the beginning of manifestations, in association with declining viral titres, recommending that pathology is driven by irritation instead of direct popular injury. Fiery markers are regularly significantly raised in patients with extreme COVID-19. Uncontrolled, self-propagating, and tissue-harming provocative action has likewise been depicted already in the pathogenesis of other human coronavirus contaminations. Acute inflammation in the lungs is a complex pathophysiological component including provocative middle people, for example, cytokines and chemokines, which animate the macrophages in the alveoli, prompting helpless guideline of the safe system. In people, the clinical movement of the novel coronavirus-incipited ailment exists in a triphasic form. The clinical highlights in first stage incorporate fever, dry hack, myalgia, and other foundational diseases that are probably going to be expanded by the replication of the virus and cell necrosis. The related element of the subsequent stage is the beginning of IgG immunoglobulins change, correlated with the lessening in viral replication. During this stage, uncontrolled viral replication happens causing serious declining of manifestations. The specific theory behind this may be the extreme harm to alveoli brought about by over rich safe reaction of the host.

In nCOVID-19-contaminated patients, the significant patient populace recouped following fourteen days, yet 33% of the patients advanced to the third stage, which is described by serious lung irritation prompting ARDS, for example acute respiratory misery syndrome. Serious adverse health result of COVID-19 contamination was discovered considerably more predominant among youngsters, particularly those underneath 12 years, the old populace, and patients with comorbid illnesses.
MATERIALS AND METHODS

This analytical study was conducted in Al Aleem Medical College Lahore with the collaboration of LGH, Lahore during April 2020 to July 2020. The data was collected from 200 patients, having confirm COVID-19 through real time PCR. Patients were divided into two categories, one was mild and second was severe. Those patients who have mild symptoms of COVID fall into the group A and those who was with severe condition, fall in Group B.

Data Collection: The data was collected from the wards of the hospitals. 3cc venous blood was drawn from the patients of both groups for biochemical analysis. This blood sample was used for the lab analysis of CBC, CRP, lactate and calcitonin levels. All these patients were also followed for the outcome.

Statistical Analysis: The data was collected and entered into the SPSS 19 for further analysis. All the values were presented in mean and standard deviation.

RESULTS

Table No.1: Baseline characteristics of selected participants in both groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mild N=130</th>
<th>Severe N=70</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.25±5.45</td>
<td>50.0±6.75</td>
<td>0.007</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>87 (66.9%)</td>
<td>58 (82.8%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Women</td>
<td>43 (33.07%)</td>
<td>12 (9.23%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>2 (1.5%)</td>
<td>7 (10%)</td>
<td>0.0805</td>
</tr>
<tr>
<td>Exposure to outside country</td>
<td>47 (36.15%)</td>
<td>16 (22.8%)</td>
<td>0.4754</td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (18.46%)</td>
<td>12 (17.1%)</td>
<td>0.0078</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22 (16.9%)</td>
<td>12 (17.1%)</td>
<td>0.3374</td>
</tr>
<tr>
<td>Malignancy</td>
<td>0</td>
<td>1 (1.4%)</td>
<td>0.2927</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>7 (5.38%)</td>
<td>2 (2.85%)</td>
<td>0.2002</td>
</tr>
<tr>
<td>Fever</td>
<td>109 (83.8%)</td>
<td>58 (82.8%)</td>
<td>0.8128</td>
</tr>
<tr>
<td>Cough</td>
<td>97 (74.6%)</td>
<td>57 (81.4%)</td>
<td>0.1289</td>
</tr>
<tr>
<td>Fatigue</td>
<td>92 (70.76%)</td>
<td>50 (71.4%)</td>
<td>0.0022</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (3.9%)</td>
<td>7 (10%)</td>
<td></td>
</tr>
<tr>
<td>Sore throat</td>
<td>22 (16.9%)</td>
<td>7 (10%)</td>
<td>0.9645</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>10 (7.69%)</td>
<td>4 (5.71%)</td>
<td>0.0078</td>
</tr>
<tr>
<td>Chest pain</td>
<td>0</td>
<td>7 (10%)</td>
<td>0.2927</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0</td>
<td>4 (5.71%)</td>
<td>0.1756</td>
</tr>
</tbody>
</table>

The data was collected from 200 COVID-19 confirmed patients. The mean age of Mild group patients was 37.25±5.45 years and 50.0±6.75 years for sever group. There were 87 males and 43 females in mild group and 58 males and 12 females in severe group. There were 1.5% deaths occur due to mild symptoms of COVID-19 and 10% deaths were due to severe condition. There were 109 (83.8%) patients have fever in mild condition and 58 (82.8%) in severe condition. There are other factors also, like hypertension 24 (18.46%) in mild group and 12 (17.1%) in severe group, fatigue and nausea which also contribute towards the severity of disease. Baseline values of patients were presented in table 01.

Biochemical analysis of all selected patients shows that young age people suffers from mild condition of disease as compared to old age. All the biochemical markers were increased significantly and shows the higher levels of ferritin, CRP, prolactin and Lactate in both groups. But the older group shows more increase as compared to younger age group.

Table No.2: Laboratory findings of both groups with respect to symptoms

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mild group</th>
<th>Severe group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.25±5.45</td>
<td>50.0±6.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>309 ± 134.6</td>
<td>1989 ±199.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>29.9 ± 45.3</td>
<td>64.9 ± 67.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>1.47 ± 0.65</td>
<td>2.10 ± 1.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>0.170 ± 0.07</td>
<td>0.61 ± 0.31</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

COVID-19, caused by SARS-CoV-2, is rapidly expanding worldwide. Regardless of the way that most cases have gentle side effects and a decent guess, COVID-19 can form into ARDS and even demise. Until this point in time, there is no successful treatment for COVID-19 [5,6]. A few examinations have demonstrated expanded pro inflammatory cytokines in serum of COVID-19 patients. Likewise, mitigating specialists for COVID-19 treatment feature the basic part of inflammation in the movement of COVID-19 [7]. Nonetheless, the function of fiery markers in observing...
the seriousness of COVID-19 is as yet dubious. In this examination, through investigating the 16 review considers, we inferred that fiery markers, particularly CRP, PCT, IL-6 and ESR, were emphatically correlated with the seriousness of COVID-19[6].

CRP is a perfectly delicate fundamental marker of acute-stage reaction in inflammation, disease, and tissue harm, which could be utilized as pointer of inflammation[10]. In the examination by other study, no measurably critical distinction was found in the degree of CRP between the no severe and the serious gathering, the mean degree of CRP was higher in the extreme gathering than in the no severe gathering[10]. Different examinations all detailed CRP level was decidedly related to the seriousness of COVID-19. PCT is likewise a principle incendiary marker regularly estimated in clinical practice. Among investigations, the degrees of PCT were all higher in the serious gathering than the non-severe gathering[11]. ESR is a vague incendiary marker, which primarily mirrors the progressions of plasma protein types. One explanation is that patients in the extreme gathering had higher inflammation. Another conceivable clarification is that patients with more established age in the serious gathering added to the more significant level of ESR thinking about that the degree of ESR expanded with age[12,13].

CONCLUSION

It is concluded that most of the patients with confirmed COVID-19 has increased values of inflammatory markers. Their values were increased significantly due to disease and these increased levels of inflammatory markers directly correlates with the severity of disease. By regular analyzing and monitoring of these markers we can control the severity of disease.

Author’s Contribution:
Concept & Design of Study: Naveed Lodhi
Drafting: Kashif Aziz Ahmad
Data Analysis: Usman Amin Hotiana, Hafiza Sobia Ramzan
Revisiting Critically: Naveed Lodhi, Kashif Aziz Ahmad
Final Approval of version: Naveed Lodhi

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

REFERENCES

A Study on Urinary Tract Infection and Metabolic Diseases in Stone Patients
Syed Muhammad Hassan Akhtar¹, Aftab Ahmad Channa² and Nadeem Shafiq²

ABSTRACT

Objective: The main objective of the study is to analyze the Urinary Tract Infection and metabolic diseases in Stone Patients among local population of Sialkot.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Allama Iqbal Memorial Teaching Hospital, Sialkot during June 2018 to June 2019.

Materials and Methods: The definite history of the multitude of patients were accumulated and 24 hour p-test was gathered from every patient and sent for PH, explicit gravity, Creatinine, uric corrosive, calcium, phosphate, oxalate, citrate and magnesium. 24 hour p-tests were gathered in plastic boxes, which don't respond artificially by standard techniques, and were put away at 2-8°C. Likewise, blood test of every patient was additionally sent for serum levels of urea, creatinine, uric corrosive, phosphate and calcium.

Results: The data were collected from 100 patients with the mean age 38 ± 7.75 years. There were 35 male and 65 female patients who were selected this investigation. The primary introducing grievance was amble torment on the influenced side for example in 79.0% patients, trailed by hematuria and consuming micturition. Dominant part of the patients for example 94.0%, were analyzed as having renal stone or ureteric stone.

Conclusion: It is concluded that recurrence of metabolic variations from the norm is exceptionally high in patients with urolithiasis and hyperoxaluria, hypercalciumia and hypocitraturia are the main metabolic irregularities saw in these patients. Stone sickness is an expanding and significant general health issue with high recurrence of bladder stone.

Key Words: Urinary, Tract, Infection, Patients, Metabolic

INTRODUCTION

Urolithiasis is a disease which is common now a days in the whole world. It is assessed that roughly 2% of the populace experience renal stone illness at times in their existence with top rate in second and third many years of life. There are a few sorts of urinary stones, and they are ordered by compound composition. Calcium oxalate is the significant segment of by far most of stones. A few components, for example, age, sexual orientation, atmosphere, metabolic variations from the norm and heredity, are related to the improvement of urinary stones. Metabolic variations from the norm are the main elements since they can be altered to forestall the danger of urinary stones. Inhabiting urinary catheters are standard clinical gadgets used in both clinic and nursing home settings to mitigate urinary maintenance and urinary incontinence. Of the very nearly 100 million catheters that are sold yearly around the world, one-fourth of them are sold in the United States. The most widely recognized urinary catheter being used is the Foley inhabiting urethral catheter, a shut sterile framework that is included a cylinder embedded through the urethra and held set up by an inflatable to permit urinary seepage of the bladder. In spite of the fact that these gadgets were initially intended for transient use in patients, inhabiting catheter use is currently typical in the long haul setting. Infections of the urinary tract related with catheter use are huge not just due their high frequency and ensuing financial expense yet additionally on account of the serious sequelae that can result. Patients with confounded UTI should be treated by compelling antimicrobial treatment just as suitable urological mediation to eliminate inclining factors when the manifestations are related, for example, micturition torment, dysuria, urinary recurrence, and low or high
fever. Paradoxically, asymptomatic bacteriuria (ASB) is recognized by segregation of a predetermined quantifiable measure of microorganisms in a properly gathered urine example acquired from a patient without indications or signs referable to urinary infection.

**MATERIALS AND METHODS**

This cross sectional study was conducted at Allama Iqbal Memorial Teaching Hospital, Sialkot during June 2018 to June 2019. The data was collected from 100 patients of both genders. The data was gathered through non probability sampling technique.

**Inclusion criteria:** Patients with one or the other various or repetitive urolithiasis were remembered for this investigation.

**Exclusion criteria:** Patients with some other sickness were prohibited from this examination. Patients with ongoing renal disappointment, persistent liver sickness and with history of any constant medication use were rejected.

**Data collection:** The data were collected from 100 patients. The positive history of the large number of patients were collected and 24 hour urine test was assembled from each patient and sent for PH, express gravity, Creatinine, uric acid, calcium, phosphate, oxalate, citrate and magnesium. 24 hour urinetests were accumulated in plastic boxes, which don't react misleadingly by standard procedures, and were taken care of at 2-8°C. Moreover, blood trial of each patient was furthermore sent for serum levels of urea, creatinine, uric destructive, phosphate and calcium. The serum levels of metabolic limits were assessed by standard compound strategy. All patients by then had legitimate method after fulfillment of all workup and stones were transported off pathology research office for compound assessment to consider the stone structure.

The data were collected and analyzed through SPSS (Version 21.0). All the values were expressed in mean and standard deviation.

**RESULTS**

The data were collected from 100 patients with the mean age 38 ± 7.75 years. There were 35 male and 65 female patients who were selected this investigation. The primary introducing grievance was amble torment on the influenced side for example in 79.0% patients, trailed by hematuria and consuming micturition. Dominant part of the patients for example 94.0%, were analyzed as having renal stone or ureteric stone. Just 38.0% patients gave intermittent stones while staying 62.0% had stone unexpectedly. Substance examination of stones after complete strategy had demonstrated calcium oxalate stone in 82.5% patients (table 01).
DISCUSSION

Urinary stones in its various structures are the third most basic difficulty of the urinary tract. Math illness is the commonest urological sickness in Sialkot. It has been evident for quite a long while that the occurrence paces of lithiasis shift significantly, from mainland to landmass as well as between neighboring areas of a nation, regardless of whether one takes into consideration contrasts in technique and models determination among the study of disease transmission studies. The lifetime perverseness of urinary stones has expanded all through the twentieth century and happens in up to 15% of the populace. It is commonly acknowledged that stones happen more ordinarily in guys than females. Our discoveries certify with this sex contrast as announced by others. No age bunch is saved to urinary stone illness in Sialkot however an adjustment in the age example of patients of urolithiasis has been accounted for in industrialized countries. In our examination, the primary introducing grumbling was bladder torment for example in 79.0% patients. Elfadil GA et al had likewise discovered flank torment as the head introducing grievance in his investigation for example in 67% patients. The consequences of our investigation have demonstrated a solid hereditary inclination to urinary stone infection as 64.0% patients had family background of urolithiasis. This hereditary factor is additionally upheld by investigations of Majalan NN et al who had discovered a positive family ancestry in 67.0% and 53.1% patient's respectively. Then again, Elfadil GA et al had discovered this in just 20% of their patients. We had additionally discovered 38.0% patients with intermittent urinary stones and the significant stone segment was calcium oxalate in our examination which was likewise found by Elfadil GA et al. But in an investigation by Androulakakis et al, the primary segments of urinary stones in Europe, in diminishing request, are struvite, calcium phosphate and calcium oxalate. In our investigation, metabolic anomalies were found in 90.5% patients, while there was no metabolic variation from the norm in just 9.5% patients which is a lot of practically identical to numerous past examinations. In an investigation by other study, 62.2% of patients had various metabolic variations from the norm; in any case, the patients didn't have repetitive calcium oxalate stones. Accordingly, it very well may be assumed that numerous metabolic anomalies are more normal in patients with intermittent calcium oxalate stones.

CONCLUSION

It is concluded that recurrence of metabolic variations from the norm is exceptionally high in patients with urolithiasis and hyperoxaluria, hypercalciuria and hypocitraturia are the main metabolic irregularities saw in these patients. Stone sickness is an expanding and significant general health issue with high recurrence of bladder stone.

REFERENCES

Role of High Mobility Group Box-1 (HMGB1) in Obesity and Metabolic Syndrome
Rabea Nasir¹, Usman Nasir³, Ghazala Khalid³, Rashid Siddique⁴, Nimra Ikram² and Akmal Khurshid Bhatti²

ABSTRACT

Objective: To determine the role of hmgb1 in obesity and metabolic syndrome.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Mohammad Islam Medical College Gujranwala and Sialkot Medical College Sialkot during Jan 2019 to March 2020.

Materials and Methods: 40 blood samples of adults Metabolic syndrome (MS) subjects and 20 samples of obese subjects between the ages 25-50 were obtained from M. Islam Teaching Hospital, Gujranwala and Sialkot Medical College Sialkot. 20 healthy subjects served as the control group. Fasting serum samples were analyzed for lipid profile, fasting blood glucose (FBG), and insulin and HMGB1 levels. Insulin and HMGB1 were estimated by commercially available ELISA kits. Insulin resistance was calculated by HOMA-IR index.

Results: Blood pressure showed significant differences among the three groups of subjects and was shown to be highest in the MS group. Significantly increased levels of FBS (124.13±8.77 mg/dl) were observed in the MS group as compared to obese and normal subjects (85.95±2.68 mg/dl and 84.50±1.06 mg/dl, respectively). Lipid profile revealed that triglycerides, LDL and cholesterol levels were significantly higher (213.78 ± 11.62mg/dl, 133.30 ± 6.45mg/dl and 218.98 ± 5.66mg/dl respectively) and HDL levels were relatively low in MS patients (44.18 ± 1.03) in comparison with obese triglycerides, LDL, cholesterol and HDL levels (133.85±6.31mg/dl, 106.15±4.31mg/dl, 166.00±5.56 mg/dl and 45.70±1.53mg/dl respectively) and normal subjects triglycerides, LDL, cholesterol and HDL levels(122.05±4.25mg/dl, 108.05 ± 3.56mg/dl, 152.15±6.00mg/dl and 46.65±1.07mg/dl respectively). Mean HMGB1 levels were maximal in patients with MS (19.68±2.58 mg/dl) and were significantly different from mean levels in subjects with obesity alone (11.06±1.12 mg/dl) and healthy subjects (13.28±0.65 mg/dl). Significantly elevated levels of insulin and insulin resistance were evident in patients suffering from MS (13.59±1.49 mg/dl and 4.06±0.54 mg/dl, respectively) as compared to healthy subjects (10.22±1.29 mg/dl and 2.13±0.26 mg/dl, respectively) and the obese group (9.95 ± 1.67 mg/dl and 2.06±0.32 mg/dl, respectively).

Conclusion: The current study demonstrates significantly higher levels of serum HMGB1 levels in MS patients in comparison with those of obese and control groups. The study suggests a role of HMGB1 as a pro-inflammatory cytokine in patients with MS. Significantly increased insulin resistance in MS patients further indicates that the HMGB1 related inflammatory pathway may be involved in pathogenesis of diabetes type 2.

Key Words: HMGB1, Metabolic syndrome (MS), obesity, insulin resistance, pro-inflammatory cytokine

INTRODUCTION

The incidence of obesity has increased phenomenally during the past 3 decades and has emerged as a pande-
between caloric intake and caloric expenditure\(^3\). Obesity is also linked to a state characterized by chronic low grade inflammation and meta-inflammation evidenced by increased pro-inflammatory and decreased anti-inflammatory markers \(^4\). In the meta-inflammatory state the usual signs of inflammation are not present that are redness, increased body temperature, pain and loss of function, but it creates a pro-inflammatory state mainly in the liver and adipose tissue as well as in muscles and pancreas. Basically the dysregulation between metabolism and immunity is considered as the starting point for obesity and the resulting disorders \(^5\). Proinflammatory factors that are increased in obesity include IL-6, TNF\(\alpha\), IL-1, leptin and others. Recently a new protein, the high-mobility group box 1 (HMGB1) was identified as a proinflammatory mediator and shown to have the ability to activate several immune cells and production of various cytokines \(^6\).

**MATERIALS AND METHODS**

This case control study was carried out on 80 subjects of both sexes 25-50 years of age. The study was approved by the Ethical Committee Sialkot Medical College Sialkot. The patients were recruited from M. Islam Teaching Hospital, Gujranwala & Sialkot Medical College Sialkot strictly on a voluntary basis. The patients were selected on the basis of BMI > 35 with or without metabolic syndrome and hence were severely obese. Height and weight measurements were recorded and BMI was calculated by using the standard formula i.e weight in kg/ height in meter\(^2\). A group of age-matched subjects was included in the study as control. The subjects were, therefore, categorized to the following 3 groups:

- **Group I:** Severely obese with metabolic syndrome (BMI > 35) n=40
- **Group II:** Severely obese (BMI>35) n=20
- **Group III.** Controls (BMI 20-25) n=20

Informed written consent was taken from all the subjects recruited in the study. Blood pressure was measured by using the standard mercury sphygmomanometer by auscultatory method. Fasting blood sample of each participant in the study was obtained by venepuncture after a 12-hour overnight fast, into a gel clotting vial. Serum was separated by centrifugation at 3000 rpm for 15 to 20 minutes after 1 hour of sample collection. The remaining samples were aliquoted into tubes and stored at -80°C until analyzed. NCEP ATPIII criteria defines metabolic syndrome as presence of three or more of the following risk factors:

1. Fasting blood glucose \(\geq 5.6\text{ mmol/l} (100\text{ mg/dl})\)
2. Blood pressure \(\geq 130/85\text{ mmHg}\)
3. Triglycerides \(\geq 1.7\text{ mmol/l} (150\text{mg/dl})\)
4. HDL-cholesterol Men: <1.03 mmol/l (40mg/dl), Women: <1.29 mmol/l (50mg/dl)

5. Central Obesity (Alberti et al.,2005)

Serum samples were analyzed for fasting blood glucose level by using the glucose oxidase method and lipid profile by automated enzymatic methods. Analysis of HMGB-1 level in human serum is carried out by ELISA kit (Bioassay Technology Laboratory, Korain Biotech Co. Birmingham, England) serum Insulin levels were also determined by ELISA using a commercially available kit (AccuBind ELISA Microwells, Monobind Inc. Lake Forest, CA 92630, USA). All assays were performed by following the manufacturers’ standard kit protocol. Inter-assay coefficient of variation was less than 10% in all cases. HOMA1-IR index was calculated by using the formula: HOMA1-IR = fasting plasma insulin (\(\mu\text{U/ml}\) x fasting plasma glucose (mmol/L))/22.5.

### Inclusion Criteria:
A group of age-matched subjects was included in the study as control.

### Exclusion Criteria:
Patients with hepatic and infectious or endocrine diseases other than diabetes or impaired glucose tolerance, syndromic obesity, pregnancy, and lactation, were excluded from the study.

**RESULTS**

The physical characteristics of all subjects are summarized in Table 1.

The study subjects and controls were within the same age range (25-50yr). The BMI of subjects with MS and obesity was greater than 35, and, therefore, belonged to the category of severe obesity. The BMI of normal healthy controls was less than 25. Both, systolic and diastolic blood pressure were markedly and significantly higher in patients with MS (150±2.67 and 98.13±1.81 mmHg, respectively) compared to subjects with severe obesity (121.50=1.81 and 81.00±1.43 mmHg respectively) and the control group (119.50±1.53 and 77.00±1.05 mmHg, respectively). No significant difference was found in the mean blood pressure values of subjects presenting obesity and those of normal subjects.

### Table No.1: Physical Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Metabolic syndrome (group-1) n=40 (mean ± sem)</th>
<th>Obese (group-2) n=20 (mean ± sem)</th>
<th>Controls (group-3) n=20 (mean ± sem)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.75±0.926</td>
<td>37.50±1.445</td>
<td>37.40±1.035</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Height (ft)</td>
<td>5.20±0.42</td>
<td>5.17±0.04</td>
<td>5.45±0.06</td>
<td>0.001</td>
</tr>
<tr>
<td>Weight(kg)</td>
<td>95.20±1.88</td>
<td>90.20±1.70</td>
<td>63.65±1.85</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Bmi (kg/m(^2))</td>
<td>37.98±0.70</td>
<td>36.33±0.41</td>
<td>22.90±0.25</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Systolic bp (mmHg)</td>
<td>150±2.67</td>
<td>121.50±1.81</td>
<td>119.50±1.53</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Diastolic bp (mmHg)</td>
<td>98.13±1.38</td>
<td>81.00±1.43</td>
<td>77.00±1.05</td>
<td>&lt;0.000</td>
</tr>
</tbody>
</table>

*Analysis of variance (ANOVA); Significant difference among the three groups; P<001
Patients with MS were hyperglycemic – mean FBG levels were 124.13±8.77 mg/dl and were significantly different from the other two groups (P=0.001). FBG levels in obese and normal subjects were not significantly different and were within the normal range (85.95±2.68 and 84.50±1.06 mg/dl, respectively). Mean values of components of lipid profile and total cholesterol levels are shown in Table 2 and Figures 2,3,4,5.

Serum triglycerides were significantly raised in patients with MS compared to the obese and control group (213.78±11, 133.85±6.31 and 122.05±4.25 mg/dl, respectively). Although mean triglyceride levels were higher in obese than in control group, the difference was statistically not significant. Low-density lipoprotein (LDL) levels were significantly (p=0.002) higher in metabolic syndrome group (133.30±6.45 mg/dl) as compared to obese group (106.15±4.31 mg/dl) and control group (108.05±3.56 mg/dl). However, in our subjects we did not find any significant difference in levels of HDL although they tended to be lower in patients with MS as compared to the other two groups, severely obese and control (44.18±1.03 vs 45.70±1.53 and 46.65±1.07 mg/dl, respectively). Mean serum total cholesterol levels were markedly and significantly higher (P<0.001) in the MS group compared to the subjects with obesity alone and the control subjects. The mean levels of cholesterol in control, obese and metabolic syndrome groups were 152.15±6.00, 166.00±5.56 and 218.98±5.66 mg/dl, respectively.

Mean serum HMGB1 levels were shown to be maximal in patients with MS (19.68±2.58 ng/ml) and differed significantly (P<0.05) from those of subjects with obesity (11.06±1.12 ng/ml) and normal body weight (13.28±0.65 ng/ml). Interestingly, HMGB1 levels were shown to be normal in patients presenting obesity alone.

**Table No.2: Biochemical Spectrum**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comparison A</th>
<th>Comparison B</th>
<th>Comparison C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic syndrome (group-1) n=40</td>
<td>124.13±8.77</td>
<td>150±6.82</td>
<td>121.50±8.12</td>
</tr>
<tr>
<td>Obese (group-2) n=20</td>
<td>133.85±8.74</td>
<td>81.00±6.40</td>
<td>106.15±19.29</td>
</tr>
<tr>
<td>Control (group-3) n=20</td>
<td>133.30±6.45</td>
<td>122.30±12.02</td>
<td>85.95±12.02</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>213.78±73.53</td>
<td>133.85±28.23</td>
<td>133.85±28.23</td>
</tr>
<tr>
<td>LDLC (mg/dl)</td>
<td>133.30±40.79</td>
<td>106.15±19.29</td>
<td>106.15±19.29</td>
</tr>
<tr>
<td>HDLC (mg/dl)</td>
<td>44.18±6.56</td>
<td>45.70±6.87</td>
<td>45.70±6.87</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>218.98±35.79</td>
<td>166.00±24.87</td>
<td>166.00±24.87</td>
</tr>
<tr>
<td>Insulin (uIU/ml)</td>
<td>13.35±9.69</td>
<td>10.00±7.91</td>
<td>13.35±9.69</td>
</tr>
<tr>
<td>HMGB1 (ng/ml)</td>
<td>19.20±18.08</td>
<td>12.27±8.26</td>
<td>19.20±18.08</td>
</tr>
<tr>
<td>IR</td>
<td>4.06±0.54</td>
<td>2.06±0.32</td>
<td>4.06±0.54</td>
</tr>
</tbody>
</table>

*Analysis of variance (ANOVA); Significant difference among the three groups; P<0.05
Although mean serum insulin levels were higher in patients with MS (13.59±1.49 μIU/ml) but the difference from obese and normal group (9.95±1.67 and 10.22±1.29 μIU/ml) was not statistically different. Insulin resistance as determined by HOMA-IR was found significantly greater with incidence of MS (4.1±0.5) whereas it was within the normal range in obese and control groups (2.1±0.26 and 2.1±0.3).

**DISCUSSION**

Insulin resistance and excessive adiposity are ascribed as the main etiological factors in the pathogenesis of MS often leading to CVD [7,8,9,15]. These conditions are characterized by an increase in inflammatory cytokines [10,11,12,16]. Only a few studies have been carried out to demonstrate the role of HMGBl in MS [13,14,17]. More recently raised levels of HMBG1 have been shown to act as a significant biomarker for development of MS [16,17]. MS is frequently preceded or accompanied by excessive adiposity. This study was primarily carried out to assess HMBG1 in obese subjects with and without MS. We have therefore investigated using HMBG1 levels as a supplementary criterion to assess the severity of MS and that of obesity without any apparent co-morbidities. Few studies have been carried out previously to determine the role of HMGBl in adult MS. This study shows that serum HMBG1 levels are significantly higher in the MS group as compared to obese and control groups. These findings are consistent with a previous study in which role of HMGBl was evaluated in children predisposed to MS. In this study serum HMBG1 levels were found to be significantly raised and closely related to other parameters of MS as shown by [18]. Some evidence also suggests that obesity is associated with higher serum levels of HMBG1 [18]. MS is characterized by low grade inflammation, oxidative stress and pro-inflammatory state. HMBG1 acts as a pro-inflammatory cytokine released in response to stress and inflammation with enhancement of further inflammatory cytokines and disease progression [18].

Interestingly, in the present study no significant increase in levels of HMBG1 were observed in subjects with 'pure obesity' indicating role of other factor in elevation of HMBG1 in patients with MS. HMBG1 levels were significantly increased in our MS patients compared to the obese and control groups.

Insulin resistance is believed to be the second most important factor in the pathogenesis of MS [17]. It has been suggested that HMBG1 plays an important role in insulin resistance through NF-κB pathway activation and its levels are found to be positively correlated with HOMA-IR [16]. The results of current study showed that insulin resistance as determined by HOMA-IR, is robustly associated and positively correlated with levels of HMBG1. On the other hand, IR as observed in patients presenting obesity alone was not significantly different from that of normal controls. A similar picture was obtained with serum insulin levels that were markedly higher in patients with MS compared to the other two groups of subjects.

**CONCLUSION**

Metabolic syndrome has emerged as a global forthcoming public health disorder over past few decades. Low grade inflammation being the prominent characteristic of metabolic syndrome leading to release of a cascade of cytokines enhancing the disease progression. Based on the findings of present study it is concluded that all the cardiovascular risk factors are vigorously higher in metabolic syndrome. HMBG1 is also found to be significantly raised and involved in individual component of MS. Depending upon the stimulus; HMBG1 is released extracellularly and binds to its specific receptors leading to activation of NF-κB signaling pathway which is central regulatory pathway of inflammation.HMBG1 has strong positive correlation with HOMA-IR and it is found to be raised in subjects having high fasting blood glucose. Significantly increased insulin resistance in MS patients revealed that HMBG1 related inflammatory pathway may be involved in pathogenesis of diabetes type 2.
Emergence of HMGB1 as a strong proinflammatory cytokine has opened a new window for future therapeutic interventions. HMGB1 blocking therapy should be considered pharmacologically to limit the inflammatory process. Blocking HMGB1 will result in improvement of all the components of metabolic syndrome. Also in future, study should be conducted on a larger population to further explore the role of HMGB1 in metabolic syndrome.

**Author’s Contribution:**

- Concept & Design of Study: Rabea Nasir
- Drafting: Usman Nasir, Ghazala Khalid
- Data Analysis: Rashid Siddique, Nimra Ikram, Akmal Khurshid Bhatti
- Revisiting Critically: Rabea Nasir, Usman Nasir
- Final Approval of version: Rabea Nasir

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

**REFERENCES**

Health Behavior of School-Aged Children in Sialkot

Usman Nasir¹, Rabea Nasir³, Ghazala Khalid², Rashid Siddique⁴, Nimra Ikram¹ and Akmal Khurshid Bhatti¹

ABSTRACT

Objective: To determine Health Behavior of School-Aged Children in Sialkot.

Study Design: Observational Study

Place and Duration of Study: This study was conducted at the Sialkot Medical College Sialkot during Jan 2019 to Dec 2019.

Materials and Methods: Health Behavior in School aged Children (HBSC) questionnaire was used in this study. Questionnaire survey was carried out in 2 schools of Sialkot. One school was private and one school was public. There were 300 participants and majority of them were 14 and 15 years old. Health behavior was measured with questions concerning adolescent’s nutritional habits (breakfast, fresh fruit and vegetable, sweets, fast food and soft drinks with sugar consumption), health-risk behavior (cigarette use, injuries) and physical activity. Statistical data was analyzed using the statistic package SPSS 15.0 for Windows.

Results: Two thirds (78.5%) of respondents thought they are in good health and just 4% claimed having excellent health. Results of this work showed, that forty one percent students of school exercise two-three times a week and seven point three percent less than once a month. It was determined that more than half of Sialkot teen agers eat morning food every day on end of the week, but on end of the week less than one third have morning food at home. One third of respondents stated, that eat fresh vegetable and 20.1% of then eat fresh fruit every day. Unhealthy diet products such as sweets, soft-drinks with sugar, fast food adolescents consumed (from 0% till 24.6%) every day or 4-6 times a week. Current study indicates that girls were less habitual to use carbonated drinks and junk foods as compared to opposite sex. They ingest more balanced diet. The results showed that 12.1% of adolescents reported smoking once a week. Statically significant differences were found among respondent gender and injuries. Young Girls were harm more often than boys in the past twelve month. Teenagers in Sialkot thought they are in excellent health less frequent than teenagers in Lithuania. Study result showed that statistically significant differences were found between breakfast consumption on weekends, nutritional habits, smoking of adolescents in Sialkot.

Conclusion: Adolescents in general experience good health in Sialkot. Physical activity of the majority adolescents did not meet the global WHO recommendations for school-aged children. Children above twelve years of age are used to intake raw vegetables frequently than the raw fruits. Majority of adolescent’s unhealthy diet products consumed rarely. Less beneficial foods is being more frequently ingested by males as compared to females. Teenagers in Lithuania enjoy very good health more often than teenagers in Sialkot. Health behavior of teenagers were different in Sialkot.

Key Words: Health habits, Children above 12 years, nutritional habits, health risk behavior


INTRODUCTION

Health behavior is one of the most important determinants of health. These are labors being adopted by persons regardless of their own condition of health in order to propagate, shield and perpetuate health. It may either effect positively or negatively. Multiple studies are needed to get data about health of babies and adolescents. These studies should encompass various activities related to health in order to collect data for health education. World health organization has defined health as well being physically, socially, and emotionally¹.

Thus, work into children’s health requires to consider the positive characteristic of health, as well as danger factors for future ailment and disease. Positive or health promoting behavior needs to be studied, as well as health-damaging or risk behavior.

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Printed: December, 2020
Certain behavior is initiated in the adolescent years, while some patterns of behavior, such as eating patterns, become established in earlier childhood. Taking a social as opposed to a purely biomedical research perspective means studying the social, environmental and psychological influences or determinants of child and adolescent health and health behavior.

This study was carried out in relation to health, taking food, tobacco and exercises. Adolescence is defined as the period from the onset of puberty to the termination of physical growth and attainment of final adult height and characteristics that occurs during the second decade of life. It can be known by abrupt physical growth, remarkable physical and psychological changes, and unfolding personal relationships. Children above 12 years and abrupt changes linked with it may have major effects on the health of individuals, and, conversely, variations in health may significantly affect the transitions of adolescence.

MATERIALS AND METHODS

The survey was conducted during Jan 2019 to Dec 2019 in 2 different types (one private and one public) of schools in Sialkot. Class was chosen as a sampling unit. The data was collected from 9th grade primary school students. The participants were 300 (200 boys and 100 girls). One hundred boys and fifty girls were from public school and hundred boys and fifty girls were from private school. Majority of respondents were 14 and 15 years old and just 3% of participant were 16 years old. More than 90% of participants lived in urban areas (cities, towns) and 5.5% in countryside.

Health Behavior in School aged Children (HBSC) questionnaire was used in this study. Health Behavior in School aged Children (HBSC), a world health organization (WHO) coordinated transnational work, collects data on 11-, 13- and 15-year-old boys’ and girls’ health and comfort, sociocultural context and combination of knowledge, practices, and attitudes that together contribute to motivate the actions we take regarding health, repeated after four years. This study used questions regarding health behaviors of adolescents. Data concerned, combination of knowledge, practices, and attitudes that together contribute to motivate the actions we take regarding health was collected with the help of survey questioning about measured with questions concerning adolescent’s the way a person or group eats various food items, Diseases causing habits like cigarette smoking and habits of doing exercise.

Adolescents were asked to fill in the questionnaire in school classroom during ordinary school hours. Written informed consent was obtained from the students after explaining the study objectives. The students were free to withdraw at any time without giving any reason.

Complete secrecy was observed during the process of data collection, entry and analysis. All attempts were made in this research to complete the ethical considerations in accordance with the ‘Ethical principles for medical research involving human subjects’ of Helsinki Declaration. The response rate was 100 percent.

RESULTS

The incidence of adolescent from City was maximum 204 (68.3%) and Minimum 16(5.5%) from Village as shown in table no 1.

Table No 1: Distribution of adolescent place of residence

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Place of residence</th>
<th>No of cases</th>
<th>age%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>City</td>
<td>204</td>
<td>68.3%</td>
</tr>
<tr>
<td>2</td>
<td>Town</td>
<td>80</td>
<td>26.7%</td>
</tr>
<tr>
<td>3</td>
<td>Village</td>
<td>16</td>
<td>5.5%</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

The incidence of adolescent male was 200 (66.66%) and 100 (33.33%) in female as shown in table no 2.

Table No 2: Gender Distribution of Adolescent

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Gender</th>
<th>No of cases</th>
<th>age%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>200</td>
<td>66.66%</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>100</td>
<td>33.33%</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

Fresh fruit and vegetable consumption is very important determinant regarding healthy lifestyle. Longitudinal studies suggest that fruit and vegetable consumption tracks into adulthood which points at the importance of establishing healthy eating behavior among children and adolescent.

One third (32.6%) of respondents stated, that eat fresh vegetable and 20.1% of them eat fresh fruit every day. This suggests that, fresh vegetables are more popular than fruits among adolescents. It was determined that no significant differences were found among gender and fresh fruit, vegetable consumption (Table 3). Other studies in Europe confirm opposite results, that vegetable intake was in general lower than fruit intake and boys consumed less fruit and vegetables than girls did.

Table No 3: Correlation between gender and exercise hour a week

<table>
<thead>
<tr>
<th>Exercise hour a week</th>
<th>Boys % (n)</th>
<th>Girls % (n)</th>
<th>Total % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.5 (3)</td>
<td>0</td>
<td>1 (3)</td>
</tr>
<tr>
<td>1/2 hours</td>
<td>12.5 (25)</td>
<td>16 (16)</td>
<td>13.7 (41)</td>
</tr>
<tr>
<td>1 hours</td>
<td>38 (76)</td>
<td>40 (40)</td>
<td>38.7(116)</td>
</tr>
<tr>
<td>2-3 hours</td>
<td>37 (74)</td>
<td>33 (33)</td>
<td>35.7(107)</td>
</tr>
<tr>
<td>4-6 hours</td>
<td>11 (22)</td>
<td>11 (11)</td>
<td>11 (33)</td>
</tr>
</tbody>
</table>

\( \chi^2 = 2.466; df = 4; p> 0.05 \)
Unhealthy diet products such as sweets, soft-drinks with sugar, fast food adolescents consumed (from 0% till 24.6%) every day or 4-6 times a week. It was determined that significant differences were found among gender and soft-drinks with sugar and fast food consumption – girls consumed unhealthy diet products less frequent than boys. No significant differences were found among gender and sweets consumption. Other studies confirmed that consumption of sugar-sweetened beverages, including soft drinks, has risen across the globe, accompanied by an increase in the prevalence of overweight and obesity. In summary every second 9th grade student in Sialkot has breakfast every day. Fresh vegetables are more popular than fruits among adolescents. Unhealthy diet products such as sweets, soft-drinks with sugar, fast food are more popular between boys than girls.
fresh fruits and vegetables than teenagers in Sialkot (Table 7).

**Table No 9: Correlation between fresh fruit and vegetable consumption of adolescents in Sialkot**

<table>
<thead>
<tr>
<th>Consumption Frequency</th>
<th>Sialkot % (n)</th>
<th>χ² = 39.9; df = 1; p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every day and 4-6 times a week</td>
<td>20.1 (60)</td>
<td></td>
</tr>
<tr>
<td>1-3 times a week and never</td>
<td>79.9 (239)</td>
<td></td>
</tr>
<tr>
<td>Total % (n)</td>
<td>100 (299)</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

Physical activity is an important lifestyle factor that is associated with a wide range of health benefits. Participation in regular physical activity in childhood and adolescence has also been reported to positively influence physical activity levels in adulthood.

Study results showed, that 41% of school students exercise 2-3 times a week and 7.3% less than once a month. No significant differences were observed between gender and student physical activity. In the survey information were collected regarding the time used to perform exercise. It was established that 11% of boys and girls spend 4-6 hours a week being physically active (Table 1). Which means, that small part of adolescents meet the global recommendations for school-aged children physical activity (participate in at least 60 minutes, and up to several hours, of at least moderate physical activity on a daily basis). Nutritional habits of adolescents in Sialkot the habitual decisions of individuals or group of people regarding what foods they eat are important relating to the activity undertaken by people for the purpose of maintaining or enhancing their health. Epidemiological research claims that youth breakfast consumption is very important part of young people future health. Regular breakfast consumption is associated with higher intakes of micronutrients, a better diet that includes fruit and vegetables and less frequent use of soft drinks. Despite the potential importance of breakfast consumption, the prevalence rates of breakfast skipping among children and adolescents have increased in the past few decades.

The study result showed that more than half (53.8%) of Sialkot adolescents eat breakfast every day on weekdays, but on weekends less than one third (28.1%) have breakfast at home. It was known, that there were gross variances between breakfast consumption on weekends and gender – girls eat breakfast less frequent then boys (Table 2). It should be noted, that 14% of despondences reported, never eat breakfast on weekends.

A recently published WHO/HBSC international report confirmed these study findings, determining that girls eat breakfast less frequent than boys. Adolescents in Lithuania consume sweets more frequent than school children in Sialkot, opposite findings were determined in soft-drinks with sugar consumption – adolescents in Lithuania consume soft-drinks with sugar less frequent than teenagers in Sialkot.

**CONCLUSION**

Adolescents in general thought they are good health in Sialkot. Physical activity of the majority of adolescents did not meet the global WHO recommendations for school-aged children. No statistically significant differences were found between the gender and physical activity. Every second 9th grade student had breakfast every day in Sialkot. Fresh vegetables were more popular than fresh fruits among adolescents. Boys and girls consumed fresh fruits and vegetables equally often.

2. Majority of adolescent’s unhealthy diet products such as sweets, soft-drinks with sugar, fast food consumed rarely (1-3 times a week or never). Unhealthy diet products were more popular between boys than girls in Sialkot.

3. The percentage rate of teenagers, who smoked daily, were small, girls smoke cigarette less frequent than boys. Adolescents smoking were related to self-rated poor health.
Author’s Contribution:
Concept & Design of Study: Usman Nasir
Drafting: Rabea Nasir, Ghazala Khalid
Data Analysis: Rashid Siddique, Nimra Ikram, Akmal Khurshid Bhatti
Revisiting Critically: Usman Nasir, Rabea Nasir
Final Approval of version: Usman Nasir

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

REFERENCES
Effects of Kalapather Poisoning on CPK, LDH, Blood Pressure and Heart Rate in Children

Mohammad Sarwar, Nighat Sultana, Umar Waqar, Fareeha Kausar, Anila Jamil and Ghazala Shaffqat

ABSTRACT

Objective: To study the Effects of Kalapather Poisoning on CPK, LDH, Blood Pressure and Heart Rate in Children.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the ICU children hospital Lahore during Jan 2014 to Dec 2019.

Materials and Methods: It was retrospective study. Sample size was 52. It was carried out in ICU of Children Hospital Lahore. SPSS version 25 was used for statistical analysis. Descriptive data and person correlation coefficient were measured. Informed written consent of parents was taken before start of study. The permission of Ethical Committee was considered before start of study and get published in Medical Journal.

Results: Mean values of CPK, LDH, heart rate, systolic blood pressure and diastolic blood pressure were much increased as compared to normal. CPK showed statistically significant and positive correlation with systolic and diastolic blood pressure.

Conclusion: Phenylenediamine PPD poisoning causes severe derangements in all systems of body in children. Blood pressure and heart rate increases along with CPK and LDH values yet if proper measure are taken timely then mortality may be reduced to minimum.

Key Words: CPK (creatine phosphokinase), LDH (Lactate Dehydrogenase), PPD (p-Phenylenediamine)


INTRODUCTION

Manner of poisoning in children is predominantly accidental.1 Accidental poisoning is a major cause of accidental hurts that take place in children which may cause loss of life or damage to body leading to disability. More than 50% total cases which attend poisoning emergency centers belong to accidental poisoning in few countries2. Various studies carried out in different countries of the world clearly indicate that accidental poisoning is more in male gender as compared to females. This is due to the fact that males are more agile than females. Children with less than six years of age more come across the accidental poisoning3. Different studies carried out to know the various reasons leading to accidental poisoning show that various elements like, how many are members of family, poverty, education, care of children and keeping the poisons and drugs separately are major facets influencing the occurrence of poisoning from things commonly used in houses like hair dye 4,5. Kala Pathar (black stone) is a low-cost and readily available hair dye in Pakistan. Its chemical ingredient PPD is a toxic and lethal substance when ingested6,7. After ingestion, PPD causes edema of face, neck, tongue, pharynx and larynx. Its poisoning also causes angioneurotic edema, rhabdomyolysis and renal failure8,9. Serum bilirubin, SGPT, SGOT, and serum alkaline phosphatase serum creatinine and CPK raised in its poisoning10,11.

MATERIALS AND METHODS

Sample Size: Fifty two patients of kala pather poisoning

Inclusion Criteria: Any children with history of poisoning of kalapather regardless of age, sex, socioeconomic condition and whose parents consented to take part in the study were included in the study.

Exclusion Criteria: Children with known heart disease were excluded from study.

This retrospective study was conducted on 52 patients of PPD (hair dye) poisoning, hospitalized in the Intensive Care Unit of children hospital Lahore during Jan 2014 to Dec 2019. Age, gender and body weight were recorded. History was taken. Heart rate, systolic and diastolic blood pressure was recorded. Physical
examination was performed. Blood was taken for measuring serum levels of CPK and LDH. Intubation, tracheostomy was performed where needed. Ventilators were provided to save life when required.

**Statistical Analysis:** It was performed by SPSS version 25. Descriptive data of age, weight, sex, CPK, LDH, heart rate, systolic and diastolic blood pressure was measured. Graphs and table were made. Pearson correlation coefficient was measured between cardiac enzymes and blood pressure and heart rate.

**RESULTS**

Mean values of CPK, LDH, heart rate, systolic blood pressure and diastolic blood pressure were much increased as compared to normal. CPK showed statistically significant and positive correlation with systolic and diastolic blood pressure.

**Table No. 1: Descriptive data of age, weight, sex, CPK, LDH, heart rate, systolic and diastolic blood pressure**

<table>
<thead>
<tr>
<th>Descriptive Statistics</th>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52</td>
<td>2.00</td>
<td>8.00</td>
<td>4.7196</td>
<td>1.57440</td>
</tr>
<tr>
<td>CPK</td>
<td>52</td>
<td>243.00</td>
<td>9175.00</td>
<td>1452.4231</td>
<td>2153.52173</td>
</tr>
<tr>
<td>LDH</td>
<td>52</td>
<td>432.00</td>
<td>8671.00</td>
<td>1296.8077</td>
<td>1586.30653</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>52</td>
<td>121.00</td>
<td>190.00</td>
<td>144.8462</td>
<td>15.68987</td>
</tr>
<tr>
<td>BP systolic</td>
<td>52</td>
<td>55.00</td>
<td>123.00</td>
<td>85.4231</td>
<td>17.24148</td>
</tr>
<tr>
<td>BP diastolic</td>
<td>52</td>
<td>38.00</td>
<td>90.00</td>
<td>55.0000</td>
<td>9.57939</td>
</tr>
</tbody>
</table>

**Table No. 2: Correlation between LDH and heart rate, systolic blood pressure and diastolic blood pressure LDH**

<table>
<thead>
<tr>
<th>Pearson correlation coefficient value</th>
<th>Value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>0.294</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.07</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>-0.03</td>
</tr>
</tbody>
</table>

**Table No. 3: Correlation between CPK and heart rate, systolic blood pressure and diastolic blood pressure CPK**

<table>
<thead>
<tr>
<th>Pearson correlation coefficient value</th>
<th>Value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>0.260</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.561</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.550</td>
</tr>
</tbody>
</table>

**Table No. 4: Correlation between CPK and LDH**

<table>
<thead>
<tr>
<th>Correlations</th>
<th>LDH</th>
<th>CPK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>.590*</td>
<td>.590*</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.000</td>
<td>.000</td>
</tr>
<tr>
<td>N</td>
<td>52</td>
<td>52</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In this study effects of kalapather poisoning on CPK, LDH, blood pressure and heart rate were studied. Correlation between all these variables was done on SPSS 25 version. 34 needed inotropes and only one patient developed arrhythmia which led to his death. Mortality was 1.9% only. Minimum heart rate noted was 121/min and maximum heart rate was 190/min. Minimum systolic blood pressure was 55 and maximum was 123 mm of Hg. Similarly minimum diastolic blood pressure was 38 and maximum was 90 mm of Hg. There was no statistically significant correlation between CPK and heart rate. But there was statistically positive and significant correlation between CPK and systolic as well as diastolic blood pressure. In case of LDH and heart rate there was weak correlation with value of r equal to 0.294. LDH did not give any significant correlation with systolic as well as diastolic blood pressure. In a study carried out in Nawab Shah12 it was found that mean value of CPK was 28.43 mg/dl while in this study minimum value of CPK was 243 mg/dl and maximum value was 9175 mg/dl.37.63 U/L was maximum value of CPK in a study in India13. But those for adults and this study was carried out in children. In another study it was found that tracheostomy was essential to save life of patient14. In another study in South India it was found that 92% patients had elevated levels of CPK15. In a study values of CPK and LDH were 3700 and 1854 U/L respectively. In this study values of CPK and LDH were drastically elevated yet mortality was very low. Only one death took place that developed arrhythmias.

**CONCLUSION**

Phenylenediamine PPD poisoning causes severe derangements in all systems of body in children. Blood pressure and heart rate increases along with CPK and LDH values yet if proper measure are taken timely then mortality may be reduced to minimum.

**Author’s Contribution:**

Concept & Design of Study:  Mohammad Sarwar, Nighat Sultana

Drafting:  Mohammad Sarwar, Nighat Sultana, Umar Waqar

Data Analysis:  Fareeha Kausar, Anila Jamil

Revisiting Critically:  Ghazala Shaffqat

Final Approval of version:  Mohammad Sarwar, Nighat Sultana

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


Frequency of Proximal Migration of Ureteric Stone during Ureteroscopic Pneumonic Lithotripsy in KPK
Shaukat Fiaz¹, Ikram Ullah, Noorul Hayat² and Muhammad Shahab³

ABSTRACT

Objective: To Study the Frequency of Proximal Migration of Ureteric Stone during Ureteroscopic Pneumonic Lithotripsy.

Study Design: Descriptive / cross sectional / Experimental study

Place and Duration of Study: This study was conducted at the department of Urology, Lady Reading Hospital Peshawar, from Jan 2019 to May 2020.

Materials and Methods: Sample size was calculated using WHO calculator and total 160 patients were enrolled with 5% margin of error and 95% confidence interval and consecutive nonprobability sampling technique was used. All patients having urinary stone of size less than or equal to 15mm, age 30-70 years and both genders were included in the study whereas all those who had previous history of ESWL, dj stent placement, age less than 30 and > 70 were excluded from the study.

After taking permission from ethical committee of the hospital, patients were admitted in the department and informed consent was taken. Detailed history and examination was performed and diagnosis was made by using x-ray KUB, Ultrasound abdomen and CTU or IVU (having normal RFTs). Data was recorded on a predesigned proforma and was analyzed using the statistical program SPSS version 20. Frequency and percentages were calculated for categorical variables like gender and stone migration. Descriptive statistics like mean ± standard deviation was calculated for numerical variable age and size of stone.

Results: During the study period 160 cases (83 male and 77 female) of ureteric stones were included in the study. In total 20 (12.5%) patients proximal stone migration was observed.

Conclusion: It is concluded from our study that proximal stone migration during pneumatic lithotripsy was major complication. And preventive measures were made for it.

Key Words: proximal migration of urteric stone, intra corpore lithotripsy, pneumatic lithotripsy


INTRODUCTION

Urolithiasis is a major clinical and economic burden for health care system. Stone disease incidence and prevalence is increasing as suggested by International epidemiological data. Worldwide 2 and 20% of population has stone disease. Prevalence of urolithiasis in Pakistan is from 4% to 20%, ureteric stones most often present with acute flank pain and hematuria. Patients can present with severe pain in emergency. Most common between 30 to 60 years. Most of the stones pass by itself without intervention. 77% of stones having size less than 5mm pass spontaneously, while more than 5 mm have a lesser than 46% chances of spontaneous passage. Distal and proximal ureteric stones have chances of spontaneous passage of 71% and 22% respectively. Intervention is required in patients having solitary obstructed kidney, unbearable pain, failure of conservative treatment, uro sepsis due to stones and sometimes on patient choice. Treatment options for ureteric stones include extracorporeal shock wave lithotripsy (ESWL), ureteroscopic lithotripsy, and ureterolithotomy (open and laparoscopic). Choice of Treatment is dependent upon stone size, location, patient’ preference and end urological facilities availability. Ureteroscopy (URS) with lithotripsy is most commonly performed procedure. Transurethral lithotripsy (TUL) is the treatment of choice for lower
and middle ureteric calculi. It has also been used for treatment of upper ureteral and renal stones. Based on recent studies, its use as a tray treatment modality for upper third ureteral stones has become popular; however, extracorporeal shockwave lithotripsy (ESWL) is still the treatment of choice. Multiple modalities are used for intra corporeal lithotripsy, including electrohydraulic, ultrasonic, and pneumatic laser lithotripters. In early 1990 Pneumatic lithotripsy (PL) was introduced several reports indicate very high success rates. It is less-costly and simple to manage as compared to laser, ultrasonic and electrolydraulic lithotripsy. For larger stones it is safe and highly efficacious procedure particularly in distal ureter. Complication of Pneumatic Lithotripsy include ureteral perforation, mucosal trauma, avulsion, ureteric stricture, urosepsis, stone migration, postoperative hematuria, fever, flank pain. Proximal stone migration is a common problem during ureteroscopic lithotripsy, especially when the pneumatic lithotripter is used. The documented incidence of stone migration is 11.36%.

MATERIALS AND METHODS

A descriptive cross sectional study was performed at the department of Urology, Lady Reading Hospital Peshawar, from 1 Jan 2019 to 30 May 2020. Sample size was calculated using WHO calculator and total 160 patients were enrolled with 5% margin of error and 95% confidence interval and consecutive nonprobability sampling technique was used. All patients having urinary stone of size less than or equal to 15mm, age 30-70 years and both genders were included in the study whereas all those who had previous history of ESWL, DJ stent placement, age less than 30 and >70 were excluded from the study.

After taking permission from ethical committee of the hospital, patients were admitted in the department and informed consent was taken. Detailed history and examination was performed and diagnosis was made by using x-ray KUB, Ultrasound abdomen and CTU or IVU (having normal RFTs). Data was recorded on a predesigned proforma and was analyzed using the statistical program SPSS version 20. Frequency and percentages were calculated for categorical variables like gender and stone migration. Descriptive statistics like mean ± standard deviation was calculated for numerical variable age and size of stone.

All results organized in the form of tab

Inclusion Criteria: Proximal Migration of Ureteric Stone during Ureteroscopic Pneumatic Lithotripsy

Exclusion Criteria: All the patients without stone of kidney were excluded from the study.

RESULTS

Duration of my study was from 1 Jan 2019 to 30 May 2020.

A total of 160 patients (51.8%) males and (48.2%) female) were included (TABLE 1)

Proximal migration of stone noted in 20 patients (12.5%). (TABLE 2)

Among the male patient 11 (13.25%) and in female 11.6% were noted with stone migration. P value > 0.05 (0.924). (Table 3)

Patients further categorized on basis of stone size.

Group 1 (stone size from 8-10mm), including 46 patients. Stone migrated in 5 (10.86%) patients.

Group 2 (stone size from 11-15mm, including 114 patients. Stone migration occurred in 15 (13.15%). P value 0.846 (>0.05). (Table 4)

Age limit was 31-70 years. Further distributed in 4 groups.

Group A age limit (31-40 years) include 62 patients. Stone migration was noted in 8 (13.33%) patients.

Group B age limit (41-50 years) included 56 patients. Stone migration was noted in 6 (10.7%) patients.

Group C age limit (51-60 years) included 26 patients and stone migration reported in 3 (11.5%).

Group D age limit (61-70 years) including 16 patients with incidence of stone migration in 2 patients (12.5%). P value was <0.05 (0.867) non-significant. (Table 5)

Mean age of the patient is 45 years and standard deviation of 10.1. Mean of stone size is 11.9 mm and standard deviation 10.1.

Table No.1: Frequency Distribution of Gender (N=160)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>83</td>
<td>51.8</td>
</tr>
<tr>
<td>Female</td>
<td>77</td>
<td>48.2</td>
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<tr>
<td>Total</td>
<td>160</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table No.2: Frequency Distribution of Upward Migration of Stone (N=160)

<table>
<thead>
<tr>
<th>Stone Migration</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>20</td>
<td>12.5</td>
</tr>
<tr>
<td>No</td>
<td>140</td>
<td>87.5</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table No.3: Cross Table of Gender with Upward Migration of Stone (N=160)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of patients</th>
<th>Stone migration</th>
<th>Percentage</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>83</td>
<td>11</td>
<td>13.25%</td>
<td>0.912</td>
</tr>
<tr>
<td>Female</td>
<td>77</td>
<td>9</td>
<td>11.6%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>20</td>
<td>12.5%</td>
<td></td>
</tr>
</tbody>
</table>
Table No.4: Cross Table of Upward Stone Migration with Stone Size (N=160)

<table>
<thead>
<tr>
<th>Stone size (mm)</th>
<th>No of Patients</th>
<th>Frequency of stone migration</th>
<th>Percentage</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 to 10</td>
<td>46</td>
<td>5</td>
<td>10.86%</td>
<td></td>
</tr>
<tr>
<td>11 mm to 15 mm</td>
<td>114</td>
<td>15</td>
<td>13.15%</td>
<td>0.814</td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>20</td>
<td>12.5%</td>
<td></td>
</tr>
</tbody>
</table>

Table No.5: Cross Table of Age with Upward Stone Migration (N=160)

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>No of patients</th>
<th>Frequency of stone migration</th>
<th>Percentage</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>62</td>
<td>9</td>
<td>14.51%</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>56</td>
<td>6</td>
<td>10.7%</td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>26</td>
<td>3</td>
<td>11.5%</td>
<td></td>
</tr>
<tr>
<td>61-70</td>
<td>16</td>
<td>2</td>
<td>12.5%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>20</td>
<td>12.5%</td>
<td></td>
</tr>
</tbody>
</table>

Table No.6: Mean and Standard Deviation of Stone Size and Age (N=160)

<table>
<thead>
<tr>
<th>Stone Size</th>
<th>n</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>160</td>
<td>8 mm</td>
<td>15 mm</td>
<td>11.919</td>
<td>2.1656</td>
</tr>
<tr>
<td>Age of Patient</td>
<td>160</td>
<td>31 years</td>
<td>70</td>
<td>44.20</td>
<td>10.149</td>
</tr>
</tbody>
</table>

DISCUSSION

Urolithiasis has a high incidence in the countries of Afro-asian stone belt having urological workload of 40-50%.

In hospitals, Management of ureteric calculi depends upon the size and location, stone of <5 mm in distal ureter has chances of spontaneous passage up to 98%, for stone of size up to 1 cm in proximal ureter ESWL should be the first option, ESWL and ureteroscopy are the available options for urteric stones. ESWL is minimally invasive and needs no anesthesia but the retreatment rate is high, URS gives higher stone clearance, but need anesthesia. In our experience Pneumatic lithoclast was found cost effective and more user’s friendly.

In a study reported the comparison of ESWL and ureteroscopy both has an excellent stone-free rate (86% to 90%) for stones smaller than 1 cm, whereas ureteroscopy have better result for larger stones i.e Ureteroscopy vs shock wave lithotripsy (67% vs 73%).

In bleeding diathesis and pregnancy preference was given to ureteroscopy over ESWL.

SWL is non on vasive and due to this generally accepted as the prior treatment option for ureteral stones, but PL with ureteroscopy has the advantage of higher and quick stone clearance rate and is good alternative. Pneumatic lithotripsy is preferred over ESWL in cases where quick stone removal is desired like for larger ureteric stones with more chances of obstruction, impaction and infection apart from this, PL may be chosen as the first line treatment rather than SWL for stones larger than 1 cm. Main complications observed were migration of a complete stone or its fragments (7.1%), urosepsis (4.5%) and perforation of ureter (1.3%) 10.

Some Perioperative complications associated with PL includes proximal stone migration into the kidney 7.2%, Damage to ureteric mucosa in (3.5%), ureteral perforation (1.7%), avulsion of ureter in (0.4%), and in (0.2%) cases it is converted to open surgery. Early postoperative complications included, Loin pain (18.4%), pelvic discomfort (5.5%), hematuria (7.3%), and urinary tract infection (5%) 11. Proximal stone fragments migration during pneumatic ureteroscopic lithotripsy is a common issue. A study has documented this incidence of stone migration about 11.36% 6.

Another study has reported 3.1% in lower and 7.6% in upper ureteric stone 12,13,14,15,16.

CONCLUSION

Our study showed that stone or its fragments migration was a big issue which urologist encounter during pneumatic lithotripsy of urteric stone, which further resulted in the procedure incompletion, added procedure, prolong hospital stay, economical burden. That’s why use of proper measures like N trap, Stone cone, Lidocaine jelly, Lithocatch etc. Should be taken to avoid the above consequences.

Author’s Contribution:
Concept & Design of Study: Shaukat Fiaz
Drafting: Ikram Ullah
Data Analysis: Noorul Hayat,
Muhammad Shahab
Revisiting Critically: Shaukat Fiaz, Noorul Hayat
Final Approval of version: Shaukat Fiaz

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

REFERENCES
Success of Streptokinase in Diabetic Smokers with ST-Elevation Myocardial Infarction (STEMI) with Absence of Other Factors
Hasan Sohail¹, Anum Hasan², Faryal Azhar³, Muhammad Usama Faruqui⁴ and Tahir Butt⁵

ABSTRACT

Objective: The objective of this study was to find success of streptokinase in diabetic smokers with ST-Elevation Myocardial Infarction (STEMI) with absence of other factors.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Punjab Institute of Cardiology, Lahore, Imran Idris Teaching Hospital Sialkot from Feb, 2018 to Aug, 2018.

Materials and Methods: A total of 382 cases meeting inclusion criteria were taken in this study after approval from hospital ethical committee. After taking informed consent all data was taken from Emergency department of Cardiology, Punjab Institute of cardiology Lahore, Imran Idris Teaching Hospital Sialkot. Basic demographer information of all cases such as age and their address, contact details were taken. Streptokinase was given to each patient at a dose of 1.5 million units, diluted in 100 ml of normal saline, in 1 hour. Informed written consent of the patient/attendant was taken. Success of Streptokinase (SK) was determined on ECG after 90 min as per operational definition. All data was collected by researchers them self on attached Performa.

Results: The mean age of cases was 46.45 ± 11.44 years with minimum and maximum age as 25 and 65 years. There were 370(96.9%) male and 12(3.1%) female cases. According to operational definition, a total of 200(52.4%) cases had success while 182(47.6%) cases did not have success of medication.

Conclusion: The frequency of success of streptokinase in diabetic smokers with ST-Elevation Myocardial Infarction (STEMI) with absence of other factors is 52.4%. So the cases with these conditions must be managed accordingly and the treatment strategies must be revisited in order to improve the treatment outcome of these cases.

Key Words: Myocardial infarction, diabetes, smoking, Streptokinase, ST elevations, fibrinolysis


INTRODUCTION

Infarction of Heart is the rapid development of necrosis of heart caused by a specific imbalance between oxygen supply and demand of heart.¹ The acute coronary syndromes include ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina.

1. Punjab Institute of Cardiology, Lahore.
2. Department of Community Medicine, Khawaja Muhammad Saifdar Medical College, Sialkot.
3. Department of Medicine / Community Medicine, SMC, Sialkot.
4. Department of Physiology, LMDC, Lahore.

Diabetes mellitus is one of the six primary risk factors identified for myocardial infarction.² Certain risk factors predispose to acute myocardial infarction which are categorized as modifiable (smoking, hypertension, high blood cholesterol, obesity, physical inactivity and diabetes) and non-modifiable (age, sex and family history of heart disease).³ Intravenous streptokinase during acute myocardial infarction is a well-recognized and effective treatment, which has beneficial effects on cardiovascular event related mortality.⁴ Conceptually, therapeutic intervention for STEMI must minimize cell death by break the ongoing process of obstruction of the blood supply and attempt to reverse the restriction in blood supply metabolic derangement of still living cells. The aim of thrombolysis in acute myocardial infarction is early and complete reperfusion.⁵ Recently it was published that ST resolution is not affected by the presence of diabetes. Although persons having diabetes have higher incidence of heart failure and in-hospital death after treatment of acute ST-elevation myocardial infarction with streptokinase, their poor outcome is most likely due to higher load of simultaneous coronary
risk factors. Smoking is also a well-known risk factor for coronary artery disease, and is associated with increased rates of myocardial infarction and cardiovascular death. In spite the fact that smoking is a well-established danger factor for the development of heart artery disease, some examiners have noted that hospital death after acute heart obstruction of the blood supply is lower in sick persons who smoke than in nonsmoking sick persons. There is some data showing lower mortality of smokers comparing to non-smokers in patients with ST-segment elevation myocardial infarction (STEMI) when treated with thrombolysis.

MATERIALS AND METHODS

This study was conducted at emergency department of Cardiology, Punjab Institute of cardiology Lahore and Imran Idris Teaching Hospital Sialkot. The sample size is estimated as 382 cases, the sample size is calculated using success of streptokinase in diabetic smokers with STEMI with absence of other factors as 45% (results of pilot study, attached), we used 5% margin of error and 95% confidence level. 

Inclusion criteria
- Diabetic smokers diagnosed of Acute Myocardial Infraction/ ST-Elevation Myocardial Infarction presented within 12 hours of chest pain
- Aged 25-65 years

Exclusion criteria
- History of previous myocardial infarction
- History of previous streptokinase (SK)

Data Collection Procedure: A total of 382 cases meeting inclusion criteria were taken in this study after approval from hospital ethical committee. After taking informed consent all data were taken from Emergency department of PIC. Basic demographer information of all cases such as age and their address, contact details were taken. Streptokinase was given to each patient at a dose of 1.5 million units, diluted in 100 ml of normal saline, in 1 hour. Informed written consent of the patient/attendant was taken. Success of SK was determined on ECG after 90 min as per operational definition. All data was collected by researcher himself on attached Performa.

Data Analysis: All collected data was entered and analyzed using statistical package for social science (SPSS) 22. Qualitative data like success of procedure was presented as frequency and percentage. Quantitative data such as age, duration of chest pain was presented as mean ± S.D. Data was stratified for age, gender and duration of chest pain to address effect modifiers. Post stratified Chi-square test was applied by taking p-value ≤ 0.05 as significant.

RESULTS

The mean age of cases was 46.45 ± 11.44 years with minimum and maximum age as 25 and 65 years. Table -1

There were 124(32.5%) cases who were 25-40 years old and 258(67.5%) cases were 41-65 years old. There were 370(96.9%) male and 12(3.1%) female cases.

The mean duration of chest pain was 6.78 ± 3.38 with minimum and maximum of 1 and 12 hours. Table -2

A total of 140(36.6%) cases had duration of chest pain as <6 hours and 242(63.4%) cases had duration as 6-12 hours.

According to operational definition, a total of 200(52.4%) cases had success while 182(47.6%) cases did not have success of medication.

When data was stratified for age, among 200 cases who had success there were 59(29.5%) cases who were 25-40 years old and 141(70.5%) cases were 41-65 years old. The frequency of success in both age groups was statistically same, p-value > 0.05. Table -3

On stratifying for gender, among 200 cases who had success there were 192 (96%) male and 8(4%) were female cases. The frequency of success in both genders was statistically same, p-value > 0.05. Table -4

When data was stratified for duration of chest pain, among 200 cases who had success there were 71(35.5%) cases who had chest pain <6hours and 129(64.5%) cases had duration as 6-12 hours. The frequency of success was statistically same in both groups of duration, p-value > 0.05. Table -5.

Table No.1: Descriptive statistics of age (years)

<table>
<thead>
<tr>
<th>Mean</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>46.45</td>
<td>11.44</td>
</tr>
</tbody>
</table>

Table No.2: Descriptive statistics duration of chest pain

<table>
<thead>
<tr>
<th>Mean</th>
<th>Duration (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.78</td>
<td>3.38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Range</th>
<th>11.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>1.00</td>
</tr>
<tr>
<td>Maximum</td>
<td>12.00</td>
</tr>
</tbody>
</table>
Comparison of success with respect to risk factors. Incidence of coronary disease is 10−7−4.

Among patients with an acute myocardial infarction, history of inside of an artery narrows arterial disease. Diabetes mellitus is one of the 6 primary danger factors detected for obstruction of blood vessels. Incomplete or failed restoring the flow of blood is associated with an increased danger of death and left heart abnormal functions. Currently available fibrinolytic agents that dissolve vascular thrombi are: a) n 0.1). Heart failure and in-hospital death were more common in persons having diabetes (twenty five point seven vs. 14.8%, p = 0.03 and 17.8% vs. 8.4%, p = 0.03, respectively). Diabetics were more likely to have three vessel disease in coronary angiography (23% vs. 8%, p < 0.001). After controlling for baseline finding, diabetes was not alone linked with restoring the flow of blood failure and major disadvantageous heart events, including heart failure and in-hospital death. Hence it can be concluded that ST resolution is not affected by the presence of diabetes. Although persons having diabetes have higher incidence of heart failure and in-hospital death after treatment of acute ST-elevation myocardial infarction with streptokinase, their poor outcome is most likely due to higher load of at the same time coronary risk factors.

So, in current study the mean age of cases was 46.45 ± 11.44 years with minimum and maximum age as 25 and 65 years. There were 370(96.9%) male and 12(3.1%) female cases. According to operational definition, a total of 200(52.4%) cases had success while 182(47.6%) cases did not have success of medication. According to operational definition, a total of 200(52.4%) cases had success while 182(47.6%) cases did not have success of medication. In another study thrombolytic effect of streptokinase infusion was compared between diabetic and non-diabetic myocardial infarction (MI) patients. In a probable interventional work, two hundred forty consecutive sick persons who were admitted to the emergency ward and diagnosed with ST-elevation MI were registered and classified into persons having diabetes (n = 85) and non-diabetics (n = 155). Streptokinase was given to each sick person at a dose of one point five million units in 1 h. Twelve-lead Electro Cardio Graphy was noticed immediately before the start of breakdown of clot treatment and at one hundred eighty min afterwards for the sick persons with acute ST-elevation myocardial infarction. The ST-segment elevation resolution was calculated and stratified as complete resolution (> 70% ST-resolution), partial resolution (30–70% ST-resolution), or failed resolution (< 30% ST-resolution). The main findings of the study showed that complete ST-resolution occurred in 31.6% of diabetic and 51.0% of non-diabetic patients, respectively (p < 0.001). The prevalence of partial ST-aim in diabetic and non- -diabetic sick persons was forty point five percent and forty percent, whereas twenty seven point eight percent of sick persons in the diabetic group and nine percent of person in the non-diabetic group showed failed ST resolution. ST-resolution was independent of the location of MI, two or more variable quantities investigation showed that

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### Table No.3: Comparison of success with respect to age groups (years)

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Success</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-40</td>
<td>59(29.5%)</td>
<td>65(35.7%)</td>
<td>124(32.5%)</td>
</tr>
<tr>
<td>41-65</td>
<td>141(70.5%)</td>
<td>117(64.3%)</td>
<td>258(67.5%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>200(100%)</td>
<td>182(100%)</td>
<td>382(100.0%)</td>
</tr>
</tbody>
</table>

Chi-square = 1.67  
*p-value = 0.195*

### Table No.4: Comparison of success with respect to gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Success</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>192(96%)</td>
<td>178(97.8%)</td>
<td>370(96.9%)</td>
</tr>
<tr>
<td>Female</td>
<td>8(4%)</td>
<td>4(2.2%)</td>
<td>12(3.1%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>200(100%)</td>
<td>182(100%)</td>
<td>382(100.0%)</td>
</tr>
</tbody>
</table>

Chi-square = 1.01  
*p-value = 0.313*

### Table No.5: Comparison of success with respect to duration of chest pain

<table>
<thead>
<tr>
<th>Duration</th>
<th>Success</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>71(35.5%)</td>
<td>69(37.9%)</td>
<td>140(36.6%)</td>
</tr>
<tr>
<td>Female</td>
<td>129(64.5%)</td>
<td>113(62.1%)</td>
<td>242(63.4%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>200(100%)</td>
<td>182(100%)</td>
<td>382(100.0%)</td>
</tr>
</tbody>
</table>

Chi-square = 0.239  
*p-value = 0.625*

**DISCUSSION**

Acute MI may be taken as a potential outbreak for human being. Incidence of coronary disease is increasing at an alarming rate not only in Pakistan but also in our region. Death rates from coronary heart disease in the UK were amongst the highest in the world but are falling now. However, South Asians living in the UK and Canada who do not display high rates of smoking, hypertension, or elevated cholesterol still have higher rates of coronary artery disease compared with Europeans.

The acute heart blood vessel syndromes include ST segment raised MI, non-ST segment raised MI, and unstable angina. Diabetes mellitus is one of the 6 primary danger factors detected for obstruction of blood vessels of heart, others are abnormal amount of lipids, high blood pressure, smoking, male sex, and family history of inside of an artery narrows arterial disease. Diabetes is a dyslipidemia disease and increases the rate of atherosclerotic progression of vascular occlusion.

Among patients with an acute myocardial infarction, 10-25% have diabetes. Even when hourly receiving agents which cause clot to break up the outcome in diabetic person is still bad than non-diabetics, manifesting impaired after break down of clot left heart function and prediction. The aim of thrombolysis in acute myocardial infarction is early and complete myocardial reperfusion. Incomplete or failed restoring the flow of blood is associated with an increased danger of death and left heart abnormal functions. Currently available fibrinolytic agents that dissolve vascular thrombi are: a) n 0.1). Heart failure and in-hospital death were more common in persons having diabetes (twenty five point seven vs. 14.8%, p = 0.03 and 17.8% vs. 8.4%, p = 0.03, respectively). Diabetics were more likely to have three vessel disease in coronary angiography (23% vs. 8%, p < 0.001). After controlling for baseline finding, diabetes was not alone linked with restoring the flow of blood failure and major disadvantageous heart events, including heart failure and in-hospital death. Hence it can be concluded that ST resolution is not affected by the presence of diabetes. Although persons having diabetes have higher incidence of heart failure and in-hospital death after treatment of acute ST-elevation myocardial infarction with streptokinase, their poor outcome is most likely due to higher load of at the same time coronary risk factors.

So, in current study the mean age of cases was 46.45 ± 11.44 years with minimum and maximum age as 25 and 65 years. There were 370(96.9%) male and 12(3.1%) female cases. According to operational definition, a total of 200(52.4%) cases had success while 182(47.6%) cases did not have success of medication. In another study thrombolytic effect of streptokinase infusion was compared between diabetic and non-diabetic myocardial infarction (MI) patients. In a probable interventional work, two hundred forty consecutive sick persons who were admitted to the emergency ward and diagnosed with ST-elevation MI were registered and classified into persons having diabetes (n = 85) and non-diabetics (n = 155). Streptokinase was given to each sick person at a dose of one point five million units in 1 h. Twelve-lead Electro Cardio Graphy was noticed immediately before the start of breakdown of clot treatment and at one hundred eighty min afterwards for the sick persons with acute ST-elevation myocardial infarction. The ST-segment elevation resolution was calculated and stratified as complete resolution (> 70% ST-resolution), partial resolution (30–70% ST-resolution), or failed resolution (< 30% ST-resolution). The main findings of the study showed that complete ST-resolution occurred in 31.6% of diabetic and 51.0% of non-diabetic patients, respectively (p < 0.001). The prevalence of partial ST-aim in diabetic and non- -diabetic sick persons was forty point five percent and forty percent, whereas twenty seven point eight percent of sick persons in the diabetic group and nine percent of person in the non-diabetic group showed failed ST resolution. ST-resolution was independent of the location of MI, two or more variable quantities investigation showed that
diabetes mellitus, as well as higher class and lower expressed as a percentage, of how much blood the left ventricle pumps out with each contraction, could effectively predict ST-resolution failure. Thus, Failure of ST-segment aim one hundred eighty min after streptokinase infusion is notably higher in diabetic vs non-diabetic sick persons. This failure rate is correlated with higher Killip class and lower ejection fraction\textsuperscript{16,19}.

**CONCLUSION**

The frequency of success of streptokinase in diabetic smokers with STEMI with absence of other factors is 52.4%. So the cases with these conditions must be managed accordingly and the treatment strategies must be revisited in order to improve the treatment outcome of these cases.

**Author's Contribution:**
- Concept & Design of Study: Hasan Sohail
- Drafting: Anum Hasan, Faryal Azhar
- Data Analysis: Muhammad Usama Faruqui, Tahir Butt
- Revisiting Critically: Hasan Sohail, Anum Hasan
- Final Approval of version: Hasan Sohail

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

**REFERENCES**


The Functional Outcome of Minimally Invasive Plate Osteosynthesis Technique in Fractures of Proximal Tibial Shaft

Adnan¹, Waqas Javed¹, Hannah Saleemi³, Ammara Shafqat³, M Arif¹ and Kamran Hamid²

ABSTRACT

Objective: To determine the functional outcome of minimally invasive plate Osteosynthesis technique in fractures of proximal tibial shaft.

Study Design: Observational Study

Place and Duration of Study: This study was conducted at the Imran Idris Teaching Hospital Sialkot during Jan 2020 to Oct 2020.

Materials and Methods: A total of 80 cases collected from patients presenting in department of orthopedics Imran Idris teaching hospital Sialkot fulfilling the inclusion and exclusion criteria were enrolled to determine the functional outcome of minimally invasive plate osteosynthesis technique in fractures of proximal tibial shaft. The inclusion criteria were explained about the procedure and written consent was taken, risks and benefits were discussed and proper follow up plan was made. All patients were operated in elective theatre of orthopedics department by the same surgeon. Patients were discharged on post-operative day #1 and were called in outpatient department every 4 weeks for follow up of functional outcome; the functional outcome at 16 weeks was done and recorded. The permission of Ethical Committee of the institute was taken to collect the data and get publishing in Medical Journal. The data analyzed for results by SPSS version 20.

Results: A total of 80 patients fulfilling the inclusion/exclusion criteria were enrolled to determine the functional outcome of minimally invasive plate Osteosynthesis technique in fractures of proximal tibial shaft. Age distribution of the patients was done which shows majority of the patients between 30-40 years i.e. 41.25% (n=33) while 31.25% (n=25) were between 41-50 years and 27.5% (n=22) were between 51-60 years, mean and sd was calculated as 41.34+3.76 years. Gender distribution of the patients was done which shows 71.25% (n=57) male and 28.75% (n=23) were females. Frequency of outcome of minimally invasive plate Osteosynthesis technique in fracture of proximal Tibial shaft reveals 61.25% (n=49) excellent and 38.76% (n=31) were good. Stratification of functional outcome for age of the patients was done and presented in Table No. 4, out of 33 cases between 30-40 years excellent were 21.25%(n=17) and 20%(n=16) were good, out of 25 cases between 41-50 years 22.5%(n=18) excellent and 8.75%(n=7) good, while out of 22 cases between 51-60 years 17.5%(n=14) were excellent and 10%(n=8) were good. Stratification of functional outcome for gender of the patients reveal out of 57 male case, 46.25% (n=37) were excellent and 25% (n=20) good while out 23 females 15% (n=12) excellent and 13.75% (n=11) were good.

Conclusion: The results of the study concluded that functional outcome in patients of fractures of proximal tibial shaft treated with minimally invasive plate osteosynthesis technique is significantly reliable and applicable in future.

Key Words: Proximal tibial shaft fracture, minimally invasive plate osteosynthesis, functional outcome, excellent, good


INTRODUCTION

The concept of biological osteosynthesis refers to the conservation of the vascularity of the bone during surgical intervention to ensure the continued vitality of the individual fragments and to improve fracture healing. Fracture is the result of mechanical overloading with important biological consequences¹. Treatment of the tibial fractures have evolutionized over a period of time and currently there are four principal methods of treating tibial diaphyseal fractures, although each method has a number of variants. Non-operative management can be undertaken using either long leg casts, patellar tendon-bearing casts which allow knee movement, or functional braces, which permit both knee and hind foot movement. The three
basic operative techniques are plating, intramedullary nailing and external fixation. In recent years, surgeons have stopped using fracture union as the only measure of successful treatment. As they have started to examine parameters such as joint stiffness, gait abnormality, and return to function and employment, it has become clear that there are a number of drawbacks to the use of casts or braces. High rates of joint stiffness and malunion after cast and brace management.

Proximal tibial diaphyseal fractures usually follow high-energy injuries, and are often comminuted. These fractures are notoriously difficult to perform interlocking nail, as they frequently become malaligned, the most common deformities are varus or an anterior bow.

Plating is one of the four main methods of treating tibial fractures. It requires open surgery, and the location of the incision and careful handling of the soft tissues are vital in order to minimize complications. No matter how much care is taken, however, soft tissue damage and periosteal stripping is inevitable, and this is a particular problem in comminuted or open fractures. With the MIPO technique, the fracture site is not exposed and further damage to the soft tissues is prevented or minimized preserving the fracture hematoma. The philosophy is therefore similar to that of intra medullary nailing. The incision for implant insertion is distant from the fracture, the fracture is reduced closed, and the fixation of the implant to the bone does not interfere with the fracture.

Nonsurgical treatment of tibial fractures can increases the incidence of mal-alignment with unacceptable shortening. Hooper et al concluded that no operative treatment resulted in more malunion and shortening. The most common surgical methods for treating distal tibial fractures are intramedullary nailing or medial plating. However, mal-alignment of the tibia may develop after nailing.

Conventional Interlocking technique showed higher incidence of mal-alignment and deformity than MIPO for the treatment of the proximal or distal third fracture of the tibial shaft.

Classic open reduction and internal plate fixation requires extensive soft tissue dissection and periosteal stripping, with high rates of complications. Minimally invasive plating techniques reduce iatrogenic soft tissue injury and damage to bone vascularity and preserve the osteogenic fracture hematoma.

MATERIALS AND METHODS

A total of 80 cases collected from patients presenting in department of orthopedics Idris hospital Sialkot fulfilling the inclusion and exclusion criteria were explained about the procedure and written consent was taken, risks and benefits were discussed and proper follow up plan was made. All patients were operated in elective theatre of orthopedics department by the same surgeon. Patients were discharged on post-operative day # 1 and were called in outpatient department every 4 weeks for follow up of functional outcome, the functional outcome at 16 weeks was done and recorded. The permission of Ethical Committee of the institute was taken to collect the data and get publishing in Medical Journal. The data was analyzed for results by SPSS version 20.

Inclusion Criteria: Fractures of proximal Tibial shaft were included in this study.

Exclusion Criteria: Without fractures of proximal Tibial shaft were excluded from the study.

RESULTS

A total of 80 patients fulfilling the inclusion/exclusion criteria were enrolled to determine the functional outcome of minimally invasive plate osteosynthesis technique in fractures of proximal tibial shaft.

Age distribution of the patients was done which shows majority of the patients between 30-40 years i.e. 41.25% (n=33) while 31.25% (n=25) were between 41-50 years and 27.5% (n=22) were between 51-60 years, mean and sd was calculated as 41.34±3.76 years. (Table No. 1)

Gender distribution of the patients was down which shows 71.25% (n=57) male and 28.75% (n=23) were females. (Table No. 2)

Frequency of outcome of minimally invasive plate osteosynthesis technique in fracture of proximal tibial shaft reveals 61.25% (n=49) excellent and 38.76% (n=31) were good. (Table No. 3)

<table>
<thead>
<tr>
<th>Table No 1: Age Distribution of the Patients (N=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>30-40</td>
</tr>
<tr>
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<tr>
<td>51-60</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Mean and sd</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No 2: Gender Distribution of the Patients (N=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No 3: Frequency of Outcome of Minimally Invasive Plate Osteosynthesis Technique in Fractures Oproximal Tibial Shaft (N=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional outcome</td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td>Excellent</td>
</tr>
<tr>
<td>Good</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
Stratification of functional outcome for age of the patients was done and presented in Table No. 4, out of 33 cases between 30-40 years excellent were 21.25%(n=7) and 20%(n=16) were good, out of 25 cases between 41-50 years 22.5%(n=18) excellent and 8.75%(n=7) good, while out of 22 cases between 51-60 years 17.5%(n=14) were excellent and 10%(n=8) were good. (Table No. 4)

Stratification of functional outcome for gender of the patients reveal out of 57 male case, 46.25% (n=37) were excellent and 25% (n=20) good while out 23 females 15% (n=12) excellent and 13.75% (n=11) were good. (Table No. 5).

### Table No.4: Stratification of Functional Outcome for Age of the Patients (N=80)

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>No. of patients</th>
<th>Excellent (%)</th>
<th>Good (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-40</td>
<td>33</td>
<td>17(21.25%)</td>
<td>16(20%)</td>
</tr>
<tr>
<td>41-50</td>
<td>25</td>
<td>18(22.5%)</td>
<td>7(8.75%)</td>
</tr>
<tr>
<td>51-60</td>
<td>22</td>
<td>14(17.5%)</td>
<td>8(10%)</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>49(61.25%)</td>
<td>31(38.75%)</td>
</tr>
</tbody>
</table>

### Table no. 5: Stratification of Functional Outcome for Gender of the Patients (n=80)

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of patients</th>
<th>Excellent (%)</th>
<th>Good (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>57</td>
<td>37(46.25%)</td>
<td>20(25%)</td>
</tr>
<tr>
<td>Female</td>
<td>23</td>
<td>12(15%)</td>
<td>11(13.75%)</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>49(61.25%)</td>
<td>31(38.75%)</td>
</tr>
</tbody>
</table>

### DISCUSSION

Minimally invasive techniques in proximal tibial fractures are technically feasible and may be advantageous in that it minimizes soft tissue compromise and devascularization of the fracture fragments.8-10 Indications for minimally invasive plate osteosynthesis of proximal fractures include displaced fractures involving the tibial plafond and those unstable fractures too proximal for safe stabilization with intramedullary nails.10 This technique involves conventional open reduction and internal fixation of the associated fibular fracture when present, followed by minimally plate osteosynthesis of proximal tibia utilizing precontoured plates and percutaneously placed cortical screws. Post-operatively early active and passive motion is permitted while weight bearing gradually progress. Minimally invasive techniques maintain alignment without compression; the operative exposure and soft tissue stripping are minimized with vascular pedicle preserved throughout.11

We planned this study considering the fact that the sample size of previous studies was very small, and in Pakistan no study was conducted on this technique and international studies are also constraint on this technique which emphasizes the need of further studies to determine its outcome.

The results in this study reveal that majority of the patients were between 30-40 years i.e. 41.25%(n=33), mean and sd was calculated as 41.34±3.76 years, 71.25%(n=57) were male and 28.75%(n=23) were females, frequency of outcome of minimally invasive plate osteosynthesis technique in fracture of proximal tibial shaft reveals 61.25%(n=49) excellent and 38.76%(n=31) were good.

These findings are in agreement with a study1 of 15 cases of proximal tibial fractures, they recorded 10 patient (i.e. 66.67%) achieved 0° to 110° of movement at the knee, in 4 patients (i.e. 26.67%) range of movement at the knee achieved was 90-110° (flexion) and in only one patient (i.e. 6.67%) the range of motion was 0 to 90° (flexion).

Another study by Mahajan N revealed Out of 20 patients, 14 (70%)had excellent results, 4 (20%)had good results and 2 (10%)patient had a fair result, these findings are in agreement with the results of the study but the difference with this study was that they used this technique in distal tibial fracture and we used in proximal tibial fractures, but the out of both studies are consistent.12,13,14

MIPO, however relies primarily on the indirect reduction of the fractures using various techniques and in this way, the fracture environment is better preserved, as well as the blood supply to the bony fragments is not disturbed, which finally leads to decreased infection rate better fracture healing. MIPO offers several theoretical advantages compared to conventional open plating technique. A mechanically stable fracture-bridging osteosynthesis can be obtained without significant dissection and surgical trauma to the bone and surrounding soft tissues. As a consequence, the vascular integrity of the fracture and the osteogenic fracture hematoma are preserved.15,16,17,18,19

### CONCLUSION

The results of the study concluded that functional outcome in patients of fractures of proximal tibial shaft treated with minimally invasive plate osteosynthesis technique is significantly reliable and applicable in future.

### Author’s Contribution:

**Concept & Design of Study:** Adnan
**Drafting:** Waqas Javed, Hannah Saleemi
**Data Analysis:** Ammara Shafqat, M Arif, Kamran Hamid
**Revisiting Critically:** Adnan, Waqas Javed
**Final Approval of version:** Adnan

### Conflict of Interest:

The study has no conflict of interest to declare by any author.
REFERENCES

Prevalence of Depression and Anxiety among Patients of Cardiovascular Diseases

Javaria Khan¹, Hena Athar¹ and Marryam Riaz²

ABSTRACT

Objective: To determine the prevalence of anxiety and depression among the patients having cardiovascular conditions.

Study Design: Cross sectional Study

Place and Duration of Study: This study was conducted at Chaudhry Muhammad Akram Teaching Hospital / Azra Naheed Medical & Dental College, Lahore for a duration of six months from February 2020 to July 2020.

Materials and Methods: One hundred and forty-two patients of cardiovascular disease were selected. Patients' detailed demographics including age, sex, marital status, socioeconomic status, profession and education were recorded after taking written consent. Patients were issued with a questionnaire. These patients were selected randomly with the help of hospital administration. AKUADS questionnaires were used to estimate the prevalence of anxiety and depression among CVD patients. Patients who scored 19 or above were considered as suffering from anxiety and depression. Data was analyzed by using SPSS-24.0 software

Results: The mean (SD) age of the patients was 45.4 (8.1) years. Female patients were in majority (58.5%). 96 (67.06%) had depression and anxiety. Patients with family history of anxiety and depression were 29%. Most of the CVD patients belonged to the middle socio-economic class. Majority were suffering from dysfunctional behavior, agoraphobia, and obsessive-compulsive disorder.

Conclusion: It is concluded that depression and anxiety are strongly linked with cardiovascular diseases such as Hypertension, Ischemic heart Disease and Heart Failure. These risks must be identified by the treating physician and hence appropriate interventions be taken for managing these symptoms. The awareness of mental stress and conditions needs improving and addressed accordingly as it is often forgotten while prioritizing cardiovascular illness.

Key Words: Depression, Anxiety, Cardiovascular disease, Hypertension, Ischemic heart Disease, Heart failure.

Citation of article: Khan J, Athar H, Riaz M. Prevalence of Depression and Anxiety among Patients of Cardiovascular Diseases. Med Forum 2020;31(12):187-190.

INTRODUCTION

Enormous studies have been done on the impact of depression and anxiety in patients with heart diseases and the aggravation of mental health issues concomitantly with cardiovascular conditions. Cardiovascular disease promotes depression and anxiety and their coexistence may affect the QoL (quality of life) of patients and may cause mortality. Previous several researches have confirmed that the patients of early forties and fifties were diagnosed with cardiovascular disease.

¹ Department of Family Medicine, Primary Healthcare Corporation, Locum General Practitioner, UK.
² Department of Physiology, Azra Naheed Dental College, Lahore.

The patients with CVD showed significant impact of depression and anxiety on their efficacy towards treatment and prognosis. Approximately 1 out of every 5 patients with CVD has major Depressive Disorder (MDD). In 2002, it was revealed that MDD was the ⁴th major cause of worldwide disability and by 2030 it is anticipated to become the ²nd major cause of worldwide disability. It is observed that post-myocardial depression increasingly prevailed in younger population. Depression and anxiety causes behavioral and physical changes which promotes the occurrence of CVD and these may facilitate and progress to disturb the neuroendocrine and autonomic nervous system, which ultimately leads to disturbance in cardiac rhythm regularities. Depression may play as a catalyst between CVD and psychosocial factors as it may cause smoking as well as other substance misuse. Further it may reduce physical activity, improper diet, and failure to act in accordance with medical advice. Mental disorders like depression and anxiety mostly occur in long running and chronic cardiovascular diseases as they are related to an increased risk of hospitalization and as a result of this the overall mortality increases.
There is need to focus more on the recognition of such mental disorders with their interventions so that the patients with CVD may be provided with good care leading to better outcomes for both physical as well as mental health.

MATERIALS AND METHODS

This cross-sectional study was done at Chaudhry Muhammad Akram Teaching Hospital/ Azra Naheed Medical & Dental College. Lahore for duration of six months from 1st February 2020 to 31st July 2020. A self-administered questionnaire was given to the patients. These patients were selected randomly with the help of hospital administration. Current research was conducted with the approval of the head of the department. Full consent was taken from the patients for this study. AKUADS (Agha Khan University Anxiety and Depression Scale) was used to access the anxiety and depression levels. Patients who scored 19 or greater were considered as suffering from anxiety and depression. AKUADS has specificity of 81%, sensitivity of 74%, a positive predictive value of 63%, and negative predictive value of 88% at a cut off score of 19 points. All data was analyzed by using SPSS-21. Additional questions were also included in this study to examine the correspondence between socio-demographic characteristics and the frequency of depression and anxiety. It was made possible to ensure the full confidentiality of the identity of the respondents as they were asked not to write any identifying explanations on the questionnaires. To investigate the distribution of our data, descriptive analysis was made.

RESULTS

Table No.1: Descriptive Characteristics of Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency n</th>
<th>%</th>
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</thead>
<tbody>
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<td>Mean age (SD)</td>
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<td>-</td>
</tr>
<tr>
<td>Age:</td>
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<tr>
<td>30-40</td>
<td>25</td>
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<td>41-50</td>
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</tr>
<tr>
<td>51-60</td>
<td>72</td>
<td>50.7</td>
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</tr>
<tr>
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<tr>
<td>Male</td>
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<td>41.5</td>
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<td>Female</td>
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<td>58.5</td>
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<td>Socio-economic Status</td>
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<td>Low</td>
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<td>43.67</td>
</tr>
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<td>High</td>
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<td>23.94</td>
</tr>
<tr>
<td>Education</td>
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<tr>
<td>Literate primary</td>
<td>55</td>
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<td>High school</td>
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<tr>
<td>Intermediate</td>
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<td>14.79</td>
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<td>Family History of CVD</td>
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<tr>
<td>Yes</td>
<td>38</td>
<td>26.76</td>
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</table>

Table No 2: Risk Factors Associated with Depression and Anxiety

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency</th>
<th>Depression and anxiety</th>
<th>Depression and anxiety</th>
</tr>
</thead>
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<tr>
<td>Age:</td>
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<td></td>
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<tr>
<td>30-40</td>
<td>25</td>
<td>9 (36)</td>
<td>16 (64)</td>
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<tr>
<td>41-50</td>
<td>45</td>
<td>21 (46.67)</td>
<td>25 (55.56)</td>
</tr>
<tr>
<td>51-60</td>
<td>72</td>
<td>66 (91.67)</td>
<td>6 (8.33)</td>
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<tr>
<td>Marital Status</td>
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<td>Married</td>
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<td>89 (66.92)</td>
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<td>9</td>
<td>7 (77.77)</td>
<td>2 (22.23)</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>59</td>
<td>30 (50.85)</td>
<td>29 (49.15)</td>
</tr>
<tr>
<td>Female</td>
<td>83</td>
<td>66 (79.52)</td>
<td>17 (20.48)</td>
</tr>
<tr>
<td>Socio-economic Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>46</td>
<td>40 (86.96)</td>
<td>6 (13.04)</td>
</tr>
<tr>
<td>Middle</td>
<td>62</td>
<td>37 (59.68)</td>
<td>25 (40.32)</td>
</tr>
<tr>
<td>High</td>
<td>34</td>
<td>19 (55.88)</td>
<td>15 (44.12)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literate primary</td>
<td>55</td>
<td>45 (81.82)</td>
<td>10 (18.18)</td>
</tr>
<tr>
<td>High school</td>
<td>66</td>
<td>40 (60.61)</td>
<td>26 (39.39)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>24</td>
<td>11 (45.83)</td>
<td>13 (54.17)</td>
</tr>
<tr>
<td>Family History of CVD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>38</td>
<td>33 (86.84)</td>
<td>5 (13.16)</td>
</tr>
<tr>
<td>No</td>
<td>104</td>
<td>63 (60.58)</td>
<td>41 (39.42)</td>
</tr>
</tbody>
</table>

Depression and anxiety were found in 96 (67.06%) patients while 46 (32.94%) patients had no depression and anxiety. (Figure 1).

Out of 142 patients, 59 (41.5%) were male while 83 (58.5%) were females. 25 (17.6%) patients were in between 30 to 40 years of age, 45 (31.6%) patients were in between 41 to 50 years and 72 (50.70%) patients were in between 51 to 60 years, mean age of patients was 45.4±8.1 years. 133 (93.7%) patients were married while 9 (6.3%) were unmarried. 46 (32.39%) patients...
had low socio-economic status, 62 (43.67%) had middle and 34 (23.94%) patients had high socio-economic status. 55 (38.7%) patients had primary level education, 66 (46.4%) had high school and 21 (14.79%) had intermediate. Different levels of anxiety and depression were noted after the careful evaluation and calculations of all the variables. Low socio-economic status, low education, older age, disease duration, female gender, and family history of CVD were the significant risk factors for depression and anxiety with p-value <0.05. (table 2)

DISCUSSION

CVD is often followed by anxiety disorders and is often imitable as cardiac functional syndromes. Depression induces behavioral and physiological changes that can lead to and accelerate the development of CVD\[13, 14\]. Smoking, alcohol and substance misuse, physical activity reduction, an inappropriate diet and compliance to medical advice cannot be accommodated immediately due to depression. Factors including autonomic nervous system activation and hormone disturbances, metabolic disorders and inflammation can be the trigger due to psychosocial factors with CVD. These factors may then result in an increased accumulation of platelets as well as endothelial dysfunction.

In present study 59 (41.5%) were male while 83 (58.5%) were females. 25 (17.6%) patients had ages of 30 to 40 years, 45 (31.6%) patients were having ages 41 to 50 years 72 (50.70%) patients had ages 51 to 60 years, mean age of patients was 45.4±8.1 years. 133 (93.7%) patients were married while 9 (6.3%) were unmarried. 46 (32.94%) patients had low socio-economic status, 62 (43.67%) had middle and 34 (23.94%) patients had high socio-economic status. 55 (38.7%) patients had primary level education, 66 (46.4%) had high school and 21 (14.79%) had intermediate. These results were comparable to many of previous studies [15-16].

We found that 96 (67.06%) patients had depression and anxiety (alone or combined) while 46 (32.94%) had no symptoms of depression and anxiety. A study conducted by Dhital PS et al [17] regarding depression and anxiety in cardiac patients and they reported depression found in 23.8% patients and anxiety found in 27.4% patients.

The findings and the results after the analysis of all the data from 142 patients with cardiovascular disease proves that the frequency of depression and anxiety increased as the disease progressed. In this study, we observed the risk factors like age, sex, marital status, family history of CVD, education, low socio-economic status and low education were correlated with the frequency of anxiety and depression among the patients of cardiovascular diseases.

These results were comparable to many of previous studies [18-19]. It is found that participation in social activities and patient’s quality of life plays key role in prevention from depression and anxiety. The significant impact of depression and anxiety on quality of life and its potential relation to mortality has been reported. An expert working group of the National Heart Foundation of Australia that reviewed the evidence had mixed findings. They concluded that there is an independent causal association between depression, its etiology, and prognosis of CVD, but did not find such a strong relationship with anxiety disorders/panic disorder [20]. On the other hand, Kawachi et al [21] showed an increase risk of sudden cardiovascular death among patients with panic and phobic symptoms. Many studies point toward an increased risk of sudden cardiac death in patients with depression as well [22-23].

Many observational studies suggest that the lack in social support play a key role in delaying the complete prognosis of cardiovascular diseases in depression patients [24]. For the improvement of depressive symptoms, exercise interventions can be more effective as pharmacotherapy [25-26]. However, it is difficult particularly for the depressed individuals to achieve motivation to begin and sustain behavioral change. It is need of the hour to focus on how these patients could be engaged and motivated in behavioral change plans and how to get support for these patients from health care providers, family, and social networks [27-28].

More studies are however needed to support the link between the socioeconomic factors and chronic cardiovascular conditions. Individual risk factors and their association to the CVS conditions, if done, will support our study.

Moreover, cardiovascular conditions with grave outcomes or lesser survival years might as well be linked to more psychological adverse outcomes. This requires a separate research.

CONCLUSION

There is a close association between anxiety and depression with the increased risk of cardiac-related events and morbidity and mortality in patients with CVD. Depression and anxiety prevailed among the cardiovascular disease patients particularly in the chronic disease patients. There was the lack of acceptance of psychological diseases by the patients and hence, they had less response towards the interventions. Low socio-economic status and low literacy rate of patients were the major reasons behind the increased prevalence of anxiety and depression among cardiovascular patients.

Author’s Contribution:
Concept & Design of Study: Javaria Khan
Drafting: Hena Athar
REFERENCES


**Relevance of High Sensitivity C-Reactive Protein (hs-CRP) Level in Patients with Acute Coronary Syndrome (ACS) and Short Term Outcome**

Gul Hassan Brohi¹, Shahzeb Rasool Memon², Shahbaz Ali Shaikh³, Kamran Ali Shahani⁴, Sarfraz Hussain Sahito⁵ and Mukhtiar Abro⁵

**ABSTRACT**

**Objective**: To evaluate the relevance of High Sensitivity C-Reactive Protein (hs CRP) level in patients with acute coronary syndrome (ACS) and short term outcome.

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

**Place and Duration of Study**: This study was conducted at the Department of Cardiology, Liaquat University Hospital Hyderabad for six months from 15th March 2018 to 14th September 2018.

**Materials and Methods**: The ACS (ST elevated MI, non-ST elevated MI, and Unstable Angina) patients were confirmed based on clinical history, ECG, Cardiac Enzymes, cardiac markers (Troponins), and further evaluated for hs-C-reactive protein levels. The data were analyzed in SPSS version 16.

**Results**: A total of 60 patients with acute coronary syndrome were recruited i.e. 40(00.7) STEML, 14(23.3%) NSTEMI, and 6(10%) unstable angina. The mean CRP level of intermediate-risk was 2.51±0.51, p<0.001, high-risk 10.95±7.7, pp<0.001, and low risk 0.862±0.51. There are significant values (<0.05), and 2(9.5%) died in the low-risk group. Six (85.7%) alive and 14 (43.75%) die in a high-risk group, 4 (19%) in the low-risk group, 1(14.3%) in the intermediate-risk group, and 8(25%) high-risk group were hospitalized within three months. The mean ± SD of CRP with STEMI, NSTEMI, and UA was 6.82±8.0, 5.11±5.9, and 4.77±8.2 (p=0.05).

**Conclusion**: Serum hs-CRP levels show a significant correlation with the acute coronary syndrome. Measurement of C-reactive protein may have clinical significance in the management of patients hospitalized for the confirmed acute coronary syndrome.

**Key Words**: C-reactive protein, acute coronary syndrome, short-term outcome, high sensitivity.

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**INTRODUCTION**

Cardiovascular diseases remain the leading cause of death worldwide, making it essential to realize the causes, pathogenesis of these diseases, and improve their diagnostic and treatment capabilities as well as prophylactic programs.¹ Numerous research has shown the correlation of pro-inflammatory biomarkers with recurrent hypertension, cardiovascular, coronary artery disease (CAD) disorder (ACS), peripheral artery disease, stroke and repeated coronary and cerebrovascular disorders, with the investigator (checked-case and prospective cohort) as well as with randomized controlled trials (RCTs).² A meta-analysis of such measurement trials has found that the high-quartile hsCRP levels are 1.5 in contrast to the lowest quartile has, after the modification of the established risk factors for significant cardiovascular events.² C-reactive protein (c-reactive protein CRP) is a much better indicator of outcome than CRP through conventional assays, which is separately correlated with cardiovascular events in all low-density cholesterol lipoprotein types.² People of land- Asian origin have one of the highest susceptibilities to Coronary artery disease (CAD) in the world,¹,² and it is therefore not surprising that CAD is

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Printed: December, 2020
now the leading cause of death in the Indo-Pakistan subcontinent.\(^3\)

C reactive protein is an acute phase reactant synthesized in the liver. It is a predictor of mortality and morbidity independent of LDL cholesterol levels.\(^5\) Elevated CRP level indicated the consequences of the active coronary atherosclerotic lesion in inflammation or tissue injury.\(^4\) CRP is considered as a cardiovascular predictor when a baseline of more than 10 mg suggests a non-cardiogenic vascular source of inflammation such as infection, or a chronic inflammatory state. Its clinical diagnosis based on the history of chest pain, ECG showing with or without ST-segment changes. Non-ST EMI myocardial infarction is based on whether an elevation in myocardial protein such as creatinine kinase/Troponins.\(^5\) The research dealt with the pertinence of high-sensitivity C-reactive protein (hs CRP) levels in acute syndrome patients and short-term effects.

**MATERIALS AND METHODS**

This cross-sectional study was carried out on 60 consecutive patients confirmed as Acute Coronary Syndrome in the Department of Cardiology Liaquat University Hospital Hyderabad for six months from 15\(^{th}\) March 2018 to 14\(^{th}\) September 2018. All patients presenting as ACS, diagnosed based on clinical history, ECG, Cardiac Enzymes, Cardiac markers were included in the study while all those patients who do not fulfill the inclusion criteria and atypical chest pain were excluded from the study.

Informed written consent was taken from all patients for participation in the study. All such patients were further evaluated for their hs-CRP levels and divided into three groups based on the level of hs-CRP i.e. low risk, intermediate-risk, and high risk. Data was collected on pre-designed proforma, a high standard of Medical ethics was observed.

**Data Analysis:** The data was evaluated using program SPSS version 22.0. The chi-square test was applied among the categorical parameters at 95% confidence interval and the p-value < 0.05 was considered statistically significant.

**RESULTS**

A total of 60 patients were included in the study. The mean CRP levels were found to be 10.95 mg/L in the total no. of patients with acute coronary syndrome included. There was no significant correlation between age and CRP level (r=0.11, p<0.05) in total subjects meaning that there is no influence of age on elevated c-reactive protein in acute. The total subjects were divided into three groups based on CRP, of low risk consists of 21 patients while 7 patients were included in the intermediate-risk group. High-risk Group comprised of 32 patients. The mean CRP levels of intermediate risk (2.51) ± 0.51, p < 0.001), and high risk (01.59 ± 7.7 p< 0.001) are significantly higher as compared to low risk (0. 862 ± 0.51). Table: 05, there is a significant relationship between mortality rate and three groups based on the risk of CRP levels. Lt means that high levels of CRP in ACS patients have been proved to be a good mortality predictor in this study. and Table: 06 showed a comparison of 3 months' pre-hospitalization among total patients in three groups. There is no significant relation between pre-hospitalization and the three groups based on CRP levels. When three groups were compared based on risk factors, Table: 05 shows the comparison of the groups based on no risk while Table: 07 shows the mean values of CRP along with standard error of the mean. There is a significant difference between CRP levels of both groups of low risk and high risk (p=0.04). CRP levels are significantly higher in high-risk groups as compared to low-risk groups (p<0.001) showing that smoking has a great influence on CRP levels, there is no significant difference between the levels of CRP in the three groups divided based on diabetes mellitus (p=0.11). Lt is suggested on this basis that Diabetes mellitus has no independent effect on CRP levels in these three groups. Hyperlipidemia was not found in three groups. Statistical analysis shows a significant association between the three groups and two combined risks (p<0.05) but due to variation and sample size in three groups, CRP levels are not found significantly higher with the increase in high risk when groups were compared based on two risk factors.

**Table No.1: Baseline characteristics of the patients (n = 60)**

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Number</th>
<th>%age</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-</td>
<td>-</td>
<td>55.2 ± 11.4 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender: Male</th>
<th>50</th>
<th>83 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>10</td>
<td>17 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors: Smoker</th>
<th>28</th>
<th>47 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>06</td>
<td>10 %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>06</td>
<td>10 %</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>Nill</td>
<td>Nil</td>
</tr>
<tr>
<td>CRP levels</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table No.2: C-Reactive protein levels in three groups**

<table>
<thead>
<tr>
<th>Level</th>
<th>Mean CRP ±SEM</th>
<th>Mean Age ±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Low risk (hs CRP &lt;2Mg/L)</td>
<td>0.862±8.81</td>
<td>52.23±8.81</td>
</tr>
<tr>
<td>2. Intermediate Risk (hs CRP=23 mg/L)</td>
<td>2.51 ±0.51***</td>
<td>51.85±6.51</td>
</tr>
<tr>
<td>3. High Risk (hs CRP&lt;3v mg/L)</td>
<td>10.95 ± 7.7 ***</td>
<td>55.2±11.4</td>
</tr>
</tbody>
</table>

***p<0.001 with respect to the low-risk group.
The diabetic hypertensive patients of intermediate-risk groups have significantly higher CRP values (p = 0.048) when compared with diabetic hypertensive patients of low-risk groups, but the high-risk group has non-significant higher CRP levels when compared with a low-risk group (p = 0.499). Whereas the smoking hypertensive patients of intermediate-risk groups have significantly higher CRP values (p = 0.031) when compared with smoking hypertensive patients with the low-risk group. The high-risk group in smoking hypertensive has a significantly higher CRP level when compared with the low-risk group (p = 0.008). This study shows mean values of CRP in three groups divided based on the type of ACS i.e. STEMI, NSTEMI, and UA. There is a significant association between mortality rate and type of ACS (p = 0.05). The present study also found that increased CRP levels were associated with increased risk for death in three months follow-up.

Table No.3: The outcome of patients based on mortality, re-hospitalization, and risk factors (n = 60)

<table>
<thead>
<tr>
<th></th>
<th>Low risk (hs CRP&lt;2 mg/L) n = 21 (%)</th>
<th>Intermediate Risk (hs CRP=2-3) n = 7 (%)</th>
<th>High Risk (hs CRP&lt;3 Mg/L) n = 32 (%)</th>
<th>X² value</th>
<th>df</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>19(60.5%)</td>
<td>6(85.7%)</td>
<td>18(56.25%)</td>
<td>151.5</td>
<td>2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Died</td>
<td>2(9.5%)</td>
<td>1(14.3%)</td>
<td>14(43.75%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re- Hospitalization</td>
<td>04(19%)</td>
<td>01(14.3%)</td>
<td>08(25%)</td>
<td>5.695</td>
<td>01</td>
<td>(&lt;0.05)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>07(33.4%)</td>
<td>01(14.3%)</td>
<td>10(32%)</td>
<td>28.86</td>
<td>04</td>
<td>(&lt;0.05)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>04(19%)</td>
<td>0(0.0%)</td>
<td>02(6.25%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>0(0.0%)</td>
<td>02(28.6%)</td>
<td>04(12.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTN + DM</td>
<td>02(9.5%)</td>
<td>02(28.6%)</td>
<td>03(9.4%)</td>
<td>90.537</td>
<td>04</td>
<td>(&lt;0.05)</td>
</tr>
<tr>
<td>HTN + Smoker</td>
<td>06(28.6%)</td>
<td>01(14.3%)</td>
<td>06(18.75%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker + DM</td>
<td>0(0.0%)</td>
<td>01(14.3%)</td>
<td>02(6.25%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table No.4: CRP levels among three groups based on no risk

<table>
<thead>
<tr>
<th>No of Patients</th>
<th>Percentage</th>
<th>Mean CRP levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk(hs CRP&lt;2 mg/L)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intermediate Risk(hs CRP=2-3mg/L)</td>
<td>01</td>
<td>14.3</td>
</tr>
<tr>
<td>High Risk(hs CRP&lt;3 Mg/L)</td>
<td>08</td>
<td>25</td>
</tr>
</tbody>
</table>

Table No.5: Comparison of CRP levels Among three groups on the basis of one risk factor

<table>
<thead>
<tr>
<th>Smoker</th>
<th>Diabetes Mellitus</th>
<th>Hypertension</th>
<th>Dyslipidaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (hs CRP&lt;2 mg/L)</td>
<td>1.09±0.564</td>
<td>0.85± 0.436</td>
<td>Nil</td>
</tr>
<tr>
<td>Intermediate Risk (hs CRP=2-3mg/L)</td>
<td>2.1± 0.00</td>
<td>Non-significant</td>
<td>2.45± 0.07</td>
</tr>
<tr>
<td>High Risk (hs CRP&lt;3 Mg/L)</td>
<td>8.14± 4.92***</td>
<td>P&lt;0.01</td>
<td>23.4± 2.5</td>
</tr>
</tbody>
</table>

Table No.6: Comparison of CRP Levels Among Three Groups On the Basis of Tow Risk Factors

| 1. Low risk (hs CRP<2MG/l) | 1.20 | 0.85 0.436 | Nil | Nil |
| 2. Intermediate Risk (hs CRP=2-3mg/L) | 2.35 | 0.05 | 2.30 0.01 | P=0.031 | Nil | 2.9 0.0 |
| 3. High Risk (hs CRP>3 mg/L) | 10.33 9.67 | P=0.499 | 8.8 3.45 | P=0.008 | Nil | 10.65 3.04 | P=0.27 |

Table No.7: Comparison of CRP levels among three groups on the basis of type of ACS

<table>
<thead>
<tr>
<th>Mean value of CRP ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. STEMI</td>
</tr>
<tr>
<td>2. NSTEMI</td>
</tr>
<tr>
<td>3. UA</td>
</tr>
</tbody>
</table>
DISCUSSION

The present study includes a group of 60 patients with acute coronary syndrome, including 50(83%) males and 10(17%) females. This age group analysis showing the youngest patient in the study was 34 years and the oldest patient was 78 years with the mean age group of 56.1 which is consistent with the study of Vythilin gam KT. PrashanthPanduranga's study also shows a mean age group of 51.28 years in coronary artery disease patients. The gender analysis shows a male predominance in the current study, which resembles the Nadogome study. HRT may be cardio protective since it impacts female cell procoagulants. In this study, the group analyses show 06(10%) cases to be hypertensive, 06(10) cases suffering from diabetes mellitus, 28(47%) were smokers. Morrow et al study showed an association of risk factors like hypertension (64%). Diabetes(44%) in CAD. In current study group, 47% of patients are smokers and a population-based survey found a high prevalence of smoking in both urban and rural populations among CAD. In the present study, all the patients with CAD diagnosis of stable and unstable angina were confirmed both clinically as well as with relevant investigation. 

The elevated incidence of stroke, acute ischemic attack, fever, peripheral artery disease, and accidental coronary failure has also been linked with higher hs-CRP. The hs-CRP values do not correlate explicitly on the simulated tomographic or authentic plaque pressure with the rate of the coronary artery calcification. Kaptoge et al. meta-analysis. Hs-CRP applies a statistical benefit to certain cardiovascular risk factors, including obesity and cholesterol, to nearly all of the research to date. The chances for coronary heart disease is roughly 1.5 in Danesh et al. in the patients with the largest tertile hs-CRP, as opposed to the patients with The Tertile Lowest. Specific prognostic details will be given by applying the High Sensitivity C-Reactive Protein to the Framingham danger ranking. Cushman et al. Women over 65 with hs-CRP > 3mg / L and 10-year frequency framing ham> 20% had 31% coronary heart disease compared to 16% with hs-CRP. The Reynolds Hazard Assessment ranks all men and females for cardiovascular risk more reliably, according to previous research. Ridker et al. have found that the Reynolds Risk Rating scale is Either higher or lower than 40% of the sample women's health (age < 45 years of age) and about 20% of the sample women's health doctors were classified as being at interim risk for cardiovascular problems in their health survey (aged > 50 years). These instructions were however written in 2003, while they followed the outcomes of the reasoning for utilizing rosuvastatin (JUPITER) trial. Current recommendations taking into account JUPITER results such as those released by the Canadian Cardiovascular Society in 2009 allow for hs-CRP assessment across all intermediate-risk individuals. Patients with higher hs-CRP coronary artery disease anticipate potential harmful medical conditions, like MI, premature mortality, and Cardiac Failure equivalent, are more prone to suffer negative consequences including MI and mortality of patients receiving low hs-CRP treatments.

In patients with coronary artery bypassing grafting of hs- > mg / L (15 of 59 patients), Milazzo et Al. have been finding a 25% potential for repeated ischemic attacks, relative to a 4% frequency (1 of 27 patients) in patients with a hs- < 3 mg / L. Milazzo and Al. observed a 25% risk for frequent ischemic attacks for patients with coronary artery bypassing hs- > mg / L (15 out of 59 patients), contrasted with the 4% incidence (1 out of 27 patients), in patients with hs<-3 mg / L.

CONCLUSION

This study showed the persistent elevation of CRP in unstable angina which indicates further continuing inflammation. Serum hs-CRP levels show a significant correlation with the acute coronary syndrome.

Author’s Contribution: Gul Hassan Brohi
Concept & Design of Study: Shahzeb Rasool Memon, Shahbaz Ali Shaikh
Drafting: Kamran Ali Shahani, Sarfraz Hussain Sahito, Mukhtiar Abro
Data Analysis: Gul Hassan Brohi, Shahzeb Rasool Memon
Revisiting Critically: Gul Hassan Brohi
Final Approval of version: Gul Hassan Brohi

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

REFERENCES
