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Technically smog is ground level ozone. It is caused when air population and fumes combined with fog and sunlight, forming a thick layer of smoke like film in the atmosphere. Smog is an urban phenomenon. Its reasons are varied. Firstly, big towns are becoming bigger because the smaller towns and rural areas have little to offer to their residents in terms of economic opportunities and municipal services.

Health experts around the world had been apprehensive about the confluence of Covid-19 and winter season, which pushes more people indoors and leads to a spike in instances of seasonal flu. In cities like New Delhi and Lahore, however, the current weather ushers in another hazard, now dubbed smog season.

While the news of Pfizer’s vaccine trials showing 90% effectiveness against Covid-19 is encouraging, the accessibility of this vaccine in poorer countries like ours will remain limited at best. Even if the Pfizer vaccine gets expedited approval and begins production in quantities enough to make its way over to countries like ours, it needs to be stored at temperatures below -70 degree Celsius. Pakistan hardly has the infrastructure to offer a vaccine with such stringent storage requirements to the masses. Perhaps the phase three Chinese vaccine trials ongoing in Pakistan will yield more positive results, in terms of accessibility and effectiveness.

Meanwhile, Pakistan may have been spared from the first coronavirus wave, but the country is now experiencing a second wave of infections. Pakistan’s positive test rate has overtaken India’s and tripled over this past month, according to the ‘Our World in Data’ website run by Oxford University. Conversely, in India, which already has the world’s second highest number of cases, there is growing evidence of air pollution causing increased Covid deaths in major cities like New Delhi, which is a trend that should be ringing alarm bells for Pakistan too.

With all the bluster about trying to balance livelihoods with the need to isolate, the ruling PTI has been busy congratulating itself for its smart-lockdown strategy to pay attention to the impending danger of coronavirus causing havoc in major cities of Punjab, with the onset of another smog season.

Our policymakers and health experts should have paid more attention to a recent Harvard University study, which has noted how even small increase in long-term exposure to PM2.5 leads to a large increase in Covid-19 death rate. This study has predicted how places with higher pollution levels will see higher numbers of hospitalisations and more Covid-19 deaths.

New Delhi and Lahore have now again begun trading places for topping the list of most polluted cities in the world. Despite the impending threat of smog season fueling coronavirus fatalities, there seems to be no significant let-up in emissions by the transport sector, or coal and other waste-based energy generation activities in industries and brick-kilns, or even in terms of averting other hazardous activities such as trash burning.

The EPA in Lahore seems blissfully unaware of the pollution problem, having declared air quality to be ‘good’ on the same day other air pollution measures deemed it ‘hazardous’.

There has been a growing wave of clean-air activism and even foreign embassies using new sources of pollution data have applied some pressure on government. Afforestation efforts have been afoot to contend with the drastic deforestation of the city due to years of aggressive road-building and unthinking urban development schemes. Yet, these have been unable to stem the tide of another smog season in Lahore, Gujranwala, Multan or Faisalabad.

All through the year, our policymakers and relevant officials should have been thinking about the arrival of another smog season in larger cities of Punjab, and the possibility of it coinciding with a resurgence of Covid-19. They should have been working double-time to ensure main contributors which cause air pollution to become untenable during winter were kept in check, especially when the coronavirus threat had not yet dissipated.

Instead of putting in place pre-emptive measures to avert the onset of smog season, the provincial government and ruling party remained busy discrediting opponents and hanging onto power. A confluence of smog season and Covid-19 has now descended upon Lahore and other large cities of Punjab, and this dual threat seems poised to extract its pound of flesh.

Measures which shall propose in the policy document if implemented efficiently could certainly help reduce air population and therefore, smog but a more protective policy stance could lie in decentralization of municipal services.

According to a report on the density a smog and air population, Lahore is the fourth worst city of the world. Followed by the Beijing, Ahwaz and Mongolia. It would be interesting to know and learn from what these countries are doing to deal with the problem.
Comparative Study Levels of Salivary Epidermal Growth Factor Between Normal Patients and Patients with Gingivitis & Periodontitis
Saqib Ghafoor Kayani¹, Syed Ali Asad Raza Naqvi², Muhammad Farooq³, Sharaz Ahmed⁴, Wajeeha Jabeen⁵ and Faiqa Hassan⁶

ABSTRACT

Objective: An important polypeptide molecule known as epidermal growth factor (EGF) has significant importance in wound healing and aids in epithelial growth. Its mechanism of action is such that it binds with receptors present on the surface of cell. The main objective of present research is to access, evaluate and make comparison of levels of salivary EGF in individuals having medical conditions like oral gingivitis and advanced periodontitis along with patients with healthy oral cavity conditions.

Study Design: Comparative Study

Place and Duration of Study: This study was conducted at the Watim Medical and Dental College Rawalpindi September 2019 to January 2020.

Materials and Methods: The samples of saliva that were unstipulated gathered from mouth of patients having oral conditions like advanced periodontitis, gingivitis and from individuals with healthy oral conditions at Watim medical and dental college Rawalpindi at September 2019 to January 2020. The clinical parameters that were measured during this case study were bleeding on probing (BOP), plaque index (PI), clinical attachment level (CAL) and probing pocket depth (PPD) with the help of a Williams probe. EGF levels were recorded by using enzyme-linked immune sorbent assay (ELISA). For data analysis and evaluation, One-way ANOVA was used.

Results: In Individuals with healthy oral conditions, EGF levels were noteworthy higher (99.00) as compared to patients suffering from gingivitis (62.49). EGF value was still higher in patients with gingivitis as compared to patients with advanced stage periodontitis (37.12) (P<0.001).

Conclusion: The decline in mean levels of EGF in individuals suffering from periodontal disease may be due to periodontal diseases.

Key Words: Gingivitis; Epidermal Growth Factor; Salivary Proteins and Pep-tides; Periodontitis and Salivary Glands


INTRODUCTION

In the whole world, periodontal disease is considered to be the most prevailing oral problem⁴. Presence of deep periodontal pockets are indication of Advanced periodontal disease (≥5 mm), that influence 10–15% of adolescents globally⁴. Some researchers say that this periodontal disease has some risk factors involved, like individual poor oral hygiene, stress, usage of tobacco and alcohol and diabetes.

Chronic periodontal disease on the other hand is linked with interaction between the host’s inflammatory responses and gram-negative bacteria that eventually lead to tissue destruction and finally end with tooth loss⁴. Microorganisms play a vital role in periodontitis pathology. Clinically, extend and severity of disease depends on host immune responses to gram negative bacteria There is release of pro-inflammatory mediators by immune cells of periodontium to fight against periodontal pathogens⁷. Cytokines plays a key role among all the immunologic and inflammatory

¹ Department of Oral Medicine, WATIM Medical & Dental College Rawalpindi.
² Department of Oral Medicine, Foundation University College of Dentistry,
³ Department of Oral Medicine, Avicenna Dental College Lahore,
⁴ Department of Operative Dentistry / Periodontology⁴ / Oral Medicine⁶, HITEC Institute of Medical Sciences (Dental College) Taxila Cant.

Correspondence: Dr. Saqib Ghafoor Kayani, Assistant Professor/HOD Oral Medicine, WATIM Medical & Dental College Rawalpindi.
Contact No: 0321-5562777
Email: saqib206@gmail.com

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mediators in the saliva as well as in gingival crevicular fluid (GCF). Epidermal growth factor is an important multifactorial cytokine along with biological effects. A polypeptide molecule EGF, has its unique property of aiding in wound healing and epithelial growth. Its mechanism of action is that it attaches itself on cell surface receptors. In the gingival epithelium, EGF receptors are present in great quantity on basal cell surface.

Periodontal disease can be defined as mixture of acute and chronic inflammatory reactions of body as a result of bacterial invasion. The detection of disease is done on basis of extracellular matrix destruction as well as bone resorption. Due to increased activity of proteinases, there is brutal destruction of periodontal tissues. Proteinases are derived from gelatinase and collagenase since as EGF is a potent activator of gelatinase as well as collagenase, its presence in saliva and tissues of gingiva showed confirmation. Moreover, during inflammatory process, expression of gingival receptors of EGF was found. Therefore, EGF proved to be the main mediator in periodontal pathogenesis.

In periodontal disease, the important source that could serve for evaluation of inflammatory mediators includes saliva, GCF and urine. According to the research work done by Laurina et al., in case of periodontal disease there is quantitative and qualitative relationships of expression of cytokines, growth factors, apoptosis and defensing. The results of his case research depicted that large number of epithelial cells cause expression of IL-10 in individuals suffering from periodontitis.

According to the Oxford et al. research, study there was decline in mean EGF serum levels in individuals suffering from diabetes. Their study proved that it was due to decline levels of EGF that was responsible for systemic and oral health destruction especially in diabetic patients.

This case study also analyzes the salivary EGF levels in individuals suffering from gingivitis and severe periodontitis and also compared these individuals with healthy controls. The main hypothesis that was under test was that decrease in EGF expression might cause bone loss of high degree.

MATERIALS AND METHODS

Study Population: This cross-sectional study was performed on samples obtained from patient’s saliva who were healthy as well as one having oral conditions like gingivitis and advanced periodontitis at Watim Medical and Dental College Rawalpindi.

This case study included about 11 individuals having periodontitis of advance stage, 17 individuals suffering from gingivitis and 20 individuals having optimum oral conditions, free from disease. The sampling was done non-randomly. The selection of patients was made on basis of following criteria:

Inclusion Criteria: In case of advanced stage periodontitis, the inclusion criteria include attachment loss ≥5 mm, bone loss visible on radiograph and systemic health. In case of gingivitis, the inclusion criteria include age range between 16–55 years, no radiographic bone loss, depth of periodontal pocket ≥5 mm and systemic health.

Exclusion Criteria: This include patient history suffering from systemic disease that has its effects on periodontal tissues, antibiotic intake history in the past month, history of positive periodontal treatment in past, any prophylactic procedures performed, stubborn patient, compliance and pregnancy.

Registry of Clinical Findings: With the help of Williams probe, the clinical parameters like BOP, PI, CAL and PPD were recorded (Hu-Friedy, Chicago, IL, USA). By spitting, salivary samples (unstimulated) were taken from the patients between 9 to 11 a.m. The test samples were shifted to Eppendorf tubes, immediately that consist of Tris-HCl buffer solution because of fear of disruption of the test results as samples contain protease enzymes (Figure 1). we prepared the buffering solution by dissolving 1.18 g of Tris (hydroxymethyl) amino- methane in water 80 mL in a flask of 100-mL flask. By the use of 0.5 mmol/L hydrochloric acid, the PH of solution was maintained at 7.8. Finally, with the use of distilled water, the volume was adjusted at 100 mL. The preparation of solution this way aids in its stability and also increases its shelf life for 6 months at - 4°C. By transferring 300 μL of the solution to each Eppendorf tube, we can achieve same ideal conditions for all the rest of samples. Observation of these samples was done for about half an hour before they were submitted the laboratory. All samples were at 4°C in refrigerator. The samples were further preserved in laboratory at -20°C until sufficient samples were taken with the aid of ELISA kit. Then, evaluation of each sample was carried out.

Procedure Steps: The steps followed during the procedure were as follows:

1. In the buffering solution the antigen that was dissolved was transferred to the respective wells with the help of sampler
2. The antigens in smaller quantities were absorbed by plastic surfaces.
3. Antigens that were free were separated by rinsing. Neutral protein was used to avoid binding of other proteins.
4. All the unbounded proteins were washed away.
5. Addition of another binding agent was done at this stage that has ability of antibodies identification. There was also covalent bond found between binding agent and enzyme like peroxidase. The binding molecule has ability to attach to the antibody under test.
6. The antibodies not attaching the antibody were all rinsed away.
7. Addition of coloring agent was done. This agent has ability to change itself into a colorful material as a result of enzymatic reactions so that we could identify the complex.
8. The antigen concentration was recorded was by scanning colored product optical density.

**Statistical Analysis:** For data analysis SPSS 24.0 was used. The mean salivary EGF level and mean age of patients were analyzed and documented. one-way ANOVA was applied for observing differences in EGF levels between patients suffering from periodontitis advance stage, patients suffering from gingivitis and individuals with in healthy oral conditions. Statistical significance was defined at P≤0.05.

**RESULTS**

The mean levels of salivary EGF in this case study were observed and documented in patients having pathologies like gingivitis, periodontitis at advance stage and individual with healthy oral cavity. As recorded from our tests, the mean age of patients having periodontitis of advance stage, gingivitis and individual with healthy oral conditions was 47.18 (SD=6.5), 31.13 (SD=1.4) and 31.24 (SD=4.4) years, respectively.

**Table No.1: Pair wise comparison of groups**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy controls</td>
<td>Gingivitis</td>
<td>6.97</td>
<td>0.001</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>Periodontitis</td>
<td>24.10</td>
<td>0.001</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>Periodontitis</td>
<td>16.00</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Table No.2: The mean salivary EGF level in patients with gingivitis and advanced periodontitis and healthy controls**

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Mean ± SD</th>
<th>Std. Error</th>
<th>95% CI Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>20</td>
<td>99.00 ± 28.12</td>
<td>8.72</td>
<td>84.58</td>
<td>113.88</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>17</td>
<td>62.49 ± 19.62</td>
<td>5.18</td>
<td>51.02</td>
<td>76.27</td>
</tr>
<tr>
<td>Periodontitis</td>
<td>20</td>
<td>37.12 ± 9.18</td>
<td>2.85</td>
<td>30.00</td>
<td>43.07</td>
</tr>
</tbody>
</table>

**Table No.3: Pairwise comparison of groups using the post hoc Tukey’s test**

<table>
<thead>
<tr>
<th>Group1</th>
<th>Group2</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>Gingivitis</td>
<td>38.93</td>
<td>0.001</td>
</tr>
<tr>
<td>Healthy</td>
<td>Periodontitis</td>
<td>63.12</td>
<td>0.001</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>Periodontitis</td>
<td>25.40</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Significant difference was recorded among three groups when pair wise comparisons done with post hoc Tukey’s test. (P=0.001) (Tables 1). The mean salivary level of EGF in patients suffering from gingivitis. Periodontitis of advance stage and individual with healthy oral conditions was 62.49±19.62, 36.14±9.17 and 99.00±28.12 ng/mL, respectively (Table 3).

Moreover, when comparison was made with the post hoc Tukey’s test also showed a noticeable differences between healthy individuals and individuals gingivitis (P<0.001), healthy individuals and individuals with periodontitis (P<0.001) and individuals with gingivitis and those having periodontitis (P=0.14); i.e. the mean levels of EGF in case of healthy individuals in was notably higher as compared to individuals with gingivitis; and it was observed that EGF value in patients suffering from gingivitis was noteworthy greater when comparison was made with individuals suffering from periodontitis (Table 3).

**DISCUSSION**

With the help of the ELISA technique, EFG levels in saliva were detected in normal individuals as well as in individuals suffering from periodontitis and gingivitis. The benefit of using the ELISA test as compared to other tests was that it is cost- friendly, scientifically very accurate and implementation is way too easy as it does not require any complicated and expensive tool. It has similarity with other radioimmunoassay tests but the only difference between ELISA and other radioimmunoassay test is that it involves the use of color change reaction because of the action enzyme over substrate rather than radioisotope work as indicator. In our current studies, ELISA was used to obtain data which helps in making our study reliable from future point of view.

From the results of our study, the mean salivary levels of EGF observed and came out to be 62.49, 37.12 and 99.00 ng/mL for gingivitis, periodontitis and healthy individuals, respectively. From results it was clearly noted that EGF salivary levels were lowest in patients with periodontitis of advance stage as compared to individuals with healthy oral conditions and the one gingivitis. This trend showed that as the disease progressed from gingivitis to periodontitis, there was decreasing value of salivary EGF was observed.

The studies by some researchers showed that in animals, EGF present in the saliva can be taken up systematically by the intestines and mucosa of oral cavity. Moreover, high salivary levels of EGF aids in enhancing the healing mechanism in injured parts by attaching itself to receptors of EGF and by activation of tyrosine kinase pathway. In addition, by more and more attachment of EGF to its receptors there was activation of different biological effects such as angiogenesis, epithelial proliferation, and gastric juice release inhibition. So, it was seen that with the temporary increased in levels of salivary EGF, there was increase in oral mucosal injuries.
The levels of salivary EGF were recorded by Oxford et al. pre and post oral and juxta-oral operations. The unstimulated salivary flow was obtained approximately at different intervals. The samples of saliva were collected from patients who were candidates for periodontal surgery before and after 6-, 12-, 18-, 24-, 30-, 36- and 42 hours and 2 weeks after the surgery. Then afterwards, the mean levels of salivary EGF were analyzed by the Quantikine Human EGF Immunoassay. The values from all these tests clearly showed that local cells have ability to produce as well as to secrete growth factor at the operated sites. So increased in secretion and production of salivary EGF was observed at operated site that ultimately aided in wound healing and repair. Growth factors play a vital biological role in regulation and proliferation of connective tissue cells and generation of protein synthesis as well as other extracellular matrix constituents. The target cells reaction to growth factors relay upon their particular receptors expression; they are considered as membrane antigens that help in production of intercellular signals, the time they attach themselves to growth factors and results in chemo taxis stimulation as well as, cellular growth, cellular differentiation and synthesis of the extracellular matrix. This is due to this reason, growth factor receptors play a vital and important role in the starting and progression of periodontal disease and as well as in regeneration process. Also, from some researchers EGF proved to play a key role in wound healing. The researches thought that this wound healing property of EGF might be because of the biological factor that controls the pathogenesis involved in periodontal disease. It was also shown by various researches that decline levels of EGF specially in patients suffering from diabetes mellitus is the main cause of destruction of periodontium. This finding supports our current study research. Gelatinase, prostaglandin E2, Collagenase, activators, TNF, IL-1 and plasminogen has a key involvement in destroying periodontium. It was also proven that EGF was considered to be important regulator in periodontal pathogenesis. Thus, the researchers believe that in future a strong focus should be paid on gingival receptors specifically regarding EGF or other cytokines expression involved in various periodontal pathogenesis.

CONCLUSION

In a nutshell, it was concluded that main differences were seen when comparison was made between three groups of patients with respect to salivary level of EGF, and proved that with the progression of periodontal pathologies, there was decreasing trend in salivary EGF was observed and noted. So decrease in the mean levels of salivary EGF is an important mechanism linked with periodontal destruction.

Author’s Contribution:
Concept & Design of Study: Saqib Ghafoor Kayani
Drafting: Syed Ali Asad Raza Naqvi, Muhammad Farooq
Data Analysis: Sharaz Ahmed, Wajeeha Jabeen and Faiqa Hassan
Revisiting Critically: Saqib Ghafoor Kayani, Syed Ali Asad Raza Naqvi

Final Approval of version: Saqib Ghafoor Kayani

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

REFERENCES


Cholesterol Lowering Potential of Allium Sativum Essential Oil in Type 2 Diabetic Patients
Muhammad Akbar¹ and Akram Munir²

ABSTRACT

Objective: The present study analyzed the cholesterol lowering potential of Allium sativum essential oil (ASEO) in hypercholesterolemia of type 2 Diabetes mellitus (T2DM).

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Department of Medicine, Faculty of Medicine and Allied Medical Sciences, Isra University Hyderabad from December 2018 to January 2020.

Materials and Methods: A sample of 79 diagnosed cases of T2DM was selected according to inclusion and exclusion criteria. 10 ml of venous blood was collected for the analysis of serum total cholesterol, blood glucose, glycated HbA1, BUN and serum creatinine. Ethical clearance of institute and informed consent were mandatory. SPSS 21.0 was used for data analysis at 95% confidence interval.

Results: Blood glucose, HbA1c, serum creatinine and blood cholesterol showed significant reductions at third and sixth months compared to baseline. Serum cholesterol at baseline, third and sixth month was noted as 215.2±72.6 mg/dl, 190.7±81.6 mg/dl and 162.8±76 mg/dl respectively (p=0.0001).

Conclusion: Allium sativum essential oil reduced hypercholesterolemia in diabetes mellitus. Allium sativum essential oil may prove helpful in treating hypercholesterolemia in diabetic patients as an adjunctive therapy for those intolerant to statin therapy.

Key Words: Allium sativum essential oil, Hypercholesterolemia, Diabetes mellitus

INTRODUCTION

Hypercholesterolemia is one of the most overlooked metabolic disorders in diabetics. Hypercholesterolemia is associated with atherosclerosis which is fore runner of ischemic vascular disease including the coronary artery disease (CAD). Hypercholesterolemia is an independent of CAD through atherosclerosis.¹ Strong evidence exists between CAD, hypercholesterolemia and atherosclerosis.²⁻⁴ As Diabetes mellitus is increasing in Pakistan; hence the problem is forecasted to multiply as time passes. Currently, the problem of hypercholesterolemia is highly overlooked and neglected. Despite life style modifications and pharmacological interventions, the risk of established mortality by CAD, brain stroke and peripheral arterial disease (PAD) remains known causes of mortality and morbidity in the developing countries. Hypercholesterolemia is an established risk factor of CAD and mortality, despite this majority of patients remain negligent.⁵⁻⁶ Currently, the pharmacological interventions include the HMG-coA reductase inhibitors. However, they are not much effective despite side effects such as; neuropathy, myopathy and myalgias, muscle weakness, cognitive dysfunction and Diabetes mellitus.⁷ Allium sativum (AS) is publicly known as Garlic. AS is a rich source of biologically active compounds used in folk medicine since time immemorial. It is rich in allicin which is a sulfur containing compound. Majority of biological activities of AS are attributed to its active ingredient the allicin. They include the anti-oxidant, anti-hypercholesterolemia, anti-hyperglycemia, anti-hypertensive, and anti-thrombotic activities.⁸⁻¹⁰ Allium sativum is used in folk medicine since ancient era of 1550 BC. Allium sativum is used as taste enhancer and food flavor. Allium sativum is herb with multiple biological functions. It is used for headache, cancer and cardiac diseases. Allicin exerts bactericidal and fungicidal activity. Allium sativum increases good cholesterol (HDLc) and reduces bad cholesterol (LDLc). One proposed mechanism of anti hyperlipidemic action is through inhibition of HMG CoA reductase.¹¹ Allium sativum stimulates the phagocytosis by macrophages and lymphocyte

¹ Department of Medicine, Isra University, Hyderabad.
² Department of Medicine, Liaquat University of Medical and Health Sciences, Hospital Jamshoro/Hyderabad, Sindh, Pakistan

Correspondence: Dr. Muhammad Akbar, Assistant Professor of Medicine, Isra University, Hyderabad.
Contact No: 0300 3064 840
Email: giggly786@gmail.com

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functioning. Allium sativum is reported of its hepatoprotective, antioxidant, Immunomodulatory function, anti-thrombotic, anti-hypoglycemic and anti-hypertensive efficacy. The primary objective of present study was to analyze the effects of Allium sativum essential oil (ASEO) on hypercholesterolemia of Diabetes mellitus. Secondary objectives were to observe effects of ASEO on the systemic blood pressure, blood glucose, glycated HbA1 and serum creatinine.

MATERIALS AND METHODS

The study was designed as an observational study that analyzed the effects of ASEO primarily on blood cholesterol, blood glucose, HbA1c, systemic blood pressure and serum creatinine. The study was conducted at the Faculty of Medicine and Allied Medical Sciences, Isra University Hyderabad from December 2018 to January 2020. Diabetic subjects attending the Diabetic clinic and Medicine OPD were negotiated about purpose of study. Eventually, a sample of 79 T2DM subjects was selected by non-probability purposive sampling who promised of regular drug intake and regular follow ups. Inclusion criteria were diagnosed cases of T2DM with blood cholesterol > 200 mg/dL, diabetes duration of ≥10 years, both genders and age between 40 – 60 years. Diabetics with history of tobacco smoking, high fiber diet such as Ispaghul husk, pregnancy, contraceptive procedures, and lipid lowering drugs were strictly excluded. Major systemic disease like chronic liver disease, pulmonary tuberculosis, diabetic kidney disease (DKD), menopause, vitamin therapy, malabsorption, and coronary artery disease were also exclusion criteria. Subjects were informed in detail about the purpose of study; its advantages and disadvantages and were asked for willingness. Drug intake and regular follow ups were emphasized again. They were informed that they are free to enter or not in the study protocol and this will not affect their treatment. They were informed that they have to allow for 5-10 ml of venous blood sampling for 3 times at baseline, at 3rd and 6th months respectively. Only willing volunteers were allowed to enroll in study protocol. Patient’s biodata, medical history was asked by a medical officer and recorded on a pre structured proforma. Medical officers were informed to abide by the inclusion and exclusion criteria strictly. Participants were finally examined by a Consultant Physician. Signing consent form is mandatory. Systemic blood pressure was recorded as per criteria set out by JNC VIII. Diabetes mellitus was defined as (FBG) ≥ 126mg/dl or postprandial blood glucose (RBG) ≥200 mg/dl as per ADA criteria. Soft gel of Allium sativum essential oil (ASEO) containing 13.5 mg each was given once a day orally for six months. Garlish oil soft gels were purchased forms Pharmacy (High Q International Pharmaceuticals Karachi). Blood glucose was detected by “glucose oxidase” and HbA1c by assay method on Hitachi 902, Roche analyzer. Serum creatinine and BUN were estimated by standard biochemical methods. Serum total cholesterol was detected by colorimetric method. Ethical clearance of institute and informed consent were mandatory. Confidentiality of patient data ensured. SPSS 21.0 was used for data analysis. Chi square test was used for gender analysis. Age was analyzed by one sample t-test. Paired test was used for analysis of variables at baseline, third and sixth months. P-value of ≤0.05 was statistically significant.

RESULTS

A sample of 79 T2DM subjects was studied to analyze the effects of ASEO on blood cholesterol, glycemic control, systemic blood pressure and serum creatinine in type 2 Diabetic subjects. Mean ± SD age of T2DM subjects was 41.7±8.6 years in our study population. Male and female were noted as 53 (67.1%) and 26 (32.9%) respectively. Male predominated with male to female ratio of 2.03:1. Statistical analysis of body weight, systolic BP, diastolic BP and BUN showed non-significant results at 3rd and 6th months (p<0.05) (table 1). Blood glucose, HbA1c, serum creatinine and blood cholesterol showed significant results at 3rd and 6th months compared to baseline. Blood glucose (R) at baseline, 3rd and 6th months was noted as 220.1±65.3, 206.6±70.7 and 181.6±63.4 mg/dl respectively (p=0.0001). HbA1c was 10.3±2.2% at baseline, which reduced to 9.7±1.8 at 3rd month and further decreased to 9.01±2.3% at 6th month (p=0.001). Serum creatinine (Scr) at baseline, 3rd and 6th months was noted as 1.03±0.23, 0.94±0.18 and 0.80±0.08 mg/dl respectively (p=0.009). Serum cholesterol at baseline was 215.2±72.6 mg/dl, which reduced to 190.7±81.6 mg/dl and further reduced to 162.8±76 mg/dl at sixth month (table 2).

Table No.1: Characteristics and laboratory findings of study subjects

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3rd month</th>
<th>6th month</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.7±8.6</td>
<td>-</td>
<td>-</td>
<td>0.001</td>
</tr>
<tr>
<td>Male</td>
<td>53 (67%)</td>
<td>-</td>
<td>-</td>
<td>0.0000</td>
</tr>
<tr>
<td>Female</td>
<td>26(32.9%)</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>74.8±11.0</td>
<td>75.0±10.8</td>
<td>74.6±11.0</td>
<td>0.91</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>146.4±20.2</td>
<td>145.4±20.4</td>
<td>146.4±20.1</td>
<td>0.92</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>86.6±14.2</td>
<td>87.2±14.0</td>
<td>87.0±14.0</td>
<td>0.79</td>
</tr>
<tr>
<td>Blood glucose (R) (mg/dl)</td>
<td>220.1±65.3</td>
<td>206.6±70.7</td>
<td>181.6±63.4</td>
<td>0.0000</td>
</tr>
<tr>
<td>Glycated HbA1 (%)</td>
<td>10.3±2.2</td>
<td>9.7±1.8</td>
<td>9.01±2.3</td>
<td>0.0000</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>11.9±0.73</td>
<td>11.7±0.69</td>
<td>11.03±0.70</td>
<td>0.89</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.03±0.23</td>
<td>0.94±0.18</td>
<td>0.80±0.08</td>
<td>0.009</td>
</tr>
</tbody>
</table>
DISCUSSION

The present study was undertaken to establish the efficacy of garlic lowering efficacy of ASE hypercholesterolemia of Diabetes mellitus. The present study reports a significant reduction in blood glucose, HbA1c, serum creatinine and blood cholesterol at third and sixth months compared to baseline. Serum cholesterol at baseline was 215.2±72.6 mg/dl, which reduced to 190.7±81.6 mg/dl and further reduced to 162.8±76 mg/dl at sixth month (table 2). Similarly, a decrease in blood glucose, HbA1c and serum creatinine was observed. The present study reports an improvement in glycemic control and antihypercholesterolemia effect of ASE. Finding of hypercholesterolemia effect is in keeping with previous studies. Previous studies reported total cholesterol was reduced in Diabetic subjects with hypercholesterolemia; the findings support the present study. The previous studies concluded that the inhibition of HMG-CoA reductase is responsible for its hypocholesterolemia effect. Other previous had also reported anti hyperlipidemic effects of Allium sativum. Other proposed mechanism of hypocholesterolemia is through the inhibition of lipoprotein lipase. A recent study by Lachhiramka et al reported mean cholesterol levels were reduced from baseline 265 ± 16.7 mg/dL to 232.7 ± 11.2 mg/dL, third month (90th day) at 3 gram raw garlic dose orally daily (P < 0.001). Finding of above study are in parallel to present study as the serum cholesterol was reduced significantly (table 2). A meta-analysis of 39 studies showed anti hypercholemic and anti hyperlipidemic effects of Allium sativum. This supports the findings of the present study. Our finding of improvement in glycemic control (Blood glucose and HbA1c) is in agreement with previous studies. Previous studies had reported on the improvement in glycemic control and anti hypercholesteroleic effects in Allium sativum fed patients. Anti hypercholeemic and anti hyperlipidemic effects of Allium sativum of present study are also consistent with animal studies. However, interventional clinical studies have reported positively on the anti hypercholesterolemia and anti hyperlipidemic effects of Allium sativum. The present study did not observed any anti-hypertensive effects of ASE which is in contradistinction to previous studies reported anti-hypertensive effects of ASE. Another previous study reported Allium sativum reduces Diastolic blood pressure (DBP). This contradistinction might be due to different study subjects of various studies such as the present study selected Diabetics while above studies selected non diabetic hypertensive population. The present has certain limitations first; small sample size, second; total lipoproteins were not estimated which might have produced effect on complete lipid profile and third; dietary factors might have affected the results towards alternate hypothesis. The findings of anti-hypcholesterolemia, improved glycemic control and serum creatinine were evaluated in prospective design; hence they are worth to report. However, the findings are worth to report as the Allium sativum is easily available, palatable and inexpensive which may be used even as home remedy. The strength of study lies in its participants who showed regular follow ups and regular use of drug. Allium sativum essential oils (ASEO) is purified compared to raw garlic used by previous studies hence our findings should be interpreted in proper clinical context. The findings of present cannot be generalized to other populations.

CONCLUSION

The present study reports Allium sativum essential oil improves hypercholesterolemia and hyperglycemic in diabetic subjects. Allium sativum essential oil may prove helpful in treating hypercholesterolemia in diabetic patients as an adjunctive therapy for those intolerant to statin therapy. However, the present study is a preliminary report conducted on a small number of diabetics, hence large sample elaborate studies may be conducted to substantiate the use Allium sativum essential oil.

Author’s Contribution:
Concept & Design of Study: Muhammad Akbar
Drafting: Akram Munir
Data Analysis: Akram Munir
Revisiting Critically: Muhammad Akbar, Akram Munir
Final Approval of version: Muhammad Akbar

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

REFERENCES
3. Patty W, Siri-Tarino, Qi Sun, Frank B. Hu, Ronald

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**Table No.2: Serum cholesterol levels**

<table>
<thead>
<tr>
<th>Serum Cholesterol (mean ± SD (mg/dl))</th>
<th>3rd month</th>
<th>6th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>219.2±42.5</td>
<td>199.5±31.6</td>
</tr>
<tr>
<td>P=0.0003 Baseline vs. 3rd month month</td>
<td>P=0.0007</td>
<td>P=0.0001</td>
</tr>
</tbody>
</table>

**Drafting:** Muhammad Akbar

**Data Analysis:** Akram Munir

**Revisiting Critically:** Muhammad Akbar, Akram Munir

**Final Approval of version:** Muhammad Akbar

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5. India Disease Incidence & Prevalence Report # CS303IN – April 2013.


The Diagnostic Accuracy of Urine Dipstick in Early Detection of UTI in Children Keeping Urine Culture as a Gold Standard

Maryam Naseem¹, Aroma Tariq¹, Sumbal Saeed², Maryam Rafiq Ghuncha³, Nighat Jabeen⁴ and Mariam Raza¹

ABSTRACT

Objective: To determine the diagnostic accuracy of urine dipstick in detection of UTI in children keeping urine culture as a gold standard.

Study Design: Cross sectional validation study

Place and Duration of Study: This study was conducted at the Paediatric department, KRL Hospital, Islamabad from July 2015 to December 2015.

Materials and Methods: 406 female patients age 2 months to 5 years with signs and symptoms of urinary tract infection were included. Urine was collected using a midstream clean catch sample or suprapubic aspiration. A rapid dipstick analysis for leukocyte esterase and nitrite was done. All dipstick positive and dipstick negative samples underwent cultures by sending samples in a clean container to the pathology lab. A study proforma was used to record the information regarding patient age, gender and the results of urine dipstick and urine culture tests.

Results: The diagnostic accuracy of urine dipstick in detection of UTI in children keeping urine culture as a gold standard was recorded as 80.95%, 62.42%, 35.98%, 92.63% and 66.26% for sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate.

Conclusion: The diagnostic accuracy of urine dipstick in detection of UTI in children keeping urine culture as a gold standard is higher and this cost effective technique may be used in our routine practice for early detection and treatment of UTI in children in order to avoid renal damage and when urine cultures are available only after 7 days.

Key Words: Urinary tract infection, diagnostic accuracy, urine dipstick

INTRODUCTION

A UTI is defined as colonization of a pathogen anywhere along the urinary tract: upper urinary tract infection (kidney, ureter), and lower urinary tract infection (bladder, and urethra).

1. Department of Pediatrics, PAF hospital, Fazaia Medical College, Islamabad
2. Department of Pediatrics, Children Hospital PIMS, Islamabad
3. Department of Pediatrics, Ruthpfau Fazaia Medical College, Karachi
4. Department of Pediatrics, Quetta Institute of Medical Sciences, Quetta

The prevalence of UTIs ranges from 1-73% worldwide. In Pakistan UTI is one of the common problems for hospital visits in pediatric ages and girls are the most affected. A recent study from Karachi reported 18% prevalence. The overall prevalence of UTI among infants presenting with fever, was 7.0% (CI: 5.5– 8.4). The pooled prevalence rates of febrile UTIs in female aged 0–3 months, 3–6 months, 6–12 months, and more than 12 months was 7.5%, 5.7%, 8.3%, and 2.1% respectively. Among febrile male infants less than 3 months of age, 2.4% (CI: 1.4 – 3.5) of circumcised males and 20.1% (CI: 16.8 –23.4) of uncircumcised males had a UTI. Among older children (>9 years) with urinary symptoms, the pooled prevalence of UTI (both febrile and afebrile) was 7.8% (CI: 6.6–8.9). The Incidence in the term neonate is approximately 1% & in the preterm3%, both with male preponderance (male to female ratio is 5:1). During infancy, risk of developing UTI is equal in boys and girls and thereafter higher in girls. Pediatric urinary tract infections (UTI) account for 0.7% of physician office visits and 5–14% of emergency department visits by children annually.
Clinical features suggesting UTI include a history of prior UTI, temperature greater than 39°C or 40°C, duration of temperature for more than 24 hours, suprapubic tenderness, and lack of circumcision. The clinical presentation of UTI depends on the age of the child. Neonates may present with poor feeding, vomiting, jaundice, irritability, sepsis, lethargy, or failure to gain weight, and may not always have fever. Infants most commonly present with fever, diarrhea, vomiting, irritability, foul smelling diapers and constipation. In older children with pyelonephritis, fever is the predominant symptom, often without dysuria. In children older than 2 years with febrile UTIs, only 32% of boys and 40% of girls had dysuria. Flank pain was even more uncommon. However, due to the lack of reliability of clinical features any child presenting with fever without a localizing source should undergo workup for a UTI. Most uncomplicated UTIs are caused by a large family of gram negative, aerobic bacilli known as Enterobacteriaceae. Others include Escherichia, Klebsiella, Enterobacter, Citrobacter, Proteus, Providencia, Morganella, Serratia, and Salmonella species. Of these, Escherichia coli is by far the most frequently isolated organism, being responsible for approximately 80% of UTIs. The most common gram-positive organisms found in UTIs are Staphylococcus and Enterococcus sp. Anaerobic fecal flora rarely produce UTIs despite being 100 to 1000 times more abundant than E. coli in stool.

The gold standard for the diagnosis of UTI is the urine culture. However, culture results are not typically available until 24 to 48 hours after the initial patient evaluation. Early identification is particularly important in attempting to avoid renal involvement. Rapid screening performed by a urine dipstick test primarily looks for the presence of leukocyte esterase (LE) or nitrites in the urine sample. Nitrites are far more specific than LE in identifying likely UTI; however, sensitivity is quite poor. The meta-analysis by Williams and colleagues produced sensitivity and specificity estimates of nitrite only positive dipstick as 49% (95% CI, 41%–57%) and 98% (95% CI, 96%–99%), respectively. Williams and colleagues found that the presence of either nitrites or LE was more accurate than LE alone, with a sensitivity and specificity of 88% (95% CI, 82%–91%) and 79% (95% CI, 69%–87%), respectively.

The traditional cutoff for urine obtained by noninvasive collection methods (clean-catch or clean bag) has remained 10^5 (100K) CFU/mL for decades. Investigators use a cutoff of 10^4 (10K) CFU/mL to define infection with specimens obtained by catheterization. Because it was recognized very early that urine obtained by suprapubic aspiration (SPA) in non-infected children is almost invariably sterile, most authorities use 10^2 (0.1K) CFU/mL as the cutoff for defining a positive culture in an SPA sample. Urine culture is the gold standard for diagnosing UTIs, however, the time span for results is a serious issue similarly urine analysis is time consuming, a urine dipstick for a lab analysis may be less time consuming. However, a recent study done in 2010 has shown that urine dipsticks are moderately sensitive (75%) and less specific (66%) in predicting UTI.

### MATERIALS AND METHODS

This study was conducted at Pediatric department KRL Hospital Islamabad from 1st July to 31st December 2015.

**Sample Size:** Sample size has been calculated by using sensitivity and specificity sample size calculator with following statistical assumptions:

- **Confidence level:** 95%
- **Sensitivity:** 75%
- **Specificity:** 66%

Our study sample size came out to be 406 children with suspicion of UTIs.

**Inclusion Criteria:**

- Females
- Age from 2 months to 5 years
- Fever up to 101°F
- Presenting complaints (lower suprapubic abdominal pain), burning micturition and frequency of micturition 10 to 15 times per day.

**Exclusion Criteria:**

- Patients who have taken antibiotics in the previous 48 hours.
- Those with underlying congenital renal anomalies i.e. cystic kidney, obstruction in renal tract, Renal Tumors, Renal Syndromes, Acute Renal failure and CKD.

**Data Collection Procedure:** After taking permission from the hospital ethical committee all female patients age 2 months to 5 years presenting in the inpatient or outpatient department with signs and symptoms of urinary tract infection were included. Urine was collected using a midstream clean catch sample or suprapubic aspiration.

A rapid dipstick analysis for leukocyte esterase and nitrite was done by a staff nurse using Meditest Combi 10 SGL. The reaction of dipstick strip was read visually. Similarly urine analysis is time consuming, a urine dipstick for a lab analysis may be less time consuming.

**Data analysis:** SPSS version 10 was used for the analysis. Mean and standard deviation was calculated for all quantitative variables i.e. age. Frequency and
percentage was presented for all qualitative variables i.e., true positive, false positive, false negative and true negative. Sensitivity, specificity, positive and negative predictive value was calculated using 2x2 table (Table 1).

RESULTS

A total of 406 cases were enrolled. Age distribution of the patients is shown in Table No. 2. Frequency of UTI in children on urine culture as a gold standard with positive results were 20.69% (n=84) while 79.31% (n=322) were not positive. (Table No. 3).

Table No.1: Urine dipstick with urine culture

<table>
<thead>
<tr>
<th>Urine dipstick</th>
<th>Urine culture</th>
<th>Test result</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
<td>Tp</td>
<td></td>
<td>Fp</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td>Fn</td>
<td>Tn</td>
<td></td>
</tr>
</tbody>
</table>

Table No.2: Age distribution (n=406)

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-3yrs</td>
<td>281</td>
<td>69.21</td>
</tr>
<tr>
<td>4-5yrs</td>
<td>125</td>
<td>30.79</td>
</tr>
<tr>
<td>Total</td>
<td>406</td>
<td>100</td>
</tr>
</tbody>
</table>

Table No.3: Frequency of UTI in children on urine culture as a gold standard (n=406)

<table>
<thead>
<tr>
<th>Ti</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>84</td>
<td>20.69</td>
</tr>
<tr>
<td>No</td>
<td>32</td>
<td>79.31</td>
</tr>
<tr>
<td>Total</td>
<td>406</td>
<td>100</td>
</tr>
</tbody>
</table>

Table No. 4: Diagnostic accuracy of urine dipstick in detection of UTI in children (n=406)

<table>
<thead>
<tr>
<th>Urine dipstick</th>
<th>Urine culture</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant (positive)</td>
<td>Malignant (negative)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>True positive 68 (16.75%)</td>
<td>False positive 121 (29.80%)</td>
</tr>
<tr>
<td>Negative</td>
<td>False negative 16 (3.94%)</td>
<td>True negative (d) 201 (49.51%)</td>
</tr>
<tr>
<td>Total</td>
<td>84 (20.69%)</td>
<td>322 (79.31%)</td>
</tr>
</tbody>
</table>

Sensitivity = 80.95%, Specificity = 62.42%, Positive predictive value = 35.98%, Negative predictive value = 92.63%, Accuracy rate = 66.26%

Diagnostic accuracy of urine dipstick in detection of UTI in children was recorded as 80.95%, 62.42%, 35.98%, 92.63% and 66.26% for sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate (Table No. 4).

DISCUSSION

Urinary tract infection (UTI) is one of the most common sources of infection in children under five. Prompt diagnosis and treatment is important to reduce the risk of renal scarring.

Rapid cost-effective, methods of UTI diagnosis are required as an alternative to culture. The current study was planned to detect UTI early by the use of urine dipstick as it is an easy modality, an inexpensive test to reduce the complications associated with late detection of UTI.

In our study, frequency of UTI in children on urine culture as a gold standard was recorded in 20.69% (n=84), the diagnostic accuracy of urine dipstick in detection of UTI in children was recorded as 80.95%, 62.42%, 35.98%, 92.63% and 66.26% for sensitivity, specificity, PPV, NPV and accuracy rate. A recent study done by Eric in 2014 showed that PPV of dipstick was significantly greater than combined urine analysis (66.8% -67.4% vs 51.2% (50.6%-51.8%)16. Our study findings are in agreement with the above study. Contrary to above, in 2007, American Academy of Pediatrics discouraged the use of dipstick in detecting UTI as it has low diagnostic yield.

Smith P and others17 evaluated the sensitivity, specificity, positive and negative predictive values of microscopy and dipstick to predict culture results and recorded sensitivity 83%, specificity 76%, PPV 94%, NPV 76%, which is supporting our study results. A study by whiting et al18 revealed similar results.

In a study conducted at turkey where urine cultures were compared with dipstick analysis for detection of UTI, negative predictive values for LE, nitrite, bacteriuria and WBC were very close to 100%.19

In a recent randomized controlled trial done in 2010, it was concluded that use of targeted antibiotics with dipstick testing becomes the most cost effective strategy but there are insufficient local data available.20

In summary, the results of our study supports the use of urine dipstick to detect UTI early as it is an easy modality, an inexpensive test and we can start early treatment with antibiotics and hence can decrease the complications associated with late detection of UTI. Though, it is not routinely performed in our hospital setting however, considering the results of our study in accordance with other studies, the use of this effective modality may guide us towards the early treatment and hence prevention of complications.
CONCLUSION

We conclude that the diagnostic accuracy of urine dipstick in detection of UTI in children keeping urine culture as a gold standard is higher and this cost effective and easy technique may be used in our routine practice for prediction and early treatment of UTI in children.

Author's Contribution:
Concept & Design of Study: Maryam Naseem
Drafting: Maryam Naseem, Aroma Tariq, Sumbal Saeed
Data Analysis: Maryam Rafiq Ghuncha, Nighat Jabeen, Mariam Raza
Revisiting Critically: Maryam Naseem, Aroma Tariq
Final Approval of version: Maryam Naseem

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

REFERENCES

Compare the Outcomes of Mini-Plate versus K-Wire Fixation in Patients with Shaft of Metacarpal Fractures

Azhar Rashid¹, Ghulam Qadir Khan¹, Muhammad Ishfaq¹, Muhammad Badarud Din², Zafir², Azmat Rasool² and Mukhtar Ahmad Tariq²

ABSTRACT

Objective: To compare the outcomes of mini plate versus K-wire fixation in patients undergoing surgical treatment for fractures shaft of metacarpal.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Orthopaedics, Nishtar Hospital Multan from January 2019 to June 2020.

Materials and Methods: Forty patients of both genders presented with fractures shaft of metacarpal were enrolled. All the patients were divided equally into two groups. Group I with 20 patients received mini plate internal fixation and group II with 20 patients received K-wire fixation. Functional outcomes were analyzed by DASH scoring system. Post-operative complications were examined.

Results: In group I, 12 (60%) patients were male and 8 (40%) were females with mean age 32.22±8.96 years and in group II 13 (65%) were male and 7 (35%) were females with mean age 33.86±7.48 years. In group I, 13 (65%) patients had excellent, 4 (20%) had good, 2 (10%) had fair and 1 (5%) had poor functional outcomes, in group II 7 (35%) patients had excellent, 7 (35%) had good 4 (20%) had fair and 2 (10%) had poor functional outcomes as per DASH criteria. In group I, 2 (10%) patients and in group II 4 (20%) patients had developed postoperative complications.

Conclusion: Internal fixation with miniplate for shaft of metacarpal fractures showed better functional outcomes with fewer rate of postoperative complications and earlier union as compared to K-wire internal fixation.

Key Words: Shaft of metacarpal fracture, Internal fixation, Mini-plate, K-wire, DASH scoring system

INTRODUCTION

Metacarpal fractures represent 18-44% of all fractures in the hands.¹³ The active and working population, particularly adolescents and young adults, has the most metacarpal fractures. The occurrence of hand trauma has evolved over the years, sometimes leading to metacarpal, fractures and dislocations.³⁴

The metacarpal bone of the hand is one of the most common orthopaedic wounds, accounting for 14-28 percent of all hospital visits followed by trauma by various means such as auto fall, attack, road accidents, industrial accidents, and farm accidents.⁵

¹ Department of Orthopedic / Orthopedic Surgery Ward No 21², Nishtar Medical University Hospital Multan.

Correspondence: Dr. Azhar Rashid, Senior Registrar, Department of Orthopedic Nishtar Medical University Hospital Multan.
Contact No: 0333-6162782
Email: drazharrashid@gmail.com

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Metacarpal fractures are frequently disregarded or treated as minor injuries, which lead to major impairment and distortions with the constant paralysis of fine hand movements. The deformity due to non-treatment, stiffness due to over-treatment and malformation and steepness due to poor treatment can complicate metacarpal fractures.⁶

Many factors, such as responsive handling of the tissues, protection of gliding tendon planes, infection prevention and early and suitable physiotherapy, apart from precise reduction and fixation, affect good mobility recovery. The lack of radiological or clinical recovery after four months of fixation determines the non-union of the metacarpal fracture.⁷ For metacarpal fracture patients the rate of union or delayed union may be up to 6%.⁸

We conducted present study with aimed to compare the functional outcomes of mini-plate versus K-wire for shaft of metacarpal fractures.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Orthopedics Nishtar Hospital Multan from 1⁴ January 2019 to 30⁰ June 2020. A total of 40
patients of both genders presented with fractures shaft of metacarpal were enrolled. Patient’s detailed demographics including age, sex, and side of fracture were recorded. Patients with osteoporosis, fractures with bone loss, comminution to the extent that accurate reconstruction with firm cortical apposition is impossible and refractures were excluded. Pre- and postoperatively complete radiological assessment was done. All the patients were divided equally in to two groups. Group I with 20 patients received mini plate internal fixation and group II with 20 patients received K-wire fixation. Post-operative complications such as superficial infection, delayed union, and finger stiffness were examined. Functional outcomes were analyzed by DASH scoring system. Patients were followed for 3 months.

All the data was analyzed by SPSS 24.0. Chi-square test was done to compare the outcomes and postoperative complications between both groups. P-value <0.05 was taken as significant.

RESULTS

In group I, 12 (60%) patients were male and 8 (40%) were females with mean age 32.22±8.96 years and in group II 13 (65%) were male and 7 (35%) were females with mean age 33.86±7.48 years. 11 (55%) patients had right side fracture and 9 (45%) had left side involvement in group I and in group II 10 (50%) patients had right side and 10 (50%) had left side fracture. No significant difference was observed between both groups regarding age, gender and side of fracture (p-value >0.05) [Table 1]. At 4th postoperative week union was achieved in 4 (20%) and 2 (10%) patients in group I and II, at 8th postoperative week in group I 16 (80%) patients achieved union of bone while in group II 12 (60%) patients had union, at 12th postoperative week 20 (100%) patients in group I and II had union of bone. We found no significant difference was observed between both groups with p-value >0.05 (Table 2).

In group I, 13 (65%) patients had excellent, 5 (25%) had good, 2 (10%) had fair and none of patient had poor functional outcomes, in group II 7 (35%) patients had excellent, 7 (35%) had good 4 (20%) had fair and 2 (10%) had poor functional outcomes as per DASH criteria. A significant difference was observed between both groups with p-value 0.036 (Table 3). In group I, 2 (10%) patients in which 1 (5%) had superficial infection and 1 (5%) had stiffness and in group II 4 (20%) patients had developed postoperative complications in which 2 (10%) patients had finger stiffness, 1 (5%) patient had superficial infection and 1 (5%) patient had delayed union. No significant difference was observed between both groups with p-value >0.05 (Table 4).

DISCUSSION

Fractures shaft of metacarpal bone are commonly encountered fractures in orthopedic settings. Many of surgical modalities have been applied for the treatment of these fractures but mini-plate fixation and internal fixation with K-wire are the most performing procedures due to high rate of excellent functional outcomes and fewer rate of complications. Majority of patients were male in both groups and overall accounted 57.5% while females were 42.5%. Majority of patients were ages between 25 to 45 years. These results were comparable to many of previous studies in which male patients population was high 60% to 70% and average age of patients was 30 years.

In present study, we found that at 4th postoperative week union was achieved in 4 (20%) and 2 (10%) patients in group I (mini plate) and II (k-wire), at 8th postoperative week in group I 16 (80%) patients achieved union of bone while in group II 12 (60%) patients had union, at 12th postoperative week 20 (100%) patients in group I and 19 (95%) patients in group II had union of bone. We found no significant
difference between both groups. But patients received mini plate fixation had earlier union of bone as compared to k-wire fixation. None of patient had non-union of bone at final follow-up. A study conducted by Agarwal et al\textsuperscript{13} reported that time of union was better in patients received mini plate as compared to patients with k-wire fixation but the results were statistically insignificant. Another study by Ali et al\textsuperscript{14} reported that Fifteen patients showed union after six post-op weeks, out of these 1 (4%) cases, K-wires were handled and fourteen (56%) were treated with miniplate. After 8 weeks of surgical treatment, 27 patients showed union, 7 cases (28%) with k-wires and 20 (80%) with miniplates were treated. During the 10th post-op week, 43 cases existed with Union, of which 18 (72%) with K-wires were treated and 25 (100%) with Miniplate were treated. On the 3rd and 4th months of post-operative procedures, 49 cases showed an X-ray union, of which 24(96%) cases were handled with K-wires and 25(100%) with a miniplate. There was a statistically insignificant gap between the postoperative unions. In our study we found that among patients who received mini plate fixation, 13 (65%) patients had excellent, 5 (25%) had good, 2 (10%) had fair and none of patient had poor functional outcomes, in group II (K-wire) 7 (35%) patients had excellent, 7 (35%) had good 4 (20%) had fair and 2 (10%) had poor functional outcomes as per DASH criteria. A significant difference was observed between both groups with p-value 0.036. Agarwal et al\textsuperscript{13} reported that patients received mini plate fixation had better functional outcomes as compared to k-wire fixation.

A research by Zhang et al\textsuperscript{15} found that 21 excellent and 46 good results have been achieved in the bone cement group k-wire fitting; and 9 very good, 50 good and 5 fair plate and screw group results. The functions of the fingers were significantly different (p< 0.05).

We found that 2 (10%) patients had postoperative complications in mini plate group while 4 (20%) patients had developed postoperative complications in K-wire group, no significant difference was observed between both groups however, 1 (5%) patient had delayed union in k-wire group. These results showed similarity to some previous studies.\textsuperscript{16,17}

CONCLUSION

Internal fixation with miniplate for shaft of metacarpal fractures showed better functional outcomes with fewer rate of postoperative complications and earlier union as compared to K-wire internal fixation.

Author’s Contribution:
Concept & Design of Study: Azhar Rashid
Drafting: Ghulam Qadir Khan, Muhammad Ishfaq
Data Analysis: Muhammad Badarud Din Zafir, Azmat Rasool,

Revisiting Critically: Mukhtar Ahmad Tariq
Final Approval of version: Azhar Rashid

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

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Liver Toxicity Incited by Rifampicin & its Remedy by Aqueous Extract Preparation of Stem Bark of Barberry (Berberis Lycium Royale) in Male Mice Model

Saima Rafique¹, Ayesha Afzal¹, Abeera Sikandar¹, Lubna Ghazal², Lubna Ehtizaz² and Khalida Ajmal¹

ABSTRACT

Objective: To investigate the liver toxicity produced by Rifampicin and its amelioration by using aqueous extract of stem-bark of Barberry (Berberis Lycium Royale) in male mice.

Study Design: Randomized control trial study.

Place and Duration of Study: This study was conducted at the animal abode of National Institute of Health (NIH), Islamabad in cooperation with Riphah Institute of Pharmaceutical Sciences (RIPS), Islamic International Medical College (IIMC) & Army Medical College (AMC) for 1 month from April 2014 to May 2014.

Materials and Methods: This research study was conducted on 56 male mice. Animals indiscriminately allotted into 4 groups (n=14). Group I: Control group fed on rodent pellet food and tap water. Group II: Drug toxicity induced group put up on Rifampin 50mg/kg BW. Group III: Lower dose aqueous extract group given Rifampicin & (150mg/kg BW) aqueous extract of stem bark of Barberry. Group IV: High dose aqueous extract group kept on Rifampicin & (200mg/kg BW) of aqueous extract of Barberry via gavage tube orally. Baseline blood samples stockpiled at day 0 and serum values of Alanine aminotransferase (ALT) were recorded. Progress of experimental research was evaluated by serum measurement of Alanine aminotransferase (ALT) at day 15. At the end of experimental research on day 30 blood samples were collected by intra-cardiac puncture technique. Serum separated from blood samples were preserved in sterile containers at temperature of 4°C for analysis of serum Alanine aminotransferase (ALT). SPSS version 20 utilized for analysis of statistical data & p-value (<0.05) regarded as significant.

Results: Serum Alanine aminotransferase (ALT) level (17-77 U/L) was recognized as normal range. Group I showed normal level of (56 U/L). Group II displayed extreme drug hepatotoxicity with very high value of (188.3 U/L). Serum value of ALT measured in Group C was (96.6 UL) & (56 UL) in Group D. Aqueous extract of stem-bark of Barberry restored serum Alanine aminotransferase (ALT) levels in group III (98.8 UL) & more remarkable improvement in Group IV with level of (58 UL).

Conclusion: Aqueous extract of stem-bark of Barberry (Berberis Lycium Royale) proved amazing protective activity for rifampicin induced liver toxicity in high doses in comparison to less doses.

Key Words: Aqueous extract, Barberry, Hepatoprotective, Rifampicin, Alanine Aminotransferase (ALT)


INTRODUCTION

1. Department of Pharmacology & Therapeutics / Pathology, Wah medical College, Wah Cantt, Pakistan.

Correspondence: Saima Rafique: Assistant Professor of Pharmacology & Therapeutics, Wah Medical College, Wah Cantt, Pakistan.

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Tuberculosis (TB) prevailed as one of the devastating disease in the history of mankind by affecting one-third of the human population all over the world. In 2018, around 10 million persons suffered from TB, and 1.5 million demise occurred because of tuberculosis. The microbe Mycobacterium tuberculosis is responsible for pathogenesis of tuberculosis. The first line anti-TB drug Rifampicin was discovered in 1957 and approved for therapeutic use in 1968 due to its tremendous sterilizing activity and reducing time span of treatment. Rifampicin acts by binding to DNA dependent RNA polymerase and blocking its action. It stops RNA synthesis of Mycobacterium tuberculosis leading to its demise. It has verified to be one in all the foremost helpful initial line anti-TB agent, however it conjointly causes severe hepatotoxicity because of being a...
powerful inducer of varied metabolic accelerator pathways of the body significantly of haemoprotein P450 (CYP3A4) system.\(^5\)

PPAR\(\gamma\) signal mechanisms and aerophilic stress were conjointly found to be greatly coupled to Rifampicin-induced toxicity to liver.\(^6\) Medications resulting liver toxicity can be depicted by increased serum markers of liver i.e liver function tests (LFT’s).\(^7\) *Berberis lycium* Royle is famous for its hepatoprotective potential.\(^8\) It is renowned by its numerous regional names like Barberry, Kashmal, Sumblool, Ishkeen & ziarlargay\(^9\) Major component of stem-bark of Barberry is Berberine (4.2%) that has vital hepatoprotective effect.\(^10\) Barberry has wide implication in treatment of diabetes.\(^12\) It's been used for polygenic disorders like jaundice, rheumatism, ear & eye infections.\(^13\) The rationale of this randomized control trial intended to investigate hepatoprotective role of the aqueous extract preparation of stem-bark of Barberry (Berberis lycium Royle) in dose dependent manner against rifampicin induced hepatotoxicity in male mice.

**MATERIALS AND METHODS**

This randomized control trial study has been conducted in research & analysis institute, National Institute of Health (NIH), Islamabad after getting ethical approval by RARE (Riphah Academy of Research & Education) from 12\(^{th}\) April 2014 until 12\(^{th}\) May 2014. Male mice of weight 28-50 grams, of age 6-8 weeks having normal serum Alanine aminotransferase (ALT) levels were kept in NIH underneath environment with standardized conditions in wire lidded cages at temperature of (21-24\(^{\circ}\)C) and accustomed for one week.

**Animals’ Groups:** Group I was considered control group fed on rodent pellet food and tap water. Group II: Drug toxicity induced group kept on Rifampin 50mg/kg BW\(^11\). Group III: Low dose aqueous extract group given Rifampicin & (150mg/kg BW) aqueous extract of stem bark of Barberry. Group IV: High dose aqueous extract group put on Rifampicin & (200mg/kg BW) of aqueous extract of Barberry via gavage tube orally.

**Aqueous extract preparation:** Bark of the stem of genus *Berberis Lycium Royle* (Barberry) stockpiled from one of the small town of Charsadda i.e Prang, Charsadda. A renowned botanist Ghulam Jillani of Peshawar University authenticated it. It was completely washed with water and dried in shade. Dried Barberry was crushed into fine powder by using electric grinder and stored in non-metallic jar. Distilled water was used for soaking fine Barberry powder for 72 with intermittent stirring. Filtration of soaked Barberry powder was done by Whatmann’s filter paper no.1. Barberry’s filtrate vaporized at 56 \(^{\circ}\)C by using the rotary evaporator at premises of research lab of Riphah Institute of Pharmaceutical Sciences (RIPS), Islamabad. Aqueous extract acquired found to be dark brown in color thick sticky paste in consistency. Air tight small glass bottles were used for its storage in refrigerator at 2-6\(^{\circ}\)C for future use in research. 25% yield was obtained of aqueous extract of Barberry as compare to original dried plant material.

**Collection of Blood Samples:** Two mice from each cluster were used for collection of blood samples by cardiac puncture at day zero as baseline of serum markers. Mid-study cycle blood sample of 2 mice was drawn at day fifteenth from every cluster so as to gauge progress of research. Finally, blood samples of all remaining mice were drawn at the last thirtieth day of research for measuring of serum Alanine Aminotransferase (ALT). Cardiac puncture technique was applied for drawing blood samples and transferred to sterile red cap serum tubes. Bench top centrifuge machine was used for segregation of serum from blood samples by doing centrifugation at (3000 rpm). Segregated serum was transferred for storage in serum cups.\(^16\) ALT kit from Merck company having Lot No. 505 was used for estimation of serum Alanine Aminotransferase (ALT) on Micro lab 200 (Merck) following International Federation of Clinical Chemistry (IFCC) principles.

**Statistical analysis:** Data analysis done on software SPSS 20. Means and Standard Error of Means (S.E.M) calculated from final results of the serum analysis. Comparison between the different groups was done by applying Post-hoc analysis. P-value <0.05 regarded as significant.

**RESULTS**

Serum Alanine Aminotransferase (ALT) levels were highly raised in drug treated group II in comparison to control group I due to hepatic damage produced by Rifampicin (p<0.001).

<table>
<thead>
<tr>
<th>Table No.1: Mean ± SEM Values of ALT</th>
<th>Animal group no. (n=10)</th>
<th>ALT(17-77 U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>56±7.99</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>188.1±68.32</td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>98.6±17.34</td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>58 ± 6.89</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
</tbody>
</table>

\(*= p\) - value Significant (ALT= Alanine aminotransferase, S.E.M= Standard Error of Means)

<table>
<thead>
<tr>
<th>Table No.2: Post-Hoc Comparison of ALT</th>
<th>Group Comparisons</th>
<th>ALT(17-77 U/L)</th>
<th>Mean Difference</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I vs. Group II</td>
<td>-134.3</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I vs. Group III</td>
<td>-44.8</td>
<td>0.079</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I vs. Group IV</td>
<td>6</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II vs. Group III</td>
<td>91.7</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II vs. Group IV</td>
<td>136.3</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group III vs. Group IV</td>
<td>47.8</td>
<td>0.050*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Serum ALT levels were strikingly normalized in group IV kept on high dose of aqueous extract of Barberry in comparison to group III which were given low dose of aqueous extract of the herb. Results have been briefed in the given table I. Post hoc comparison of ALT is also shown in table 2.

DISCUSSION

This randomized control trial was conducted to identify the degrees of hepatotoxicity produced by Rifampicin by measuring serum Alanine Aminotransferase (ALT) levels and to explore hepatoprotective activity of low & high doses of aqueous extract of Barberry in vivo in male mice. Serum Alanine Aminotransferase (ALT) levels were highly deranged in Group-II animals due to hepatotoxic nature of rifampicin with statistically significant difference in values between Group I & Group II. Serum Alanine Aminotransferase (ALT) levels were highly raised to (188.1±68.32) in Group-II mice from (56±7.99) in Group-I. Kim JH et al in 2017 observed alike results during research on investigating mechanisms involved in rifampicin induced liver injury. Analogous findings were detected by Ramappa V et al in 2013 while studying mechanisms & management of hepatotoxicity related to anti-tuberculosis drugs. Comparable results were noticed by Issabagloo in 2012 by triggering hepatotoxicity in rats with combination of rifampicin & isoniazid. Free radical ions and oxidative stress produced by the drug leads to severe damage to hepatocytes. Hepatotoxicity produced by rifampicin is because of induction of many oxidizing enzymes specifically of cytochrome P450 (CYP3A4) enzyme system resulting in increase in oxidative trauma & hepatotoxicity. It is widely accepted regarding reactive oxygen species (ROS) & free radicals being main culprit of inflammatory cascade and subsequently tissue damage. Antioxidants are scavenging compounds by nature and play a vital role in reducing oxidative stress to the tissues from free radical ions. Herbal medicine are known for their excellent safety profile since earliest times. Berberis lycium Royle, (Barberry) is widely recognized for its anti-oxidant & hepatoprotective activity. Barberry is commonly used for different ailments. Major constituent of Barberry is berberine. It is tremendously effective in improving body’s immune system. Our randomized control trial was planned to investigate the hepatoprotective activity of lower & higher doses of aqueous extract of stem bark of Barberry. This randomized control trial manifested that aqueous extract of Barberry have astonishing hepatoprotective potential (p <0.001) in dose-dependent manner. Higher dose of aqueous extract (200mg/kg BW) significantly dropped serum Alanine Aminotransferase (ALT) levels in comparison to low dose of aqueous extract (150mg/kg BW.). A higher peak was depicted in serum Alanine Aminotransferase (ALT) levels in group II kept on Rifampicin as compare to Group-I without administration of any drug. Increased serum Alanine Aminotransferase (ALT) level is a key diagnostic criteria of hepatic damage. Concurrent administration of Rifampicin besides with lower and higher doses of aqueous extract of stem-bark of Barberry in group III and IV re-establish serum Alanine Aminotransferase (ALT) to normal level owing to its anti-oxidant potential. Khan & his colleagues in 2011 observed hepatoprotective effects of aqueous extract of Berberis Lycium Royale (Barberry) in combination with Gallium aparine & Pistacia Integerrima in CCl4 treated rabbits. Similar findings established in the research done on hepatoprotective activity of Berberis Lycium in 6 herbal formulations alongwith Livokin (Herbo-med, Kolkata) on hepatotoxicity produced by paracetamol in mice model.

CONCLUSION

The remunerative effect of aqueous extract of stem bark of Berberis Lycium Royale (Barberry) is proven in hepatotoxicity and this herb has promising potential in ameliorating liver function at low & high doses in drug Rifampicin induced liver damage in male mice.

Recommendations:
- Other serum LFT’s should also have been performed.
- Histopatholgical studies of liver should also be planned for future research.
- Active components of stem bark of Barberry (Berberis lycium Royle) extracts should be isolated and evaluated regarding their hepatoprotective potential.

Acknowledgements: We are grateful to Riphah International University, Pakistan for providing financial grant for this research study.

Author’s Contribution:
| Concept & Design of Study: | Saima Rafique |
| Drafting: | Khalida Ajmal |
| Data Analysis: | Abeera Sikandar, Lubna Ghazal, Lubna Ehtizaz |
| Revisiting Critically: | Saima Rafique, Ayesha Afzal |
| Final Approval of version: | Saima Rafique |

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

REFERENCES


Corelation of Mesiodistal Width of Upper Anterior Teeth with Inner Canthal Distance in Population of Hyderabad Region

Sandeep Kumar¹, Kashif Ali Channar², Abdul Bari Memon¹, Irfan Ahmed Shaikh², Almas Rahoojo¹ and Deepak Kumar²

ABSTRACT

Objective: To determine the corelation of mesiodistal width of upper anterior teeth with inner canthal distance in population of Hyderabad region.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Department of Prosthodontics, Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro from June 2018 to January 2019.

Materials and Methods: Total 122 subjects were included with convenient sampling technique. The data was collected by measuring the inner-canthal distance (ICD), with Vernier caliper by placing against the forehead and lowered towards the eyes. The external arms of the Vernier caliper were adjusted so that they were in gentle contact with medial angles of the palpebral fissures of the eyes. The distance between these two anatomical landmarks were recorded as the ICD represented in millimeters.

Three readings of ICD were done to ensure precision and the mean value was recorded. The mesiodistal widths (MDW) of each maxillary central incisor, lateral incisor and canine were recorded intra-orally. The combined width of upper anterior (CWUA) teeth was calculated by summing up the widths of central incisors, lateral incisors and canine of both contralateral sides. Then the combined widths of maxillary anteriors were co-related with the ICD. The readings were recorded in proforma. The Data was analyzed by SPSS version 16.

Results: The mean age was 28.16±5.508. The males were 61% and female were 39%. Comparison of mean score of ICD in male was 29.38±2.44 and in female was 28.97±2.01 which is statistically not significant. Comparison of mean score of CWUA teeth in male was 32.68±2.69 and in female was 32.02±2.31; statistically not significant. Pearson correlation of ICD with CWUA was positive and statistically significant.

Conclusion: The results of the present study suggest that ICD may be a reliable predictor to determine the MDW of upper anterior teeth. The relationship between ICD and CWUA a ratio between ICD and CWUA was found. The overall mean ratio between ICD and CWUA was found to be 1.10. This indicates that the MDW of upper anterior teeth can be obtained by multiplying ICD with 1.10.

Key Words: Inner-canthal distance, Mesio-distal width, Correlation


INTRODUCTION

Esthetics is one of the primary concerns of all individuals and it has importance in the field of dentistry.

¹ Department of Bibi Aseefa Dental College @ SMBBMU Larkana Sindh.
² Department of Prosthodontics, LUMHS, Jamshoro.

Correspondence: Abdul Bari Memon, PhD Scholar (LUMHS) and Assistant Professor, Bibi Aseefa Dental College @ SMBBMU Larkana Sindh.
Contact No: 0300 2426578
Email: drabmemon@yahoo.com

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Esthetics plays a crucial role in complete denture prosthodontics. One of the important tasks in esthetic dentistry is the creation of harmonious smile. To achieve a harmonious smile, the Prosthodontist has to carefully blend the science and art with regards to selection and arrangement of teeth.¹ The size, form and color of the teeth must be in harmony with surrounding oral and facial structures. Selection of appropriately sized teeth requires both artistic skill and scientific knowledge.²

Most important step in denture esthetics is the selection of suitable size of maxillary anterior teeth.¹ The accurate size estimation of combined width of maxillary anterior teeth become very difficult in the absence of preoperative clinical records. Several anatomic measurements, including bi-zygomatic width (BZW), inter-pupillary distance (IPD), inter-alar width (IAW), ICD, and inter-commissural width have been suggested to aid in the estimation of a combined width
of the maxillary anterior teeth (inter-canine width).\textsuperscript{3} Controversial studies have been reported regarding correlation between the width of the mouth and the MDW of the upper anterior teeth. Clapp and Tench published that the distal surfaces of the maxillary canines should be located at the commissural of the mouth, but Al Wazzan and colleagues, found no correlation between the width of the mouth and the MDW of upper anterior teeth.\textsuperscript{4} Scandrett et al evaluated BZW, IAW, ICW, sagittal cranial diameter, inter-buccal frenum distance, philtrum width, and age as predictors of the width of maxillary anterior teeth and central incisors.\textsuperscript{5} Kumar and Gupta investigated facial measurements was the width of the nose. When measured in bone structure, the nasal width showed equal or nearly equal measurements to the width of the four maxillary incisors in 93% of the skulls analyzed.\textsuperscript{1} However, when measured in soft tissue, the inter-alar width (IA) is not correlated to the width of the four maxillary incisors but rather to the width of the six maxillary incisors. On the other hand, Smith, in 1975, found that neither the nasal width nor the IA correlated to the width of the six upper anterior teeth.\textsuperscript{6} Naeem et al found that IPD is different in males and females and is not correlated with the selection of artificial teeth.\textsuperscript{7} Another facial anthropometric measurement is the distance between the inner canthus of the eyes. The investigators concluded that no single predictor was accurate enough for clinical application. Therefore, it appears that more than one variable is needed to predict the width of maxillary anterior teeth and central incisors.

The ICD is stated as the distance between the medial angles of the palpebral fissures of both eyes.\textsuperscript{8} At 5 years of age, 93% of ICD growth has been achieved; maturity is reached between 8 and 11 years. The ICD is considered normal at a dimension of 28 35 mm.\textsuperscript{3} Selecting anterior teeth in absence of any previous record is one of major problems faced by dentists. In the absence of previous records, ICD can be helpful so the purpose of this study is to determine the correlation of ICD with MDW of maxillary anterior teeth. The results of this study will be beneficial for Prosthodontists in selecting proper anterior teeth and for patients in their appearance.

MATERIALS AND METHODS

This study was conducted at Department of Prosthodontics, Institute of Dentistry; LUMHS Jamshoro, Sindh. Ethical clearance was sought from the Ethical Review Board of University. The written informed consent was acquired from the participants. The sample size was calculated using epitoool online software by taking the standard deviation 2.81 (taken as reference the ICD from the association between the facial widths and width of upper anterior teeth \textsuperscript{3}) at 95% confidence interval at 0.5 acceptable error. The total sample size calculated was 122. Inclusion criteria were fully dentate adults of age ranging from 20-40 years irrespective of gender. Exclusion criteria were patients with attritional teeth, restored teeth, orthodontic ally treated teeth, undergone crown and bridge work or Congenital and/or acquired oro-facial deformities.

The participants were seated on a dental chair to measure the ICD and their heads were held upright towards the horizon. The Vernier caliper was put against the forehead and lowered to the eyes. The Vernier caliper's internal arms were adapted so that the palpebral fissures of the eyes were in smooth contact with the medial edges. As the ICD depicted in millimeters, the distance amid these two anatomical landmarks was documented. Three readings of ICD were made to ensure precision and the mean value was recorded. The MDW were recorded intra-orally for each central incisor, lateral incisor and canine. Cheek retractors were used to facilitate access. The readings were found with the pointed claws of the digital caliper's inner jaws placed in labial embrasures at the largest mesio-distal aspect of each tooth and the digital caliper's long axis kept parallel to the incisal corners, and the caliper's inner and outer jaws were positioned perpendicular to the tooth's long axis. The combined size of maxillary anterior teeth was computed by summing the widths of both contralateral sides of central incisors, lateral incisors and canine. Then the maxillary anterior teeth paired length was correlated with the ICD. The measurements were recorded in proforma.

Data was entered and analyzed through SPSS version 17. Mean and standard deviation were calculated for quantitative variables like age, ICD, MDW of maxillary anterior teeth. Frequency and percentage were calculated for qualitative variable like gender. Independent t test was applied to check the statistical difference between gender and ICD, MDW of maxillary anterior teeth. Pearson correlation coefficient was determined between ICD and MDW of maxillary anterior teeth. P value < 0.05 was considered as significant at 95% confidence interval.

RESULTS

The male was 61% and female were 39%. The mean age was 28.16 ± 5.50. Mean MDW of right central incisor, lateral incisor and canine was 6.04±0.61, 4.84 ± 0.62 and 5.31 ± 0.74 respectively. Mean MDW of left central incisor, lateral incisor and canine was 6.03 ± 0.64, 4.874±0.665 and 5.281±0.703. The mean ICD was 29.22 ± 2.286 (Table-1) Comparison of mean score of ICD in male was 29.38±2.44 and in female was 28.97±2.01 which is statistically not significant (Table-2). Comparison of mean score of CWUA in male was 32.68±2.69 and in female was 32.02±2.31; statistically not significant (Table-3).
Table No.1: Descriptive statistics of Gender, Age, MDW and ICD of teeth

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>75</td>
<td>61</td>
</tr>
<tr>
<td>Female</td>
<td>47</td>
<td>39</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.16</td>
<td>5.50</td>
</tr>
</tbody>
</table>

**Table No.2:** Comparison of mean score of inner canthal distance in gender (Student T-Test)

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inner Canthal Distance</td>
<td>Male</td>
<td>75</td>
<td>29.38</td>
<td>2.441</td>
<td>0.281</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>47</td>
<td>28.97</td>
<td>2.016</td>
<td>0.294</td>
</tr>
</tbody>
</table>

**Table No.3:** Comparison of mean score of combined upper anterior teeth (CWUA) in gender (Student T-Test)

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean of all</td>
<td>Male</td>
<td>75</td>
<td>32.68</td>
<td>2.694</td>
<td>0.311</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>47</td>
<td>32.021</td>
<td>2.310</td>
<td>0.336</td>
</tr>
</tbody>
</table>

**Table No.4:** Correlation of inner canthal distance with mesiodistal width of maxillary anterior

<table>
<thead>
<tr>
<th>Correlations</th>
<th>Inner Canthal Distance</th>
<th>Mean of All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inner Canthal Distance</td>
<td>Pearson Correlation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>122</td>
</tr>
<tr>
<td>CWUA</td>
<td>Pearson Correlation</td>
<td>.599**</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>122</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Enhancement of facial beauty is one of the primary elective goals of patients seeking dental care. Loss of teeth especially anterior teeth is a traumatic experience that prompts people to seek dental care. Hence the planned prosthesis should fulfill esthetic harmony, functional efficiency and structural balance with the rest of the dento-facial structures. Achieving excellent esthetics when restoring or replacing the maxillary anterior teeth is one of the most challenging tasks in dentistry. Hardy IR had stated that, “To meet the esthetic needs of the denture patient, we should make the (denture) teeth look like (the patient's) natural teeth.” In complete denture construction, selection of anterior teeth is a vital step. When no pre-extraction records are available, selecting the proper size and shape of anterior teeth for edentulous patients can be difficult. The relative stability of the ICD aroused interest in various authors who have reported using ICD as the anatomic landmark in determination of MDW of central incisor and upper anterior teeth. These studies were conducted for limited sample size and for a single ethnic group. This study has also same limitation of insufficient sample size but different ethnic groups like sindhi, siraiki and muhajir. The authors of these studies were of an opinion that, the ethnic related differences in ICD may exist and they proposed further research to validate the relationship between ICD and maxillary central incisors and maxillary anterior teeth. ICD was chosen for measurement in the present study for the following reasons: Studies have proved that the reference points (namely, medial angles of the palpebral fissures of the eyes) as a stable anthropometric parameter. These reference points can be easily located and measured with a simple instrument such as Vernier caliper. In this study Vernier caliper was one of the research gadgets. The limitations of using caliper as a measuring device was noticed during the study which includes, inability to insert the thinner beaks of the caliper in the broadest width of the tooth due to tight teeth contacts, some subjects did not cooperate to place the beaks of the caliper in the medial canthus to record ICD.

In our study it was observed that ICD was slightly more in men than in women. This is in agreement with the studies of Wazzan KAA, Sanin C& Savara BS. An analogous report in this regard was also been stated by Mavrosofoufis et al. In this study the CWUA teeth was almost equal in males and females which is not in agreement with the study conducted by Wazzan KAA and Lavelle CL who observed that all tooth dimensions and ICD were significantly larger in men than in women. CWUA teeth are the sum total width of each anterior tooth. Most of the values (95% confidence interval) of this parameter ranged between 32.68 and 32.02 with the...
mean being 32.35 mm where as it was 48.68 mm and 49.02 mm with the mean being 48.85 mm in the study conducted by Kumar A et al.1 In this study mean values of CWUA and sex showed statistically insignificant difference where as it showed statistically significant difference in the study of Kumar A et al.1 The mean value of CWUA found in present study was less than the value reported by Scandrett et al.15 (53.61 mm), Wazzan16 (45.23 mm) and Shillingburg et al.16 (45.80 mm). This variation in the measurements reported could be attributed to the difference in the ethnicity of the population evaluated. The relationship between ICD and CWUA teeth a ratio between ICD and CWUA was found. The overall mean ratio between ICD and CWUA was found to be 1.10. The mean value showed no statistically significant difference between genders. This indicates that the MDW of upper anterior teeth can be obtained by multiplying ICD with 1.10. This ratio is less than the ratio quoted by Kumar AKV et al1 (1.61) and Wazzan KAA1 (1.426). This variation in the ratio may also due to difference in the ethnicity of the sample population tested.

In this study the subjects were relatively homogeneous which relate to the study conducted at Saudi Arabia where the homogenous samples were selected, the results of this study are more applicable to the population evaluated. Comparisons with data on Western populations may be undertaken, but ethnic differences should be considered.

The mean MDW of the central (Right and Left) incisors (6.03mm) and (8.48 mm) is not in agreement with the findings of Scandrett FR et al15 (8.50 mm). The mean value of the combined width of the 6 maxillary anterior teeth (32.43) does not support the findings of Shillingburget HT15 (45.80 mm) and Abdullah M4 (43.00 mm). To some extent, the variations may be explained by differences in measuring techniques and in the ethnicities of the populations studied. In the present study the mean ICD was (29.22) less than values reported by Wazzan KAA3 (31.92), Abdullah M4 (32.00 mm) and Freihofer HP17 (31.20 mm).

The Pearson correlation coefficients were positive and highly significant for various tooth widths. These findings indicate that the ICD could be used to select maxillary anterior teeth for edentulous patients.

CONCLUSION

The results of the present study suggest that ICD may be a reliable predictor to determine the MDW of upper anterior teeth. The relationship between ICD and CWUA a ratio between ICD and CWUA was found. The overall mean ratio between ICD and CWUA was found to be 1.10. The mean value showed no statistically significant difference between sexes. This indicates that the MDW of upper anterior teeth can be obtained by multiplying ICD with 1.10. Interpretation and extrapolation of the results must be tempered, however, by an acknowledgement of the study’s limitations. Only single centered study was approached, and subjects were selected within a narrow age range. It was single operator based study. Further research is necessary to validate the outcomes of this investigation. Future research should investigate ethnic groups other than the one evaluated in the present study.

Author’s Contribution:
Concept & Design of Study: Sandeep Kumar
Drafting: Kashif Ali Channar, Abdul Bari Memon
Data Analysis: Irfan Ahmed Shaikh, Almas Rahoojo, and Deepak Kumar
Revisiting Critically: Sandeep Kumar, Kashif Ali Channar
Final Approval of version: Sandeep Kumar

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

REFERENCES


Comparison of Lung Function Changes Among Anemic and Non-Anemic Adults

Aliya Waseem¹, Shahjabeen², Syed Adnan Ahmed³, Saba Abrar³, Padma Rathore⁴ and Mohammad Saleh Soomro³

ABSTRACT

Objective: To find the correlation that exists between blood hemoglobin/ serum iron indices and lung function tests. To compare changes in lung functions amongst the anemic and non-anemic adults.

Study Design: Case control study.

Place and Duration of Study: This study was conducted at the Fatima Hospital, Baqai Medical University, Karachi and Abbasi Shaheed Hospital, Karachi from July 2017 to December 2017.

Materials and Methods: 100 males and 100 female diagnosed iron deficient anemic adults in range of 18-45 years and with no co-morbid respiratory and cardiac diseases were included. Inclusion criteria included iron deficient anemic adults with no acute emergency states and no chest and back area deformities. Blood samples were reanalyzed for blood hemoglobin (Hb) by automated cell analyzer and anemia were rechecked for confirmation of iron deficiency anemia (IDA) by doing further tests like serum iron, serum ferritin, serum Total Iron Binding Capacity (TIBC) levels by Enzyme Linked Immunosorbent Assay (ELISA). Digital spirometer was used to perform Pulmonary Function Tests (PFTs) which includes Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1st second of FVC (FEV1) in all anemic patients and lung functions were compared with lung functions of non-anemic healthy individuals.

Results: The FVC and FEV1 in male and female cases were significantly reduced (p<0.05) as compared to that in male and female controls respectively. Whereas the FEV1/FVC ratio was significantly increased (p<0.05) in male and female cases. Restrictive lung changes were observed in male and female cases.

Conclusion: In the present study positive association was observed between blood Hb/serum iron indices and lung functions in anemic patients. The results showed restrictive lung function changes in anemic subjects. While no abnormal lung function changes were found in non-anemic healthy participants.

Key Words: Hemoglobin, Iron Deficiency Anemia, Pulmonary Function Tests, Forced Vital Capacity, Forced Expiratory Volume in 1st second.


INTRODUCTION

Anemia is characterized by decreased quantity of red blood cells and/or decreased levels of hemoglobin below normal levels. Normal range of hemoglobin levels in adult males are 13.5-18.0 g/dl and in female adults are 12.0-15.0g/dl. Anemia is considered when hemoglobin levels are less than 13.5 g/dl in adult males and less than 12 g/dl in adult females. Although anemia affects any gender and age but its prevalence in lower socioeconomic population is profound. According to World Health Organization (WHO), around 528.7 million (29.4%) women of reproductive age are globally affected by anemia. According to this report severe anemia was found in 20.2 million women. In accordance with National Nutritional Survey conducted in 2018 in Pakistan, anemia was prevalent in 41.7% of women of reproductive age. This survey showed a slightly higher proportion in rural (44.3%) as compared to urban settings (40.2%). Molecular oxygen is necessary for proper functioning of all biological systems. In conditions like anemia where there is decrease in supply or decrease in the utilization of oxygen profound changes occur in cell metabolism. This causes accumulation of intermediary products of metabolism like lactic acid etc in the tissue. This may
lead to increase in fatigability and decrease work output. So respiratory efforts become less powerful and respiratory muscle’s weakness occurs. Earlier studies have proved that anemia has varied effects on various respiratory parameters. Larger percentage of anemia is due to IDA alone. IDA has been shown to result in impaired work capacity, lower cognition function and impaired immune response.

Anemic patients had significantly higher medical research council dyspnea scale and number of exacerbations than patients with normal Hb levels in a study conducted in Egypt. In asthmatics, decreased concentrations of iron can initiate pathophysiologic mechanisms leading to the development of asthma. Bronchoconstriction occurred due to inflammation and muscle contraction.

The studies establishing relationship of blood hemoglobin/ serum iron indices and dynamic lung function tests are very limited. Hence, the present study was undertaken to observe the relationship of hemoglobin/serum iron indices with dynamic ventilatory tests in iron deficient anemic patients and to compare the lung functions among anemic and non-anemic adults. By knowing the association between blood hemoglobin/ serum iron indices with lung function tests, we can detect early changes in lung functions in anemic subjects and hence by correcting anemia we can indirectly improve the function of lungs.

MATERIALS AND METHODS

The present study was carried at Fatima Hospital, Baqai Medical University, Karachi and Abbasi Shaheed Hospital, Karachi from July 2017 to December 2017. This study was approved by the Ethical committee of Baqai Medical University. An approval letter with Ref no. BMU-EC/2016-04 was issued from ethical committee of Baqai Medical University on 02-01-2017. Patients who were attending in the hospitals were screened for the presence of lung function changes in diagnosed iron deficient anemic patients. Purposive sampling was done. Written consent was obtained from all participating individuals. 100 male and 100 female patients within the age group of 18 to 45 years and 50 Male & 50 female healthy individuals were included. Diagnosed iron deficient anemic patients confirmed by blood Hb, serum Iron, serum Ferritin, serum TIBC and serum % transferrin saturation levels were included. The patients with any other diseases like cardiac, lung diseases, any infectious diseases, and any inflammatory disorders were excluded. Patients with back, chest deformities, other types of anemia, active smokers and pregnant women were also excluded.

All the participant’s blood hemoglobin and serum iron indices (serum iron, serum ferritin, serum TIBC levels) were measured by automated cell analyzer (Sysmex Kx-21) and ELISA (sandwich ELISA kit (cat # YHB2785Hu; Bio Check (Foster city, CA, USA, cat #. BC-1025)) respectively.

Hemoglobin estimation was done by diluting blood in a solution containing potassium cyanide and potassium ferricyanide. Hb is converted into cyan-methemoglobin (HiCN), which is a colored-product. The color intensity is read in the colorimeter or spectrophotometer at a wavelength of 540nm, and the absorbance is proportional to the concentration of hemoglobin in the blood.

Serum ferritin levels were measured by ELISA. The first step is adding approximately 35 μl serum and BSA-buffer (bovine serum albumin) to each well. Then for 15 minutes, plates are allowed to stand at room temperature. Then the wells are rinsed 3 times with PBS (phosphate-buffered saline) after aspiration. Then again the plates are allowed to stand for 15 minutes after adding antiferritin to each well. Again PBS is utilized for rinsing the wells. Then the substrate solution containing p-nitrophenylphosphate (PNP) is added to each well. After keeping the wells at room temperature for 1 hr, the reaction is stopped by adding one drop of 1 M sodium hydroxide to each well. Visual estimation of the intensity of the yellow color in each well is performed. Finally, color intensity of each well is compared to ferritin standards containing 0, 20, 50, 100, 200, and 500 μg/liter.

Digital spirometer (Microlab 3300 electronic spirometer, Micro Medical Limited, Kent, England) was used to measure lung volumes and capacities. Three acceptable forced expiratory readings were taken for each variable and the best value was selected. Subjects were given a rest of 2-3 minutes between the tests. Nose clips were used in our study.

Statistical Analysis: Data for blood hemoglobin, serum ferritin, total serum iron, serum TIBC, serum % Transferrin saturation and lung function tests were analyzed by using independent sample t-test, and has given numerical values between two variables that were measured on same interval and results were calculated using SPSS 22.0 at p-value< 0.05. Pearson Correlation was used to correlate between blood Hb/serum iron indices and lung functions.

RESULTS

During study period, two hundred iron deficient anemic patients (N=200) were included, that consisted of hundred male and hundred female individuals. One hundred healthy individuals (N=100) participated as controls. These healthy subjects consisted of fifty males and the same number of females.

Table 1 showed that FVC in male controls was 4.05±0.05 Liters and FVC in male cases were 3.09±0.09 Liters and the t-values and p-values are 70.13 and 0.01 respectively. FVC in female controls were 3.34±0.31 Liters and FVC in female cases were 2.40±0.59 Liters and the t-values and p values are 10.54.
and 0.01 respectively. FEV1 in male controls were 3.35±0.09 Liters and FEV1 in male cases were 2.80±0.06 Liters and the t values and p values are 40.46 and 0.01 respectively. FEV1 in female controls was 2.24±0.58 Liters and the t values and p values were 3.62 and 0.01 respectively. FEV1/VC ratio in male controls was 0.82±0.19 % and the ratio in male cases was 0.90±0.18 % and the t values and p values were -2.51 and 0.01 respectively. FEV1/VC ratio in female cases was 0.80±0.04 % and FEV1/VC ratio in female controls was 0.92±0.05 % and the t values and p values are -3.36 and 0.01 respectively.

Comparison of PFTs in Table I showed that The FVC and FEV1 in male and female controls were reduced significantly (p<0.05) than in male and female controls respectively. Whereas the FEV1/VC ratio was increased significantly (p<0.05) than in male and female cases. Therefore, Restrictive lung disease was observed in anemic subjects.

### Table No.1: Mean Comparison of Pulmonary Function Tests among control & cases

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gender</th>
<th>Control</th>
<th></th>
<th>Cases</th>
<th></th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>Male</td>
<td>4.05</td>
<td>0.05</td>
<td>3.09</td>
<td>0.09</td>
<td>70.13</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>3.34</td>
<td>0.31</td>
<td>2.40</td>
<td>0.59</td>
<td>10.54</td>
<td>0.01</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>Male</td>
<td>3.35</td>
<td>0.09</td>
<td>2.80</td>
<td>0.06</td>
<td>40.46</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2.70</td>
<td>0.97</td>
<td>2.24</td>
<td>0.58</td>
<td>3.62</td>
<td>0.01</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>Male</td>
<td>0.82</td>
<td>0.19</td>
<td>0.90</td>
<td>0.18</td>
<td>-2.51</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>0.80</td>
<td>0.04</td>
<td>0.92</td>
<td>0.25</td>
<td>-3.36</td>
<td>0.01</td>
</tr>
</tbody>
</table>

P <0.05 Significant
P>0.05 Non-significant

### Table No.2: Mean Comparison of Biochemical parameters among Control & Case

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gender</th>
<th>Control</th>
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<th>Cases</th>
<th></th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood hemoglobin(g/dl)</td>
<td>Male</td>
<td>14.01</td>
<td>1.96</td>
<td>7.05</td>
<td>1.15</td>
<td>27.36</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>12.06</td>
<td>1.89</td>
<td>6.05</td>
<td>1.32</td>
<td>22.64</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum Iron(µg/dl)</td>
<td>Male</td>
<td>144.54</td>
<td>50.32</td>
<td>20.23</td>
<td>2.36</td>
<td>24.73</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>108.66</td>
<td>15.28</td>
<td>15.0</td>
<td>3.30</td>
<td>58.79</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum Ferritin(µg/l)</td>
<td>Male</td>
<td>156.68</td>
<td>25.98</td>
<td>9.12</td>
<td>1.03</td>
<td>56.9</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>96.34</td>
<td>22.60</td>
<td>8.0</td>
<td>1.14</td>
<td>39.12</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum TIBC (µg/dl)</td>
<td>Male</td>
<td>349.60</td>
<td>51.73</td>
<td>625.01</td>
<td>10.01</td>
<td>-51.5</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>272.84</td>
<td>32.77</td>
<td>650.50</td>
<td>12.04</td>
<td>-102.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>% Transferrin Saturation</td>
<td>Male</td>
<td>35.4</td>
<td>3.13</td>
<td>9.99</td>
<td>2.56</td>
<td>53.12</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>30.42</td>
<td>2.52</td>
<td>5.23</td>
<td>2.19</td>
<td>63.1</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

P <0.05 Significant  P>0.05 Non-significant

Table 2 showed that the Mean value of hemoglobin in male controls was 14.01±1.96 g/dl and mean value of hemoglobin in male cases was 7.05±1.15 g/dl and the t values and p values were 27.36 and 0.0001 respectively. The mean value of hemoglobin in female controls was 12.06±1.89 g/dl and mean value of hemoglobin in female cases was 6.05±1.32 g/dl and the t-values and p-values are 22.6 and 0.0001 respectively. Mean value of serum Iron in male controls was 144.54±50.32 µg/dl and in male cases was 20.23±2.36 µg/dl and the t-values and p-values are 24.73 and 0.0001 respectively. Mean value of serum Iron in female controls was 108.66±15.28 µg/dl and in female cases was 15.0±3.30 µg/dl and the t-values and p-values are 58.79 and 0.0001 respectively. Mean value of serum ferritin in male controls was 156.68±25.98 µg/L and in male cases was 9.12±1.03 µg/L and the t-values and p-values are 56.9 and 0.0001 respectively. Mean value of serum ferritin in female controls was 19.34±22.60 µg/L and in female cases was 8.0±1.14 µg/L and the t-values and p-values are 39.12 and 0.0001 respectively. Mean value of serum TIBC in male controls was 349.60 µg/dl±51.73 µg/dl and in male cases was 625.01±10.01 µg/dl and the t-values and p-values are -51.5 and 0.0001 respectively. Mean value of TIBC in female controls was 272.84±32.77 µg/dl and in female cases TIBC was 650.50±12.04 µg/dl and the t-values and p-values are -102.5 and 0.0001 respectively. Mean value of % transferrin saturation in male controls was 35.4±3.13 % and in male cases was 9.99±2.56 % and the t-values and p-values are 53.12 and 0.0001 respectively. Mean % transferrin saturation in female controls was 30.42±2.52 % and in female cases was 5.23±2.19 % and the t-values and p-values are 63.1 and 0.0001 respectively. Comparison of biochemical parameters among controls and cases in Table 2 showed that blood
hemoglobin/serum iron indices of both genders were significantly (p=<0.05). lower in anemic group.

DISCUSSION

Millions of people around the world are affected by anemia. Profound prevalence of anemia has been observed in developing countries. Anemia hampers the normal metabolism of body due to anemic hypoxia, which could have different systemic effects. Out of which one effect is on the respiratory system. Therefore, anemic subjects are not able to blow out air at its maximum capacity because respiratory efficiency deteriorates due to prolonged anemia.\(^3\)

To the best of our knowledge, there is hardly any standardized literature documented on effects of Iron deficiency anemia on dynamic ventilator tests.\(^4\) According to this study iron deficiency anemia was seen more commonly in suburbs of Gadap town.\(^5\)

In the present study, patients with IDA with low Hb levels had significantly lower PFT values (FVC 3.09±0.09, FEV\(_1\) 2.80±0.06, FEV\(_1\)/FVC ratio 0.90±0.18) in males and in females (FVC 2.40±0.59, FEV\(_1\) 2.24±0.58, FEV\(_1\)/FVC ratio 0.92±0.25) (p<0.05). Several studies have supported the current findings. A study conducted on anemic Iranian male and female healthy subjects with no history of respiratory diseases showed reduced PFT values.\(^6\)

A US based cross-sectional study revealed negative correlation between serum iron indices and FVC and FEV\(_1\), which is in contradiction to the current research. In the present study, FVC showed significant positive correlation with serum iron indices. Serum iron levels were found to be positively related with the FEV\(_1\) in a nationwide study conducted in Korea.\(^7\)

In a study conducted in Austria, the subject’s PFTs declined with reduction in concentration of serum ferritin levels\(^8\). Similar significant positive (p<0.05) association was found in the present study between serum ferritin levels and PFTs in anemic adults. Until recently no association has been found between serum TIBC levels and PFTs in anemic individuals. However, the present study demonstrated negative association between serum TIBC and FVC and FEV\(_1\) but showed significant positive association with FEV\(_1\)/FVC ratio (p<0.05).

CONCLUSION

In the present study, restrictive lung function changes were found in iron deficient anemic individuals. Whereas lung functions were normal in non-anemic healthy adults.

**Recommendations:** It is suggested that early detection and correction of IDA in patients with reduced pulmonary functions may improve health status and prevent the development of respiratory diseases.

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


Adequate Crown Preparation for Porcelain Fused to Metal Crowns Among Practitioners of Hyderabad

Aqsa1, Abdul Bari Memon2, Kashif Ali Channar1, Muhammad Rizwan Memon1, Irfan Ahmed Shaikh1 and Abdul Hayee Shaikh3

ABSTRACT

Objective: To determine the frequency of adequate crown preparation for porcelain fused to metal crowns among local practitioners.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted in clinics of private practitioners and public sector hospitals of Hyderabad city from January to August 2018.

Materials and Methods: Data was collected from dies’ of tooth prepared for porcelain fused to metal crowns; dies were collected from different clinicals. Data was collected from die trimmed the plaster models after the delivery of porcelain fused to metal crowns to patients. Dies were stabilized in wax blocks, pictures were snapped in buccal and mesial view for convergence angles measurement and tooth placed with scale for height measurement. The pictures were processed through latest version of AUTOCAD software. All the data was entered in proforma. The data was analyzed by SPSS version 22.0. Chi square test was applied for checking the statistical difference.

Results: Males were 65% and females were 35%. General practitioners were 41%, P.G students were 48% and consultants were 11%. The mean Bucco-lingual convergence angle of dies was 25.79± 9.569. Mean Mesio-distal convergence angle of dies was 20.72 ± 7.180 and mean Height of dies was 5.789 ± 2.0165. Adequate crown preparation was done by 24.2% while 75.8% have not done adequate preparation. Association of adequate preparation with practitioners showed that 8% general practitioners, 32% Postgraduates students and 54% consultants prepared crowns with adequate preparation which shows statistically significant association.

Conclusion: It was concluded that adequate crown preparation standards were followed by consultants while general practitioners need to improve their skills for making proper fixed prosthesis preparation.

Key Words: Metal ceramic, convergence angle, practitioners.

INTRODUCTION

In modern era, full coverage porcelain fused to metal crowns is one of the most common practices to treat the extensively damaged teeth. The effect of treatment and the period of lasting of treatment vary on the basis of dentist’s ability to prepare teeth1.

Though the practice of using metal crown is very common for the treatment of damaged teeth but the retention has been identified as an important issue pertaining to metal crown2. The convergence angle is considered as a combination of two opposite axial walls3,4. The appropriate convergence angle plays a significant role for the purpose of retention for the metal crowns; the chances of retention fall whenever the angle goes above certain degrees; it is said that chances of retention decline as the angle increases5,6. According to Rosenstiel SF7 the convergence angle of 4- 6º is considered ideal; whereas an angle of 6-14º is considered as acceptable though retention decreases after 6%.8 Convergence angle of as great as 12 º have been seen for clinically opposing surfaces9. It was suggested by Good acre et al that 10- 20º is the ideal ocular convergence angle. The minimal occluso-cervical dimension for 10-20 degrees occlusal convergence is thought to be 3 mm for incisors and premolars, and 4 mm for molars. Axial reduction is 0.5 mm and occlusal 1mm deep for all metals, whereas it is 1 mm for axial and 2 mm for occlusal reduction in semi translucent and metal ceramic systems10. Many devices

References

1. Liaquat University of Medical and Health Sciences Jamshoro.
2. Bibi Aseefa Dental College @ SMBBMU Larkana Sindh.
3. Senior Denta Surgeon/ Lecturer, Paramedical Institute of Sindh, Jamshoro.

Correspondence: Abdul Bari Memon. PhD Scholar (LUMHS) and Assistant Professor, Bibi Aseefa Dental College @ SMBBMU Larkana Sindh.
Contact No: 0300 2426578
Email: drabmemon@yahoo.com

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have described for achieving recommended convergence angle in dental literature but none of them showed best results or achieved widespread acceptance.

The aim of this study is to evaluate the adequate crown preparation, prepared for porcelain fused to metal crowns. By doing this study we will be able to know about tooth preparation of crowns made by local practitioners, whether they consider recommended values for porcelain fused to metal crown preparation or not.

MATERIALS AND METHODS

This Descriptive study was carried out in clinics of private practitioners and public sector hospitals of Hyderabad city from January to August 2018. Sample Selection Procedure was chosen as a convenient sampling technique. The inclusion Criteria were age of dentist from 25 to 60 years, both male and female dentist, crown preparation dies of permanent teeth, preparation done for porcelain fused to metal crowns, tooth should have enough structure for good prognosis, operator must be registered dental practitioner with at-least one-year practice experience after house job and operator must be unaware of the aim before or during the preparation. The exclusion Criteria were porous dies of prepared tooth, deformed, broken dies of prepared tooth, dies with flat or negative abutment height.

Data Collection Procedure: Informed consent was taken from operator before the execution and no special instructions were given to clinician at the time of tooth preparation that might result in biasness. Data was collected from dies’ of tooth prepared for porcelain fused to metal crowns; dies were collected from different clinics. The die was prepared by trimming the plaster models after the delivery of porcelain fused to metal crowns to patients. Pin-indexed crown prepared teeth was removed from plaster model and mounted on square-shaped rigid wax block to stabilize in a fixed vertical position on horizontal table with white background. Then, the picture was snapped in buccal and mesial view for convergence angles measurement of the tooth preparation with scale placed parallel to the height of contour for height measurement, using the Nikon D500 and tripod stand at 20 cm distance in a way that it should be perpendicular to long axis of tooth. The pictures were processed through latest version of AUTOCAD software to analyse those pictures. Buccal surface view was used for mesial and distal axial walls convergence angles and mesial surface view was used for buccal and lingual axial walls convergence angles. It was made sure that the tooth structure should not be less, shouldn’t be carious, operator should not be given any instructions, there should be no faulty impression taking and die making keeping confounding variables limited to none. All the data was recorded in proforma. The data was entered and analysed by SPSS version 16. Quantitative variables like age, CA, height are presented as mean and standard deviation. Qualitative variables like gender, appropriate crown preparation are presented as frequency and percentage. Post stratification chi square was applied for significance results by taking p vale ≤ 0.05 as significant.

RESULTS

Males were 65.0% and females were 35.0%. General practitioners were 41%, P.G students were 48% and consultants were 11%. Out of 120, dies prepared for porcelain fused to metal crowns, 52.5% were of mandibular arch and 47.5% dies were of maxillary arch. Frequency of site of arch showed as mandibular right side 21%, mandibular left side 32%, maxillary right side 20% and maxillary left side 27.5% (Table-1). In this study, mean age was 34.54± 8.55. Mean Bucco-lingual convergence angle of dies was 25.79± 9.569. Mean Mesio-distal convergence angle of dies was 20.72 ± 7.180. Mean Height of dies was 5.789 ± 0.2165 (Table-1).

### Table No.1: Descriptive statistics of gender, Practitioners, Type and site of Arch

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>78</td>
<td>65</td>
</tr>
<tr>
<td>Female</td>
<td>42</td>
<td>35</td>
</tr>
<tr>
<td>Practitioners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Practitioner</td>
<td>49</td>
<td>40.8</td>
</tr>
<tr>
<td>P.G Student</td>
<td>60</td>
<td>50.0</td>
</tr>
<tr>
<td>Consultant</td>
<td>11</td>
<td>9.2</td>
</tr>
<tr>
<td>Type of Arch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandibular</td>
<td>63</td>
<td>52.5</td>
</tr>
<tr>
<td>Maxillary</td>
<td>57</td>
<td>47.5</td>
</tr>
<tr>
<td>Site of Arch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandible Left side</td>
<td>25</td>
<td>20.8</td>
</tr>
<tr>
<td>Mandible Right side</td>
<td>38</td>
<td>31.7</td>
</tr>
<tr>
<td>Maxilla Left side</td>
<td>24</td>
<td>20.0</td>
</tr>
<tr>
<td>Maxilla Right Side</td>
<td>33</td>
<td>27.5</td>
</tr>
</tbody>
</table>

### Table No.2: Descriptive statistics of Age, Bucco-lingual, Mesio-distal convergence angle and Height of Dies

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Range</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of Participants</td>
<td>120</td>
<td>26</td>
<td>59</td>
<td>33</td>
<td>34.54</td>
<td>8.55</td>
</tr>
<tr>
<td>Bucco-lingual Convergence Angle</td>
<td>120</td>
<td>9</td>
<td>50</td>
<td>41</td>
<td>25.79</td>
<td>9.59</td>
</tr>
<tr>
<td>Mesio-distal Convergence Angle</td>
<td>120</td>
<td>8</td>
<td>40</td>
<td>32</td>
<td>20.72</td>
<td>7.18</td>
</tr>
<tr>
<td>Height of Prepared tooth</td>
<td>120</td>
<td>2</td>
<td>11</td>
<td>9</td>
<td>5.78</td>
<td>2.01</td>
</tr>
</tbody>
</table>
Table No.3: Association of adequate preparation with practitioners

<table>
<thead>
<tr>
<th>Operator qualification</th>
<th>Adequate preparation</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>General practitioner</td>
<td>4</td>
<td>45</td>
<td>49</td>
</tr>
<tr>
<td>P.g student</td>
<td>19</td>
<td>41</td>
<td>60</td>
</tr>
<tr>
<td>Consultant</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>91</td>
<td>120</td>
</tr>
</tbody>
</table>

Adequate crown preparation was done by 24.2% while 75.8% have not done adequate preparation as shown in (Figure-1).

In this study, the dies for central incisors were 24%, lateral incisors were 8%, canines were 12%, first premolars were 12%, second premolars were 11%, first molars were 23% and second molars were 9% (Figure-2).

DISCUSSION

Porcelain fused to metals crowns are usually practiced as treatment of partially or fully damaged teeth. The success of such treatment depends on the ability and skills of practitioner\textsuperscript{12-14}. According to the results obtained in this study, the percentage of convergence angles and adequate preparation was done by 24% which are in agreement with El-Mubarak et al\textsuperscript{15}, and not in agreement with Ow et al\textsuperscript{16}, the possible explanation could be lack of experience, limited access, visual error and anatomical variation.

In this study, the average convergence angles i.e mesio-distal 20.72 and bucco-lingual 25.79 of groups observed were considerably greater than the recommended ones. These results are in agreement with the studies conducted by Ayad MF et al\textsuperscript{17} who have reported mean convergence angles of 19.2 mesiodistally and 23.0 bucco-lingually on vital teeth. The observed higher mean convergence angles could be due to the minimal clinical experience of the local practitioner and lack of skills.

Goodacre et al\textsuperscript{10} who regarded 10-20º as acceptable clinical range, and were even higher than what was recorded from other studies, however in this study majority of general practitioner and postgraduate students did not made crowns with adequate preparation. The crown preparation has been evaluated by several investigators to see how much it is far from the ideal. Such type of studies are done by professional students of dentistry\textsuperscript{18-20}, teaching staff\textsuperscript{21}, general practitioners\textsuperscript{8,20,22}, residents\textsuperscript{18}, and prosthodontists\textsuperscript{20,22} and the results obtained have been different. The probable reason for the same could be that the general dentists and postgraduate trainees had minimal short clinical experiences.

The height of prepared dies showed mean score than the previous studies measuring preparation height which cannot be compared because the definition of height has not been adequately addressed\textsuperscript{23,24}. In this study, post graduate students have prepared the crowns more adequately than general practitioner, this is in agreement with study results of Safa Hinnara et al\textsuperscript{25} the difference cannot be considered tangible. The GPs had recorded the highest total occlusal convergence (TOC) values. The available literature is also in support of this study in terms of adequate crown preparation values which are rarely achieved in dental practice, are in agreement with Ghafoor R et al\textsuperscript{10}, Patel PB et al\textsuperscript{26} and Nordlander J et al\textsuperscript{27}. The clinical researches spanning longer duration are required to assess the influence of
TOC on the longevity of fixed prosthodontics. The values of TOC obtained in laboratory studies were smaller as compared to the clinical studies.\textsuperscript{28,29} The appropriate TOC is essential for proper tooth preparation because it can affect the overall acceptability during crown preparation. Recommendations have been made for optimal axial wall taper of tooth preparations for fixed prosthodontics to prevent undercuts, compensate for inaccuracies in fabrication, and permit more complete seating during cementation.\textsuperscript{30,31} Every tooth is different according to shape and angles that is why no tooth should be subjected to the same recommended values. Each tooth needs to be prepared according to its own clinically recommended value for better retention of crowns.

CONCLUSION

It was concluded that adequate crown preparation standards were followed by consultants while general practitioners need to improve their skills for making proper fixed prosthesis preparation. Further clinical studies spanning longer duration with sufficient sample size are necessary to assess the longevity of fixed prosthesis, to assess the influence of less/more than ideal taper on the success of these restorations and to test all the parameters like height, width, convergence angle, line angles together and to test how they influence each other and the resulting survival of the crown.

Author’s Contribution:

Concept & Design of Study: Aqsa Abdul Bari Memon, Kashif Ali Channar

Drafting: Muhammad Rizwan Memon, Irfan Ahmed Shaikh, Abdul Hayee Shaikh

Data Analysis: Aqsa, Abdul Bari Memon

Revisiting Critically: Aqsa, Abdul Bari Memon

Final Approval of version: Aqsa, Abdul Bari Memon

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

REFERENCES

18. Dorriz H, Nokar S, Baghai Naini R, Madadi A. The convergence angle of full-coverage crown
Objective: To study the association of clinical features & comorbidity among Covid-19 patients admitted in tertiary care hospital.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the ABWA hospital and research center attached with Abwa Medical College, Faisalabad for the period of four months from April to July, 2020.

Materials and Methods: Total 142 admitted Covid-19 patients were selected as participants to assess the range of symptoms experienced during active phase of infection.

Results: Out of total 142 participants, 87.3%(n=124) complaint of shortness of breath, 57.7%(n=82) had fever & 43.3%(n=62) had cough, 27.5%(n=39) reported of body aches as compared to 14.1%(n=20) who had loose motions & 3.5%(n=5) who experienced irritability. Regarding comorbidity, 49.3%(n=70) patients had Diabetes Mellitus, 33.1%(n=47) Hypertension, 10.6%(n=15) Ischemic heart disease & 2.8%(n=4) had Chronic kidney disease.

Conclusion: During the pandemic of corona infection, majority of the symptomatic patients admitted in hospital had pre-existing health issues i.e. Diabetes, Hypertension, Renal diseases & respiratory involvement. Moreover, the concurrence of Covid-19 infection with medical syndrome serve as a vital prognosis factor linked with complications with multi organ involvement, unexpected outcome & longer hospital stay. This implies that health care emergency services should be formulated and implemented in a way where supervised intensive care should be provided to the most vulnerable group. Moreover, extensive awareness campaigns should be carried out to identify the group at risk of mortality.

Key Words: Clinical features, Comorbidity, Covid-19, Diabetes, Hypertension, Kidney disease, Ischemic Heart disease.


INTRODUCTION

Since two decades, the public health system is continually challenged by contagious viral infections which have rendered the dire need to upgrade the current healthcare system at international level in context of prevention and management of epidemics.

Currently, in the beginning of 2020, 2019-nCoV is declared by World Health Organization as a serious respiratory infection keeping in view the highly contagious nature and uncontrolled fatality rate with high probability. A shocking feature of cross specie spread from animals to human serve as a bitter evidence based reality not to be easily swallowed. As with SARS & MERS, Corona infection was expected to be same in intensity demonstrating wide but typical range of symptoms of common cold to pneumonia. Covid-19 virus is spread via respiratory droplets and direct contact from patients. Although 50% of the patients remain asymptomatic while the rest of 30% present with complications with multi organ involvement.

Regarding immunology, in response to viral attack, the human body activates the process of innate immunity as a 1st defense mechanism where interferon I/III, IL-6, IL-18 & TNF proliferates and gathers. In exponential phase of Covid-19 infection, it inhibits interferon which stimulates immune response by ceasing the signaling genes of infected cells ascertained by diminished levels of cytokines, tumor necrotic factor & interferon.
An interesting myeloid response has been postulated in context of its deregulatory mucosal cell response which renders the covid-19 virus to attack and produce serious complications such as ARDS, disseminated intravascular coagulation DIC & cytokine release syndrome 4. Being highly contagious in nature, the Covid-19 infection in its mild and asymptomatic form poses a danger of wide transmission as well as the difficulty to facilitate screening. No predictive factor has been identified for detection of asymptomatic patients although younger age group is expected to lie in this group 5.

Covid-19 syndrome is found to be similar to SARS-CoV in context of transmission, pathogenicity& nature of wide symptoms. However, in genome sequencing COVID-19 linked sequence identity is comparatively upgraded when studied with MERS CoV & SARS CoV1ab polyprotein and surface glycoprotein or S-protein are the postulated regions of genomes which are altered in covid-19 virus as compared to MERS CoV SARS CoV 6. With an incubation period of 14 days, median days of 4 to 5, is the gap between exposure and onset of symptoms of COVID-19 infection which produces common cold symptoms like fever, body aches, generalized fatigability, cough, sore throat, rhinorrhea, sneezing, difficulty in breathing & headache. However, a plethora of other non-respiratory symptoms have been reported during this COVID-19 pandemic.

For diagnosis of covid-19 infection, real time PCR serves as a vital diagnostic tool by achieving expectorated nasal, tracheal &Brongo alveolar secretion sampling (WHO recommends both upper and lower respiratory tract sample collection) as well as computed tomography of chest (CT SCAN) is used for diagnostic and prognostic tools 7.

In management of COVID-19 infection, efficient measures include quarantine to prevent spread of disease, oxygen therapy and symptomatic relief. However, antibiotics are added to the regime with acetaminophen and cold sponging to control fever. Patients with severe respiratory disease & septicemia require intravenous steroids, high flow oxygen, nutritional supplements, vasopressors, anticoagulants, ventilatory support, hemodynamic & plasma transfusion. The progress of vaccine development against covid-19 virus has been under process. To prevent against rapid spread the only solution seems fruitful is isolation of patient with distant avoidance of contact with family members and even healthcare workers along with the judicious use of alcohol based hand sanitizers, surface bleach, N95 face masks & hand gloves. Evidence based community control programmes have been implemented globally under the guidance of WHO to control the transmission of infection 8.

MATERIALS AND METHODS

During a pandemic of corona virus infection, 142 patients of Covid-19 were admitted in Abwa hospital & research center, Faisalablad. With the permission from ethical review committee, the record of Covid-19 confirmed cases were collected. The medical records of hospitalized patients were included in this study irrespective of comorbidity and severity. Patients already diagnosed with Diabetes Mellitus, hypertension, ischemic heart disease, chronic kidney disease, chronic liver disease, cerebral stroke & bronchial asthma were also included. Covid-19 patients with pregnancy were excluded. The patients with stay of more than 24 hours and long admission were included. We analyzed reported symptoms, including shortness of breath, fever, cough, body aches, diarrhea, vomiting & irritability as well as co-morbidities. The data entered and analyzed using SPSS version 20. For the purpose of analysis, participants were divided in two groups, those who were covid-19 patients along with comorbidity & others without any comorbidity. Pearson Chi Square test and Fisher’s Exact Test were used to evaluate associations between various qualitative variables of interest. For all purposes, p-value of <0.05 was considered statistically significant. Categorical variables were expressed as number (%) and compared by $\chi^2$ test.

RESULTS

Total 142 Covid-19 patients admitted in Abwa hospital and research centre, Faisalablad.

Table No.1: Demographic characteristics of study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (%)</th>
<th>n= 142</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± s.d)</td>
<td>55.57±13.6</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>108(76.1)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>34(23.9)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay days (mean ± s.d)</td>
<td>5.17±4.97</td>
<td></td>
</tr>
<tr>
<td>Recovery time(mean ± s.d)</td>
<td>4.96±4.96</td>
<td></td>
</tr>
<tr>
<td>Comorbidty</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>47(33.1)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>70(49.3)</td>
<td></td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>15(10.6)</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>4(2.8)</td>
<td></td>
</tr>
<tr>
<td>Others (hcv, asthma, thyroid disease, cld, cva)</td>
<td>7(4.9)</td>
<td></td>
</tr>
<tr>
<td>Patient status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recovered</td>
<td>108(76.1)</td>
<td></td>
</tr>
<tr>
<td>Expired</td>
<td>34(23.9)</td>
<td></td>
</tr>
<tr>
<td>Patients with covid-19 symptoms</td>
<td>140(98.6)</td>
<td></td>
</tr>
</tbody>
</table>

*Descriptive statistics. Values are reported as n (%).
The mean age of participants was (55.57± 13.6) whereas 76.1% patients were male & 23.9% females. The average stay of Covid-19 patients at hospital was (5.17±4.97) days and mean recovery duration was (4.96±4.96) days as shown in Table-1. The most striking comorbidity in our study was Diabetes Mellitus present in 49.3% admitted patients followed by 33.1% & 10.6% cases diagnosed of Hypertension & Ischemic heart disease respectively. Only 2.8% were consulting for chronic kidney disease & 4.2% belonged to a minor group (Bronchial asthma, HCV, Thyroid disease, CLD, Cerebrovascular disease). Moreover, 76.1% patients recovered from corona infection as compared to 23.9% who could not survive during their stay at hospital. Amongst Covid-19 patients who expired due to complications during hospital stay, 79.4% had a single or multiple physical illnesses concurrent with Covid-19 infection.

Out of 142 participants, the majority reported various clinical symptoms at presentation and during treatment in the corona ward whereas only 1.4% (n=2) hospitalized patients were asymptomatic. In the context of symptomatology, 87.3% (n=124) patients presented with shortness of breath, 57.7% (n=82) had fever & 43.3% (n=62) had cough. Similarly, 27.5% (n=39) Covid-19 hospitalized patients reported of body aches, as compared to 14.1% (n=20) who had loose motions & 3.5% (n=5) who experienced irritability. A minority of patients, 2.8% (n=4) experienced hemoptyis, vomiting, loss of taste and hiccups singly.

Table No.2: Commonly reported symptoms in COVID-19 patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shortness of breath</td>
<td>124(87.3)</td>
</tr>
<tr>
<td>Fever</td>
<td>82(57.7)</td>
</tr>
<tr>
<td>Cough</td>
<td>62(43.7)</td>
</tr>
<tr>
<td>Body ache</td>
<td>39(27.5)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20(14.1)</td>
</tr>
<tr>
<td>Irritability</td>
<td>5(3.5)</td>
</tr>
<tr>
<td>Hiccups</td>
<td>1(0.7)</td>
</tr>
<tr>
<td>Vomiting &amp; hemoptyis</td>
<td>2(1.4)</td>
</tr>
<tr>
<td>Loss of taste</td>
<td>1(0.7)</td>
</tr>
</tbody>
</table>

*Descriptive statistics. Values are reported as frequency (%).

In view of table-3, Amongst hospitalized covid-19 patients, 68.3% (n=97) had already diagnosed medical diseases, in contrast to 45% of patients who had no other physical illness at the time of corona infection, 31.1% (n=14) of covid-19 patients without comorbid disease detained in management ward for less than 24 hours whereas 68.9% (n=31) remained under hospital’s supervised treatment. Similarly, amongst the other group of participants of covid-19 disease along with comorbid medical condition, 88.7% (n=86) preferred to stay at hospital.

Table No.3: hospitalization of covid-19 patients vs. Covid-19 + comorbidity patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hospitalization</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>Less than 24 hours</td>
</tr>
<tr>
<td>Covid-19</td>
<td>31(68.9)</td>
<td>14(31.1)</td>
</tr>
<tr>
<td>Covid-19 + comorbidity</td>
<td>86(88.7)</td>
<td>11(11.3)</td>
</tr>
</tbody>
</table>

Values are expressed as frequency (%). Chi square test: *p < 0.05

DISCUSSION

Severity of covid-19 disease along with the deteriorating course of infection has been associated with presence of various medical diseases. The chance of contracting an infection is greater in those having medical/psychiatric illness. The current study showed the greater number of COVID-19 patients with other medical diseases; hospitalized in a greater number as compared to those who are not previously diagnosed with other illnesses. A recent meta-analysis in early 2020 shows that the most common co-morbidities elucidated in these patients of corona infection were Hypertension (15.8%), Cardiovascular disease (11.7%) and Diabetes mellitus (9.4%). Another study in Wuhan, China identified Diabetes 20%, Hypertension 15%, and Cardiovascular disease 15% along with the corona infection in hospitalized patients. However, this study reports that Diabetes Mellitus (49.3%) surprisingly predominates in participants in context of co-morbidities followed by Hypertension (33%) and Ischemic heart disease (10%) where longer hospital stays and willingness for immediate seeking for medical treatment were prominent.

As compared to milder cases of corona infection, those who are hospitalized are mostly symptomatic presenting with complaints of fever, cough and dyspnea. One study reports fever as core symptom in majority of hospitalized patients. Atypical symptomatology has been observed in high risk group which comprises of older age, immune compromised & comorbid medical illness. In contrast, in the context of symptomatology, this study identifies frequency of various clinical complaints experienced by hospitalized covid-19 patients where dyspnea stands out remarkably in 87.3%, fever 57.7% & cough in 43.7% of participants. Following this, diarrhea and irritability has been reported by 14.1% & 27.5% of participant’s respectively. A multicenter study on gastroenterological symptoms of covid-19 disease shows that myalgia, anosmia, nausea, gastric discomfort, diarrhea & vomiting are considered to be symptoms suggested of mild disease which are experienced usually prior to development of fever.
Although it was believed that the prognostic factors of Covid-19 infection are yet to be ascertained, a study was conducted during the early phase of pandemic in Changsha in 2020 where a high risk group is identified as of old age, with comorbid medical illness, bilateral lung involvement, decrease in white cell count and raised C-Reactive protein highlighting as the predictors of complications. According to the recent multivariate study carried out in Henan, certain symptoms serve as prognostic tools related to outcome of covid-19 disease in which Fever was reported by 92% of covid-19 patients but its predictability of outcome is unascertained. Although shortness of breath & cough was recognized to be associated with disease severity.12,13

Another study on healthcare workers showed 97% of negative assay results of covid-19 tested were either asymptomatic or only complain of sore throat, where higher viral load was detected in those having high grade fever and myalgia. Presentation of symptoms and their severity was considered to be a useful predictive measure of PCR result and prognosis.14

As Atypical symptoms are surprisingly common in Covid-19 infection, Helm and colleagues suggested that 69% of severely ill Covid-19 patients have irritability linked to CNS invasion of Covid-19 virus by generating a cascade of hyper activation of cytokine response leading to multiple organ failure specifically targeting brain and lung parenchyma.15 The findings of our study are consistent with those of recently published research work in terms of the similarity of co-morbidities among hospitalized patients of Corona Virus disease. However, hypertension and coronary heart diseases remained the most common category of comorbidity.16-19 The older patients with diabetes mellitus, hypertension, ischemic heart disease, and chronic kidney disease; had poor prognosis correlating with outcomes of several studies.20,23 The male predominance belonging to the mean age i.e. 55.57 ± 13.6 observed in our study also congruous with the results of a local research conducted by Asghar et al.24 Confirmed cases of corona virus disease, having any comorbidity end up with poorer clinical outcomes and the greater number of patients with co-morbidities also correlated with poorer clinical outcomes.25

CONCLUSION

There is significant association between comorbidity and COVID-19 where severity of infection and comparatively delayed recovery is associated. Similarly, presence of medical illness & severe symptoms experienced by COVID-19 patients also serve as important prognostic factors. Healthcare system should be devised effectively to screen high risk group & provide early intervention to prevent its transmission to masses.

REFERENCE


Prevalence of Placenta Previa and its Risk Factors in Pregnant Women Attending Tertiary Care Hospital
Afra Aman¹, Dawood Misbah², Mehwish Syed¹, Laiyla Shinwari³, Rabia Nawaz⁴ and Muhammad Umer Farooq²

ABSTRACT

Objective: The aim of this study is to determine the incidence of placenta previa along with its risk factors in Gynecology/obstetrics unit of Ayub teaching hospital, Abbottabad.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Obstetrics department ATH, Abbottabad, KPK from November 2018 to November 2019.

Materials and Methods: All pregnant women having POG ≥ 28 weeks were included in the study; those unsure of dates or diagnosed with eclampsia were excluded. Sample size was 426 and data was analyzed using SPSS version 23. A p-value of ≤ 0.05 was considered statistically significant for association between categorical variables.

Results: The frequency of placenta previa was found to be 6.3%. The mean age was 26.33 ± 5.36 years. Mean parity was 1.44±1.57 and mean gravida was 2.92±2.13. 22.2% of the pregnant women with placenta previa had a history of previously diagnosed placenta previa (p-value=0.047). 33.3% of patients diagnosed with placenta previa had a history of abortion (p-value=0.51). 55.6% of the patients diagnosed with placenta previa were grand multigravida followed by multigravida (44.4%) whereas there were no primigravida (p-value=0.01). 77.8% of the patients diagnosed with placenta previa were multiparous followed by primiparous (22.2%), whereas there were no nulliparous women patients (p-value=0.029).

Conclusion: The frequency of placenta previa was 6.3% which is abnormally high. History of previous placenta previa, gravida and parity were found to be major risk factors for placenta previa. History of previous caesarean section and age were also associated with placenta previa but were statistically insignificant.

Key Words: Placenta previa, previous caesarean section

INTRODUCTION

Placenta previa is an obstetrical emergency which usually occurs in 2nd and 3rd trimester of pregnancy. In this condition the placenta abnormally lies lower and near the cervical os. It poses a serious threat to the health of mother as well as the baby and is associated with an increased maternal morbidity and mortality.¹

¹. Department of Gynae and Obstet, Ayub Teaching Hospital, Abbottabad, KPK.
². Medical Officer, Ayub Teaching Hospital, Abbottabad, KPK.
³. Department of Gynae and Obstet, Govt. Maternity Hospital, Peshawar
⁴. District Gynecologist, Tehsil Hospital Headquarters Dargai

Correspondence: Afra Aman, Senior Registrar, Ayub Teaching Hospital, Abbottabad, KPK
Contact No: 0333-9199151
Email: afrahanman19@gmail.com

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Therefore, knowing its occurrence and major risk factor in a developing country like Pakistan is very important. The incidence of placenta previa has been variously reported to range from 0.1% to 0.5%.² In Pakistan, the frequency of placenta previa has been reported to be in between 0.51-3.5%.³ The maternal mortality rate secondary to placenta previa is 0.03%. The incidence of placenta previa increases with previous cesarean section i.e. 1.87% with previous one cesarean section, 2.4% for two cesarean section, 2.8% for three and 10% for four or more cesarean sections.⁴

The etiology still remains controversial, but the generally accepted theories revolve around endometrial and myometrial damage along with genetic abnormalities. Blastocyst completely embeds in the endometrium in a normal pregnancy, failure of proper vascularization of endometrium, delayed ovulation and previous trauma to endometrium due to any cause increases probability for placenta previa.⁵,⁶

The risk factors for placenta previa are smoking, previous cesarean sections, advanced maternal age, multiparity and conception by in vitro fertilization (IVF), previous abortion and placenta previa in a previous pregnancy.⁷,⁸,⁹,¹⁰,¹¹
substance abuse among mothers is also associated with placenta previa. The usual presentation of placenta previa is painless bright red vaginal bleeding most in late 2nd trimester or 3rd trimester. As the uterus grows, it, sometimes resolves. However, the more it remain over the cervix-os, less chances are there for its resolving. Its diagnosis is confirmed through an ultrasound (USG) and sometimes is discovered incidentally in an operation. 12,13

The most profound maternal risks associated with placenta previa are anesthesis and surgical complications, postpartum sepsis and placenta accrete. post-partum heavy bleeding deteriorates mother health instantly and results in increased mortality. Placenta previa increases the risk of neonatal mortality by 3 times which is primarily due to preterm birth of the baby. Perinatal mortality is currently 4-8%, due to consequences of prematurity.

Fetal and neonatal complications associated with placenta previa are congenital anomalies, respiratory distress syndrome, still birth and anemia.14 Availability of blood transfusion can significantly reduce the maternal morbidity and mortality as all complications are a sequel of blood loss, better neonatal intensive care (NICU) can reduce the perinatal mortality and morbidity. Early diagnosis by antenatal USG even before the first episode of bleeding can be significant in deciding the fate of mother and child. Once the condition is diagnosed, the case should be carefully managed and all steps required should be taken to treat the complications associated with such cases.15,16

Occurrence of placenta previa in Northern areas of Pakistan is not yet studied. Moreover, finding its incidence and major risk factor is sought important. Therefore, this study aims to determine the incidence of placenta previa along with its risk factors in Gynecology/obstetrics unit of Ayub Teaching Hospital, Abbottabad.

MATERIALS AND METHODS

This is a cross-sectional study carried out on pregnant women in gynaecology/obstetrics department Ayub Teaching Hospital, Abbottabad for 1-year i.e. November 2018 to November 2019. All pregnant women having gestational period≥ 28 weeks were included in the study. Those unsure of dates or diagnosed with eclampsia were excluded. Sample size was 426 and sampling technique was non-probability convenient sampling. Data was recorded on a structured self-made questionnaire. Participants were informed about the purpose of study and they were assuring for confidentiality of their data. Informed consent was obtained from all the women included in the study. The study was approved from the mother institutional review board. Data was analyzed using SPSS version 23. Continuous variables were measured by mean and standard deviation whereas categorical were presented as frequencies and percentages in tables. Chi square test was applied for finding a significant relation between placenta previa and other independent variables. A p-value of ≤ 0.05 was considered statistically significant for association between categorical variables.

RESULTS

Total 426 pregnant women with mean age of 26.33 ± 5.368years and mean gestational age 36.87±3.120weeks participated in current study. Majority of the women were multigravida (n=216, (50.7%), 168 (39.4%) were multiparous and 123(28.9%) women (28.9%) had a history of abortion. Table 1.

Table No.1: Demographic variables of participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.33 ± 5.368</td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>36.87±3.120</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
</tr>
<tr>
<td>Primigravida</td>
<td>126 (29.6%)</td>
</tr>
<tr>
<td>Multigravida</td>
<td>216(50.7%)</td>
</tr>
<tr>
<td>Grand Multigravida</td>
<td>84 (19.7%)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>153(35.9%)</td>
</tr>
<tr>
<td>Primiparous</td>
<td>105(24.6%)</td>
</tr>
<tr>
<td>Multiparous</td>
<td>168 (39.4%)</td>
</tr>
<tr>
<td>History of Abortion</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>123 (28.9%)</td>
</tr>
<tr>
<td>Placenta Previa</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (6.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Status of Placenta Previa</th>
<th>Total (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous Caesarean Section</td>
<td>Yes</td>
<td>18 (66.7)</td>
<td>150 (37.6)</td>
</tr>
<tr>
<td>No</td>
<td>9 (33.3)</td>
<td>249 (62.4)</td>
<td>258 (60.60)</td>
</tr>
<tr>
<td>Previously diagnosed Placenta Previa</td>
<td>Yes</td>
<td>6 (22.2)</td>
<td>12 (3)</td>
</tr>
<tr>
<td>No</td>
<td>21 (77.8)</td>
<td>387 (97)</td>
<td>408 (95.88)</td>
</tr>
<tr>
<td>History of Abortion</td>
<td>Yes</td>
<td>9 (33.3)</td>
<td>114 (28.6)</td>
</tr>
<tr>
<td>No</td>
<td>18 (66.7)</td>
<td>285 (71.4)</td>
<td>303 (71.1)</td>
</tr>
<tr>
<td>Categories of Gravida</td>
<td>Primigravida (%)</td>
<td>0 (0)</td>
<td>126 (31.6)</td>
</tr>
<tr>
<td>Multigravida (%)</td>
<td>12 (44.4)</td>
<td>204 (51.1)</td>
<td>216 (50.7)</td>
</tr>
<tr>
<td>Grand Multigravida (%)</td>
<td>15 (55.6)</td>
<td>69 (17.3)</td>
<td>28 (19.7)</td>
</tr>
<tr>
<td>Category of Parity</td>
<td>Nulliparous (%)</td>
<td>0 (0)</td>
<td>153 (38.3)</td>
</tr>
<tr>
<td>Primiparous (%)</td>
<td>6 (22.2)</td>
<td>99 (24.8)</td>
<td>105 (24.6)</td>
</tr>
<tr>
<td>Multiparous (%)</td>
<td>21 (77.8)</td>
<td>147 (36.8)</td>
<td>168 (39.4)</td>
</tr>
<tr>
<td>Total</td>
<td>27 (100)</td>
<td>390 (100)</td>
<td>426 (100)</td>
</tr>
</tbody>
</table>
Among 27 (6.3%) who had placenta previa, 18 (66.7%) of the patients had a history of previous Cesarean section. 6(22.2%) had a history of previously diagnosed placenta previa. The former had insignificant p-value of 0.086 while the later shows significant relation with previous history of placenta previa, p=0.047. Only 9(33.3%) women of placenta previa had history of abortion with insignificant p value, 0.51. However, 15 (55.6%) grand multigravida and 21(77.7%) multiparous women show cases of placenta previa with significant relation, p=0.010 and 0.029 respectively Table 2.

DISCUSSION

This study focused to find the frequency of placenta previa and its association with obstetric variables. This way, it gave a good insight into occurrence of placenta previa in developing country like Pakistan especially in Northern-Hilly areas. The frequency of placenta previa was found to be 6.3% which is higher as compared to other studies conducted previously. In Nigeria, it was found to be 2%, in Tanzania it was 0.6% and in Iran 0.7%. This could be due to difference in demographic factors.

In our study 66.7% of the patients diagnosed with placenta previa had history of previous Cesarean section. This is in conjunction with previous studies in which it was found to be 56.5%, 58.1% and 61.7% respectively. However the association was statistically insignificant in our study (p value=0.086). In our study, 22.2% of the pregnant women with placenta previa, had a history of previously diagnosed placenta previa. This is in approximate conjunction with a study conducted in Saudi Arabia (KSA) in which it was found to be 26.1%. The p-value was also significant with a value of 0.047. Hence history of previous placenta previa can be regarded as a risk factor for placenta previa. In current study, 33.3% of patients diagnosed with placenta previa had history of abortion which is higher as compared to those who did not have placenta previa (28.6%). In a study conducted in Croatia, it was found to be 45.5% in patients with placenta previa and 23% who did not have placenta previa. However, our association was found to be statistically insignificant (p-value=0.51).

Majority of the patients (55.6%) diagnosed with placenta previa were grand multigravida followed by multigravida (44.4%). However, there were no primigravida. This is comparable to a study conducted in Pakistan in which majority of the patients were grand multigravida (58.7%) followed by multigravida (36.8), and no primigravida (0%). The association was found to be statistically significant (p value=0.01). Hence, gravida of patient can be regarded as an important risk factor for placenta previa.

According to our study majority of the patients (77.8%) diagnosed with placenta previa were multiparous followed by primiparous (22.2%). Whereas there were no nulliparous women with placenta previa. This is in conjunction to several studies conducted internationally in which the frequency of placenta previa increases with increasing parity. Our results were statistically significant with a p-value of 0.029. Thus, parity of patient can be regarded as an important risk factor for placenta previa in our setting.

CONCLUSION

The frequency of placenta previa was 6.3% which is abnormally high. History of previous placenta previa, gravida and parity were found to be major risk factors for placenta previa. History of previous cesarean section and age were also associated with placenta previa but were statistically insignificant.

Recommendations: MCHC should be improved with proper awareness among women of the region. Family planning should be promoted. Mothers with more than one risk factor for placenta previa should be counselled.

REFERENCES

Immediate Induction Versus Delayed Induction of Labour in term Prelabour Rupture of Membrane: Let’s Find a Solution to Eliminate the Controversy & Reduce the Cesarian Births

Musarat Akhter, Salma Jabeen, Saeqah Manzoor, Nergis Taj Obgy, Farzana Razaque and Shazia Siddique

ABSTRACT

Objective: To compare the outcome in terms of delivery within 24 hours of induction of labour of immediate induction versus delayed induction of labour in term Pre-labour rupture of membrane.

Study Design: Randomized controlled trial

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Civil Hospital, Bahawalpur from November 2018 to April 2019.

Materials and Methods: 154 women at term (gestational age ≥37 weeks) were enrolled. All with premature rupture of membrane, & of between 18-40 years of age. They were divided in 2 equal batches (A&B). Patients with multiple pregnancy, fetal weight more than 4 kgs, uncontrolled diabetes mellitus and h/o uterine surgery were excluded. Labour induction was carried out after 6 hours and after 24 hours of presentation in group A and B patients respectively. Outcome was measured in both groups in term of delivery within 24 hours of induction of labour.

Results: The average age of participants in batch A was 27.77 ± 3.14 years and in batch B was 28.09 ± 3.38 years. The mean found for gestational age was 39.01 ± 1.31 weeks. The mean parity in batch A & batch B was 2. Satisfactory outcome in batch A (immediate induction) was seen in 68 (88.31%) while in Group B (delayed induction) was seen in 54 (70.13%) patients (p-value = 0.005).

Conclusion: This study concluded that outcome of immediate induction is better as compared to delayed induction in term, pre-labour rupture of membrane (PROM).

Key Words: Pre-labour rupture of membrane, PGE1, immediate induction, vaginal delivery, delayed induction.


INTRODUCTION

The overall incidence of Membrane rupture before the start of uterine contractions is around 20% and it doubles in cases of premature births\(^1\). At term, immediate delivery results in a lower complication rate along with greater maternal satisfaction, in contrast to expectant management without conferring additional risks to newborns\(^2\).

4 out of 5 pregnant presenting with PROM at term go into labour in first 24 hrs with majority (upto 95%) in next 72 hrs while choosing expectant management\(^3\). However, continuing expectant management comes at the cost of neonatal and maternal morbidity due to infection\(^4\), thus it’s better to choose induction in these to reduce prolong latency period.

There is still debate about the definitive management of PROM. As the time lapse between ROM and uterine contractions increases, so does the likelihood of rise in infective morbidity for mothers leading to increased operative deliveries\(^5\). Therefore, some health professionals advised that labour should be stimulated (by Oxytocin or Prostaglandin E1) at term after 6 hours of PROM, if woman does not go into spontaneous labour. Both Oxytocin and prostaglandin E1 are effective & safe in inducing labor in women with PROM at term\(^6,7\). Timing of induction is controversial. Some obstetricians are of opinion, that waiting for spontaneous onset of labour is preferable, if there is no indication of compromise (fetal or maternal), so the risk
of abdominal deliveries may be lower. A study comparing early vs delayed induction of labour (IOL) in PROM at term showed a remarkable reduction in rate of cesarean section in favor of early IOL (12% vs 28%). Without any significant difference in Apgar scores of newborns at 1 & 5 min. Another study has summarized that immediate induction of labour is more beneficial when compared with expectant management in terms of reduction in the length of latent period without any rise in abdominal deliveries. Zamzami T.Y.Y & co-workers, showed contradictory evidence that hands off strategy for managing cases of PROM at term has the advantage of high number of vaginal births without feto-maternal compromise. As the timing of labour induction is very important for better outcome and previous studies have shown argumentative results. So in order to reevaluate we carried out a research to compare the outcome of immediate induction versus delayed labour induction in cases of PROM at term. This study will not only help to resolve the controversy but will also provide the local stats & to find more suitable time for induction of labour in females with term PROM in order to reduce the caesarean rates and maternal morbidity.

MATERIALS AND METHODS

This was a Randomized controlled trial conducted at Gynecology & Obstetrics Department of, Civil Hospital, Bahawalpur. The duration of this research was 6 months (1st November 2018 to 30th April 2019). The women fulfilling the following inclusion criteria were selected: confirmed premature rupture of membrane at term (gestational age >37 weeks by LMP/first trimester USG), having singleton viable pregnancy of cephalic presentation. The age of patients ranged from 18-40 years and parity 0-5. The patients having multiple pregnancy, cephalo-pelvic disproportion, estimated fetal weight more than 4 kg were excluded from study. The women with ante partum hemorrhage, S/S of chorioamnionitis, fetal distress, history of previous uterine surgery, & pregnancy with medical disorders were also not included.

The technique used was non-probability, consecutive sampling to take sample. 154 patients in total were registered in study with 5% level of significance. After approval from ethical review committee, total 154 women fulfilling the inclusion criteria were selected after being admitted in department of Obstetrics & Gynecology, Civil Hospital, Bahawalpur. Informed consent in written was taken from each patient. The patients, who were selected were divided randomly into 2 equal batches (77 in each) i.e. batch A (immediate induction) & batch B (delayed induction) by lottery method. All selected participants were given a chance to choose a slip from total pool of slips (1/2 slips with letter ‘A’ & half-slips with letter ‘B’) and they were placed in their respective batches. In both batches bishop score was assessed. In batch A patient, IOL was done within 6 hours of presentation by giving 50 µg sublingual PGE1. The dose was repeated after 4 hours if bishop score found to be poor & uterine contractions were <2, contractions/10 minutes. If patient did not enter in active labour after 2 doses of PGE1, oxytocin infusion dose of 2-32mIU/minutes was started after the last dose of PGE1 via infusion pump. In batch B patients, induction of labour was done after 24 hours of presentation by following same regimen as used for batch A. Outcome was measured in both batches in terms of vaginal delivery within 24-hours after labour induction, & labelled as satisfactory: If vaginal delivery was occurred within 24 hours of induction otherwise taken as unsatisfactory.

All patients given i/v antibiotics, vaginal swab sent for culture & sensitivity & labours were monitored by maintaining partograph. This all data including the demographic data (age, BMI) was entered on a proforma.

Data Analysis: SPSS version 20.0 was used to enter and analyze all the information obtained. Age, gestational age, height, weight and BMI were calculated as mean & standard deviation. Parity & outcome (satisfactory/unsatisfactory) were mentioned as frequency & percentage. Chi square, was applied to compare the outcome of both batches and p-value ≤ 0.05 was labelled as significant. Effect modifiers like parity, age, gestational age and BMI were managed through stratification. To see their effects on out-come, Post-stratification chi square was used. P-value ≤ 0.05 was considered as significant.

RESULTS

Age range observed in this research was from 18 to 40 years, with mean age of 27.93 ± 3.41 years. The mean age of participants in batch A was 27.77 ± 3.14 years & in batch B was 28.09 ± 3.38 years, as shown in Table I. The mean gestational age calculated was 39.01 ± 1.31 weeks, (in batch A was 39.10 ± 1.22 weeks and in batch B was 38.94 ± 1.36 weeks) (Table I). The mean parity in batch A was 2.71 ± 0.84 and in batch B was 2.83 ± 0.89 (Table I). The mean BMI in batch A was 28.42 ± 2.36 and in batch B was 28.36 ± 2.27 kg/m². The mean height was 158.29 ± 11.43 and weight was 75.54 ± 7.61 kg.

Satisfactory outcome in batch A (immediate induction) was seen in 68 (88.31%) while in batch B (delayed induction) was seen in 54 (70.13%) patients as exhibited in Table 2 (p-value = 0.005).
**DISCUSSION**

Premature, rupture of membranes (PROM) is referred to a condition when spontaneous rupture of membranes, occurs & evident by leakage of amniotic fluid per vagina, at or after 37 completed weeks of pregnancy. The prefix 'premature' is used if it’s ahead of onset of labour. The acronym PPROM is used if it occurs before 37 weeks (preterm premature rupture of membranes). PROM affects 1 out of 10 pregnancies resulting in rise in maternal morbidity, surgical interventions & health risks for neonates.\(^{11}\)

However certain researchers found that the perinatal and maternal morbidity, does not rise, with conservative management of PROM, but immediate induction results in higher rates of surgical intervention.\(^{12}\) On the other hand, Neuhaus and colleagues reported a substantial rise in infection rates (both neonatal and maternal) along with fetal distress in patients where delivery is delayed by more than 24 hours after PROM. They observed, lower maternal and neonatal infection rates with short hospital stay when mediante IOL strategy was opted.\(^{13}\) According to Duff P & colleagues, the rate of delivery in first 24 hours after PROM was 90% for those who were induced within 6 hours with respect to 60% in those who were managed expectantly.\(^{14}\) Russel KP provided histological evidence of chorio-amnionitis associated with increased time lapse after membrane rupture.\(^{15}\)

No significant difference was found in my study & research of other colleagues between the groups regarding maternal age, parity and obstetrical complications. Age range seen in my study, ranged from 18 to 40 years, 27 years was the mean age. Majority of the participant women were (79.22%) between 18 to 30 years of age. Mean gestational age was 39 weeks. Satisfactory outcome in batch A (immediate induction) was seen in 88.31% while in batch B (delayed induction) was seen in 70.13% patients (p-value = 0.005). Firdous & co researchers also agreed with results of my study by documenting a shorter mean delivery time (13hrs group A vs 33 hours group B respectively) with immediate (in 6 hours) induction than to delayed (after 24 hours) one. The mean age of the study population was around 28 years, with 38 weeks of gestational age & with parity of 1.\(^{16}\)

A prospective case control study was carried out to compare both strategies: immediate induction of labour, & delayed induction. The study population which was shortly induced with misoprostol (intravaginal), resulted in a decline of rates of abdominal deliveries and instrumental vaginal deliveries along with a significantly elevated spontaneous vaginal birth rates.\(^{17}\) The results matched with results of my study. Immediate induction was also proven beneficial by shortening the latent phase (of labour), and pre-delivery hospital stay without any statistically significant rise in morbidity of mothers & newborns which are comparable.\(^{17}\)

Another prospective randomized study strengthened the outcome of my study. It compared term pregnancies complicated by PROM with expectant vs early management. The patients were randomized to either Group 1 (immediate IOL with oxytocin) or 2 (conservative management). Those in second group were divided in two groups A and B. In 2A, intervention was performed in terms of labour induction by oxytocin, if labour did not initiate after 24 hours of PROM. The 2nd set of participants (Group 2B) in whom uterine contractions started naturally within 24 hours. The base c-section rate was high in group 2. The subsequent rates of LSCS recorded in 1, 2A and 2B.

**Table No.1: Demographic data**

<table>
<thead>
<tr>
<th></th>
<th>Batch A (n=77)</th>
<th>Batch B (n=77)</th>
<th>Total (n=154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-30yrs</td>
<td>60 (85.81%)</td>
<td>56 (72.73%)</td>
<td>116 (74.83%)</td>
</tr>
<tr>
<td>31-40</td>
<td>11 (14.29%)</td>
<td>21 (27.27%)</td>
<td>32 (20.78%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>27.77 ± 3.14</td>
<td>28.09 ± 3.38</td>
<td>27.93 ± 3.41</td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37-39 weeks</td>
<td>49 (63.64%)</td>
<td>48 (62.34%)</td>
<td>97 (62.99%)</td>
</tr>
<tr>
<td>40-42 weeks</td>
<td>28 (36.36%)</td>
<td>29 (37.66%)</td>
<td>57 (37.01%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>39.10 ± 1.22</td>
<td>38.94 ± 1.36</td>
<td>39.01 ± 1.31</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>27 (35.06%)</td>
<td>22 (28.57%)</td>
<td>49 (31.82%)</td>
</tr>
<tr>
<td>3-5</td>
<td>50 (64.94%)</td>
<td>55 (71.43%)</td>
<td>105 (68.18%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.71 ± 0.84</td>
<td>2.83 ± 0.89</td>
<td>2.76 ± 0.85</td>
</tr>
</tbody>
</table>

**Table No.2: Comparison of outcome between both Groups (n=154)**

<table>
<thead>
<tr>
<th></th>
<th>batch a (n=77)</th>
<th>batch b (n=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients</td>
<td>%age</td>
</tr>
<tr>
<td>outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>satisfactory</td>
<td>68</td>
<td>88.31%</td>
</tr>
<tr>
<td>unsatisfactory</td>
<td>99</td>
<td>11.69%</td>
</tr>
</tbody>
</table>

P value is 0.005 which is taken as statistically significant
were 19.2%, 60% and 12.2% respectively. Group 2 showed a notable rise in cases of fetal distress (p<0.05).\textsuperscript{18}

Al calay et al. provided contradicting evidence when they discovered a reduction in duration of labour with expectant management and an increase in operative vaginal deliveries with induction secondary mainly to fetal distress. They recorded low and comparable c section rates among the groups. They inferred expectant management in cases of membrane rupture at term to be safe with reduction in operative vaginal birth rates.\textsuperscript{19}

Beyond this point of membrane rupture, the obstetrical clock starts; fetal separation & protection from external microorganisms is abolished. In 1965, Lanier and coworkers validated by observing a two-fold rise in perinatal mortality with prolong ROM. 28% of these, showed features of intra-partum (perinatal mortality was 50%.) or postpartum infection. So delay in delivery can lead to increase in feto-maternal infectious morbidity & mortality.\textsuperscript{20}

**CONCLUSION**

This study concluded that the outcome of immediate induction is better as compared to delayed induction for labour in term Pre-labour, rupture of membrane. So, we recommend that immediate induction (PGE1 or Oxytocin) is more suitable treatment strategy for patients with term Pre-labour, rupture of membrane in order to reduce the caesarean rates and maternal morbidity.

**Author’s Contribution:**

Concept & Design of Study: Musarat Akhter

Drafting: Salma Jabeen, Saeqah Manzoor

Data Analysis: Nergis Taj Obgy, Farzana Razaque, Shazia Siddique

Revisiting Critically: Musarat Akhter, Salma Jabeen

Final Approval of version: Musarat Akhter

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

**REFERENCES**


The Assessment and Evaluation of Factors of Prognostic Significance in the Management of Colorectal Cancer

Gul Sher Khan¹, Abdul Ghafoor¹, Alam Zeb², Asif Mehmood¹, Bushra Nabi³ and Rafi Ullah¹

ABSTRACT

Objective: To evaluate the association of lymph node retrieval, lymph node ratio (LNR) and various other prognostic factors in the management of colorectal cancer (CRC).

Study Design: A retrospective and longitudinal study.

Place and Duration of Study: This study was conducted at the Department of General Surgery Khalifa Gul Nawaz (KGN) MTI Bannu between July 2019 and January 2020.

Materials and Methods: This study was conducted on the data of 450 consecutive patients with colorectal cancer (CRC), admitted to the Department of General surgery KGN MTI Bannu between Jan 2010 and Dec 2014 and who underwent curative resection for colorectal cancer. The data was collected from the clinical charts, computer record and the pathological reports and were reviewed retrospectively and longitudinally for various prognostic factors in the management of CRC. Follow up period was 5 years.

The data were fed to the computer for analysis and calculation of rates, percentages, means and median of variables. Comparisons between variables were assessed for significance by using Pearson chi-square (χ²) test and Fischer exact test, with the threshold for significance the p<0.05. Kaplan-Meier curves were used to calculate and depict the overall survival in different groups of patients.

Results: A total of 450 patients with colorectal cancer were analyzed. For stage I and stage III or node negative disease, the 5yr survival was 65-70%, declining to 50% for patients with stage I11 or node positive disease. For Duke stages B and C, there was a significant difference in the overall survival (OS) in patients with <12 versus >12 lymph nodes (LNs) retrieved. There was a statistically significant difference in the overall survival (OS), disease free survival (DFS) and recurrence rates in patients with different number of lymph nodes retrieved, the number of lymph nodes with metastases and lymph nodes ratios (LNRs). Histological subtypes, the surgeon, and the pathologist also played a significant prognostic role in the management of CRC.

Conclusion: Retrieval of >12 lymph nodes, thorough evaluation of lymph nodes and decreased lymph nodes ratio have a significant effect on the long term survival and recurrence in the CRC patients.

Key Words: Colorectal cancer (CRC), Lymph nodes numbers (LNs), lymph node ratio (LNR), Lymph nodes with metastases (LNM), and factors of prognostic significance.


INTRODUCTION

Colorectal cancer (CRC) is a very common gastrointestinal malignancy and is the major cause of death in the population worldwide. Colon cancers are more common than the rectal and most of the CRC cases are treated by surgery.

The most important prognostic factors regarding the colorectal cancers treatment are, the total number of lymph nodes examined, the number of lymph nodes with metastases (nodal stage N) and the lymph node ratio (LNR). LNR=the number of lymph nodes with metastases (positive LNs) to total number of lymph nodes examined. The histology of tumour, role of the surgeon and the pathologist, the patient age and co-morbidities and mortalities due to surgical procedures are quite important regarding the prognosis of CRC. TNM (tumour, lymph node and metastasis) system is used for staging and prognosis of malignancies. The minimum number of lymph nodes required to be examined for accurate staging is ≥12.

The lymph node count in a surgical specimen positively correlates with; the age, gender, histology, location of tumour, size of the tumour, the differentiation of the tumour, the year of tumour diagnosis, the depth of...
invasion of tumour, the experience and skill of surgeon and the interest and diligence of the pathologist. Lymph nodes involvement by metastases predicts prognosis and is an important informative factor in deciding patient further treatment and also points towards tumour recurrence. These patients benefit from radio chemotherapy which decreases recurrence rate and increases disease free survival1 and overall survival2-5.

Goldstein et al6 suggested to retrieve and examined more and more lymph nodes during resection of a tumour. Many authors have reported improved survival in Dukes stages B and C with increased number of lymph nodes examined. Berger et al7 noticed the ratio of metastatic lymph nodes to the total number of lymph nodes examined and concluded that lymph node ratio (LNR) is a significant prognostic factor for overall and disease free survival. There are many factors which affect the number of lymph nodes (LN) retrieval such as the type of surgical resection e.g. segmentectomy or hemicolectomy and also the number vary between patient to patient constitutionally6,8. The possibility of detecting positive lymph nodes pathologically increases with the number of lymph nodes examined9.

Age <65yrs and right sided tumour localization, the length of resected bowel segment and the spread of the tumour positively correlate with a high number of lymph nodes examined10.

Preoperative radio-chemotherapy decreases the number of lymph nodes retrieval8. Surgeon experience in colorectal surgery is an important factor in adequate lymph node recovery11. Retrieval of lymph nodes and identification of positive lymph nodes have been shown to be significantly affected by pathologist lymph nodes examination9.

MATERIALS AND METHODS

The study was conducted on the data of 450 diagnosed cases of adenocarcinoma of colorectum who were admitted to the General Surgical Ward between January 2010 and Dec 2014. These patients underwent curative resection for colorectal cancer.

The data were collected from the clinical charts, computer record and pathological reports. Included in this study were males 290 (64.4%) and female 160 (35.5%). The mean age was 58.8±7.8yrs and the median age was 56(22-80) yrs. The mean age for female was 59.8yrs and for male was 57.5yrs.

Six experienced and skillful colorectal surgeons took part in the colorectal resection through an open approach. The surgical specimens were assessed by 2 interested and diligent pathologists. The resections were grouped as follow;

Rt hemicolecotomies __________90.
Extended Rt hemicolecotomies ______15.
Transverse colectomies __________25.

Lt hemicolecotomies __________30.
Extended Lt hemicolecotomies ______10.
Sigmoid resection ___________85.
Anterior abdominal resection _______40.
with CME (complete mesocolic excision) Abdomino perineal resection _______130.
with TME (total mesorectal excision) Rectal extirpation ____________25.

Preoperatively the patients were diagnosed by ultrasound abdomen and chest, CT scan abdomen and chest, X ray chest, sigmoid scopy and colonoscopy with biopsy and carcinoembryonicantigen (CEA) level.

Patients with more than one primary, patients with synchronous tumours, patients with distant metastases, patients with advanced irresectable tumours and patients who received neoadjuvant chemoradiation were excluded from the study.

The technique of total mesorectal excision (TME) or complete mesocolic excision (CME) was applied by sharp dissection in the developmental plane of the entire mesorectum or mesocolon with intact facial layers and ligation of the feeding vessels at their origin. The length of the bowel excised was 10cms proximal and 10cms distal to the tumour growth in colon cancer and 5cms proximal and 2cms distal in the rectal carcinoma and therssected specimen removed en bloc with the mesorectum or mesocolon.

Follow up: From the record it was apparent that the patients had been followed for up to 5yrs. Patients had follow up check once every 3 months during the first year, once every 6 months during the next year and once in a year during the next 3 years. During each follow up visit, patient physical examination, full blood count, CEA level, liver function tests(LFTs) and bone scan were repeated and surveillance colonoscopy and sigmoidoscopy done periodically. Survival data were collected by phone or interviews with patients or their relatives or from the record of our oncological department.

After a median follow up of 60 months (55-65 months); 370 patients were alive, 80 patient had died, of whom 70 patients from colorectal cancer (CRC). During each follow up check, patients were searched for any evidence of recurrence. 24.5% (n=90) patients postoperatively required radio chemotherapy within 4-8 weeks. 60 patients of rectal cancer received radiotherapy and 30 patients of colon cancer received chemotherapy.

Overall 19% patients (n=70) had cancer recurrence. Isolated liver metastases were found in 15 patients, isolated lung metastases in 8 patients and local recurrence was found in 30 patients.

Metastatic spread to liver commonly occurred from left sided colon cancer, while rectal cancers commonly metastasized to lungs and also these cancers had increase tendency for local recurrence.
RESULTS

Male patients of CRC were younger than females (p<0.05). The frequency of CRC was higher in men (64.4%, n=290) than the female (35.5%, n=160). The mean number of lymph nodes retrieved was 15.8±6.5. More lymph nodes were found in patients with age <65yrs, the average was 17.5.

Table No.1: 5yr recurrence and survival rates in CRC patients.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Recurrence</th>
<th>5yr survival rates</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Colon</td>
<td>Rectum</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3.5%</td>
<td>75</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>10.9%</td>
<td>70</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>111a</td>
<td>25.4%</td>
<td>60</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>111b</td>
<td>39.6%</td>
<td>55</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

Regarding the location, more tumour were present in the colon, especially in the left colon (numbers given in the para as group resections). The mean number of lymph nodes examined were higher in the right colon (median=16) followed by left colon (the median number=14) and rectum (median=12). In 57% (n=257) patients, the tumour showed a dimension of <5cms and in 40% (n=180), the tumour dimension was >5cms with more serosal invasion.

Histologically the tumours were mostly adenocarcinoma 78% (n=350), mucinous adenocarcinoma 15% (n=70), followed by invasive adenocarcinoma 4.4% (n=20) and the signet ring adenocarcinoma 2.2% (n=10).

Regarding the spread of tumour, T3 tumours were the most common 49% (n=210), followed by T2 27% (n=115). T4 tumours were present in 12% (n=54) and T1 in only 10% (n=45) cases.

Differentiated (low grade) tumours were more frequent 88% (n=396) than the undifferentiated (high grade) tumours 12% (n=53). In high grade tumours, the median number of lymph nodes retrieved was 17 while in low grade tumour it was 14.

Regarding the number of lymph nodes retrieved from a surgical specimen, it was <12 in 62% of cases and >12 lymph nodes per specimen were found in 38% of cases. In greater majority of cases 56.8% (n=256), no lymph node with metastasis found, while in 28% (n=126) 1-3 lymph nodes with metastases and in 14% (n=63), >4 lymph nodes with metastases found.

Table No.2: The Clinopathological data of 450 patients with CRC and the results of univariate analysis.

| Variables       | Number of pts | % of pts | 5yr survival | P values | |
|-----------------|---------------|----------|--------------|----------|
| Gender          |               |          |              |          | |
| Male            | 290           | 64.4     | 70           | 0.010    | |
| Female          | 160           | 35.5     | 75           |          | |
| Age             |               |          |              |          | |
| <65yrs          | 290           | 64.44    | 65           | 0.05     | |
| >65yrs          | 160           | 35.55    | 60           |          | |
| Depth of invasion|             |          |              |          | |
| T1              | 45            | 10       | 65           |          | |
| T2              | 115           | 27       | 60           |          | |
| T3              | 210           | 49       | 55           |          | |
| T4              | 54            | 12       | 50           | 0.001    | |
| Lymph nodes with mets |       |          |              |          | |
| N0              | 256           | 56.8     | 75           |          | |
| N1              | 126           | 28       | 60           |          | |
| N2              | 63            | 14       | 50           | 0.001    | |
| Lymph nodes examined |       |          |              |          | |
| <12             | 280           | 62.22    | 55           | 0.005    | |
| >12             | 170           | 37.77    | 70           |          | |
| Tumour size     |               |          |              |          | |
| >5cms           | 180           | 40       | 60           |          | |
| <5cms           | 257           | 57       | 65           | 0.001    | |
| Low grade       | 396           | 88       | 70           |          | |
| High grade      | 54            | 12       | 55           | 0.001    | |
| Tumour type     |               |          |              |          | |
| Adeno Ca        | 350           | 77.7     | 60           |          | |
| Mucinous adeno Ca |    | 15.5     | 55           |          | |
| Invasive Ca     | 20            | 4.44     | 45           |          | |
| Signet ring Ca  | 10            | 2.22     | 50           | 0.001    | |

Figure No.1: Kaplan Meier survival curves according to the number of lymph nodes with mets.

There was a significant correlation between the number of lymph nodes removed and the lymph nodes with mets (Nstage) (r=0.138, p<0.001). While there was no significant positive correlation between the number of lymph nodes examined, the LNR and survival (r=0.026, p=0.756 and r=0.138, p=0.065) respectively. In this study LNR was found to be significantly correlated with survival as the most significant prognostic factor [p<0.001, 95% CI: 3.14(1.45-5.65)].

We noticed a correlation between the number of lymph nodes examined and the number of lymph nodes with mets (LNM or N stage) (p=0.005, r=0.134). The 189 patients (with N1+N2 diseases) were divided into 4 groups according to the LNR quartiles, e.LNR<0.1 n=6, LNR ≤0.2n=50, LNR≤0.4 n=45 and LNR >0.4 n=34. The 5yr survival rates decreased as the LNR increased.
LNR < 0.1 the 5yr survival was approximately 70%.
LNR ≤ 0.2 the 5yr survival was approximately 60%.
LNR ≤ 0.4 the 5yr survival was approximately 55%.
LNR > 0.4 the 5yr survival was approximately 45%.

Figure No.2: Lymph nodes ratios and Kaplan Meier survival curves.

**DISCUSSION**

Total lymphadenectomy is a key factor in the curative surgery of CRC. The generally accepted recommendation demands at least 12 lymph nodes per surgical specimen\(^{12}\). However the harvested lymph nodes number from a colorectal specimen is always highly variable and is incompletely understood\(^{13}\).

The surgeon and his skill and the pathologist and his devotion to his job are quite important regarding the number of lymph nodes harvest and the evaluation of lymph nodes respectively.

In this study we noticed that increased lymph node harvest was correlated with an increased number of lymph nodes with metastasis and which is according to the existing literature.

Levoy et al\(^{14}\) concluded that the number of lymph nodes evaluated was a significant prognostic factor in both lymph nodes positive and negative patients of colorectal cancer.

Wright et al\(^{15}\) reported that 73% patients of CRC had < 12 lymph nodes retrieved. In our study the number of patients with < 12 lymph nodes retrieved were 62.22%.

Berger et al showed that decreased LNR was associated with increase survival. Decreased LNR shows either decreased positive lymph nodes or increase number of examined lymph nodes.

The technique of total mesorectal excision (TME) and complete mesocolic excision (CME) in colorectal surgery (the standardization of surgery) have led to improved survival and decreased recurrence\(^{16-17}\).

Several authors have reported excellent out come from TME or CME with good 5yr survival, low local recurrence and maximum lymph nodes yields.

**CONCLUSION**

In the management of CRC, the TNM staging system predicts the prognosis of the disease. The total number of lymph nodes and lymph nodes with metastases depend on the site of the tumour and extent of resection (surgeon skill), the handling of the resected specimen (histopathologist role) and the pre and post operative radiochemotherapy protocols. The staging of a tumour depends upon the extent of spread through the bowel wall, the involvement of the number of lymph nodes in the drainage area, which dictates the management and predicts the survival and the recurrence rates of the disease.

The standardization of surgery (i.e. resection of a tumour in a clean sweep) and thorough retrieval and evaluation of the lymph nodes from the resected specimen (pathologist zeal and interest in searching out lymph nodes) which dictates an accurate staging and hence the prognosis of the disease.

**Author’s Contribution:**

Concept & Design of Study: Gul Sher Khan
Drafting: Abdul Ghafoor, Alam Zeb
Data Analysis: Asif Mehmood, Bushra Nabi, Rafi Ullah
Revisiting Critically: Gul Sher Khan, Abdul Ghafoor
Final Approval of version: Gul Sher Khan

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

**REFERENCES**


Duration of Labour after Injection of Drotaverine Hydrochloride in Primigravida Presenting in Active Phase of Labour in a Tertiary Care Hospital
Seema Gul Salman¹, Maria Rafiq¹, Sania Hafeez¹, Isma Rafiq Khan² and Zartaj³

ABSTRACT

Objective: To determine the mean duration of labour after injection of Drotaverine hydrochloride in primigravida presenting in active phase of labour in a tertiary care hospital.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of gynecology and obstetrics Bacha khan medical complex Sawabi from January to July 2018.

Materials and Methods: A total of 123 patients were enrolled in the study after taking informed consent from the individual participant. Patients having age 20-36 years with singleton cephalic presentation of fetus as assessed on ultrasound and already in the active phase of labour having cervical dilation of 3-5cm with 2-3min uterine contractions for at least 30 seconds in every 10 minutes were included in the study. Data was collected using a pre designed proforma. Data analysis was done using SPSS version 20.

Results: Average age of the patients was 25.72years±3.67SD with range 20-36 years. Average gestational age of the patients was 37.26 years±2.29SD with range 33-41 weeks. The average total duration of average labor was 4.14±0.55SD.

Conclusion: Drotaverine hydrochloride in primigravida presenting in active phase of labour is effective to reduce the duration of labor

Key Words: Mean duration, labour, primigravida, active phase


INTRODUCTION

Labour is defined as process that results in the delivery of the baby. It is physiological process and can cause serious consequences during its prolongation. It can result in dehydration, infection, metabolic acidosis, fetal distress and increased intraoperative interventions.¹

Spasms in the cervical smooth muscles is commonest cause of prolonged labour. Cervical muscle spasm is the most common cause of prolonged labour.

1. Department of Gynae, Bacha Khan Medical complex, Sawabi Pakistan.
2. Department of Gynae, Pak international Medical College, Peshawar.
3. Medical Officer, Rural Health Center Shergarh Mardan, KPK

Correspondence: Dr. Seema Gul Salman, District Specialist, Gynae Department, Bacha Khan Medical Complex, Sawabi Pakistan.

Contact No: 03339885967
Email: seemagul193@yahoo.com

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It is because of over discharge of circular muscle of cervix. This over activity of cervical muscles is exaggerated in the presence of injury or inflammation, fibrosis in the cervical muscles or fear related tension syndromes.²

Obstetrician and laboring female both would like to complete the delivery process in shortest possible duration without compromising mother and fetal safety. Therefore, with early administration of oxytocin and amniotomy, antispasmodic agents may be used to accelerate the process.³

Labour is a process that involves multiple factors i.e uterine contractions, cervical ripening, dilation and delivery of baby and placenta in an ordered way. The first stage of labor is a bit longer in primigravida as compared to multigravida, 12-16 hours and 6-8 hours respectively.

Calculating the time duration of labor is difficult and very subjective. Certain reasons are there that hinders the calculation of duration of labour. First is measuring cervical dilation and secondly the process of labor varies from patient to patient. Some females presents with strong and painful uterine contractions at 2cm of cervical dilation, whereas other females feels the same intensity of pain at 4cm of cervical dilatation.
This affects the obstetrician’s perception of induction of labor. Therefore, most of studies has defined the measurement of first stage of labor as the point of administering an antispasmodic till full cervical dilatation. This intervention can be done at 3 to 6 cm of dilatation. This timing of the administration of antispasmodic agent varied from 3 cm to 6 cm cervical dilatation. Many studies have shown effectiveness of antispasmodics in increasing the rate of cervical dilatation during first stage of labor.

Second and third stage of labor was not influenced by using antispasmodics. Pain may be relieved but it is not certain that it has an analgesic effect.

Every mother and care taking obstetrician wants pain free labor and delivery. Strength and frequency of uterine contractions along with active cervical dilatation are the factors that lead the progress of labor, but often active cervical dilatation starts late even if uterine contractions are present. It can result in unrequired painful and prolonged labor which affects the health of mother and baby. Thus pharmacological drugs are used to augment cervical dilatation in the presence of good uterine contractions that results in smooth delivery of baby. Different types of agents (both mechanical and pharmacological) are used, which can cause cervical dilatation. Early amniotomy and smooth muscle relaxants are used to shorten the duration of labor.

Drotaverine hydrochloride is a muscle relaxant that has different mode of actions. Drotaverine hydrochloride or isoquinolone 1,2,3,4-tetrahydro 6,7 diethoxy-1-(C-3, 4-diethoxy phenylmethylene) is a potent spasmolytic derivative and is a smooth muscle relaxant. It does not have habit forming or addictive nature because it lacks opioid analgesic and narcotic effects. The mode of action of Drotaverine is inhibition of phosphodiesterase enzyme. It causes increase in cAMP levels which causes relaxation of smooth muscles by inhibiting muscle contractions.

The rationale of the present study is to evaluate the effect of shortening of duration of labour as in our set-up obstetrician do not give any drug or spasmytic to shorten the duration of labour as long duration of labour may cause many complications to fetus as well as laboring mother. If mean duration of labour is shortened than before then we will implement the drug in future in our set-up to save time of obstetrician and laboring women.

**MATERIALS AND METHODS**

Sampling method was non-probability (consecutive) sampling technique. Patients who were in the age group 20-36 years presenting to department/ ER having singleton pregnancy with cephalic presentation of the fetus (as assessed by ultrasound) and who were in active phase of labour with cervical dilatation of 3-5cm with 2-3 uterine contractions for at least 30 seconds in every 10 minutes were included in the study. Patients having pregnancies with medical disorders like hypertension (BP > 140/90 mmHg) or diabetes (RBS > 180 mg/dl, FBS > 126mg/dl) were excluded and patients with borderline pelvis and cephalopelvic disproportion (assessed on pelvic examination) were also excluded from the study.

After explaining the purpose and benefit of the study and procedure, an informed consent was taken and information’s were entered in a pre-designed proforma. Demographic data including gestational age was noted. These patients who were in active stage of labour were injected intramuscularly with forty milligrams (40mg) of Drotaverine hydrochloride. This injection was administered at 3-5cm of cervical dilatation by a single trained staff nurse. Then patients were followed till delivery and duration of labour from time of injection till delivery was noted by the author herself. Data was analyzed using SPSS version 20. Data were stratified for stages of labour (1st, 2nd, and 3rd).

**RESULTS**

Average age of the patients was 25.72 years + 3.67SD with range 20-36 years. Patients were divided into four categories according to age of patients. Out of which most common age group for primigravida presenting in active phase of labour was 24-28 years of age. Fifty (40.7%) patients were in the age range of 24-28 years. Frequency and percentages for age distribution is shown in table 1.

**Table No.1: Age Wise Distribution of the Patients**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Percentage/ frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 23.00</td>
<td>35.8%(n=44)</td>
</tr>
<tr>
<td>24.00 - 28.00</td>
<td>40.7%(n=50)</td>
</tr>
<tr>
<td>29.00 - 33.00</td>
<td>22%(n=27)</td>
</tr>
<tr>
<td>34.00+</td>
<td>1.6%(n=2)</td>
</tr>
</tbody>
</table>

**Table No.2: Mean Duration of Labor**

<table>
<thead>
<tr>
<th>Count</th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Stage of Labour (in hr)</td>
<td>123</td>
<td>2.65</td>
<td>4.30</td>
<td>3.51</td>
</tr>
<tr>
<td>2nd Stage of Labour (in hr)</td>
<td>123</td>
<td>.28</td>
<td>.75</td>
<td>.50</td>
</tr>
<tr>
<td>3rd Stage of Labour (in hr)</td>
<td>123</td>
<td>.08</td>
<td>.17</td>
<td>.13</td>
</tr>
<tr>
<td>Total Duration of Labour (in hr)</td>
<td>123</td>
<td>3.13</td>
<td>5.15</td>
<td>4.14</td>
</tr>
</tbody>
</table>

Average gestational age of the patients was 37.26 weeks + 2.29SD with range 33-41 weeks. Majority of patients have 36-39 weeks of gestational age. There were 27(21.95%) patients were of the less than or equal to 35 weeks and 18(14.63%) patients were in the range of more than 40 years of gestational age presenting in active phase of labour in a tertiary care hospital. (Fig 1)
Out of 123 primigravida presenting in active phase of labour in a tertiary care hospital. The average labour in 1\textsuperscript{st} stage was observed 3.51 hour $\pm$ 0.54SD followed by the 2\textsuperscript{nd} stage of average labour 0.50 hour $\pm$ 0.12SD while in 3\textsuperscript{rd} stage, it was 0.13hour $\pm$ 0.03SD. Total duration of average labor was 4.14$\pm$0.55SD. (Table 2)

Gestational age wise distribution of duration of labor shows that duration of labor was almost same in all gestational age group. (Table 3)

Age wise distribution of duration of labor shows that age has no role over average duration of labor. (Table 4).

<table>
<thead>
<tr>
<th>Gestational Age (in weeks)</th>
<th>1st Stage of Labour(in hr)</th>
<th>2nd Stage of Labour(in hr)</th>
<th>3rd Stage of Labour(in hr)</th>
<th>Total Duration of Labour(in hr)</th>
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<tbody>
<tr>
<td>$\leq 35.00$</td>
<td>N</td>
<td>27</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>3.5022</td>
<td>.4944</td>
<td>.1374</td>
</tr>
<tr>
<td></td>
<td>Std. Deviation</td>
<td>.55333</td>
<td>.11517</td>
<td>.02123</td>
</tr>
<tr>
<td>36.00 - 39.00</td>
<td>N</td>
<td>78</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>3.5606</td>
<td>.5013</td>
<td>.1336</td>
</tr>
<tr>
<td></td>
<td>Std. Deviation</td>
<td>.49999</td>
<td>.12115</td>
<td>.02777</td>
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<td>40.00+</td>
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<td>Std. Deviation</td>
<td>.53861</td>
<td>.11982</td>
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Table No.4: Age Wise Distribution of Duration of Labor Among Patients with Primigravida Presenting in Active Phase of Labour

<table>
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<tr>
<th>Gestational Age (in weeks)</th>
<th>1st Stage of Labour(in hr)</th>
<th>2nd Stage of Labour(in hr)</th>
<th>3rd Stage of Labour(in hr)</th>
<th>Total Duration of Labour(in hr)</th>
</tr>
</thead>
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<tr>
<td>$\leq 35.00$</td>
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<td>27</td>
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<td>Std. Deviation</td>
<td>.55333</td>
<td>.11517</td>
<td>.02123</td>
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<tr>
<td>36.00 - 39.00</td>
<td>N</td>
<td>78</td>
<td>78</td>
<td>78</td>
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<td></td>
<td>Mean</td>
<td>3.5606</td>
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<td>Std. Deviation</td>
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<tr>
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<td>Std. Deviation</td>
<td>.53861</td>
<td>.11982</td>
<td>.02696</td>
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</table>

DISCUSSION

Number of cesarean sections, prolonged labor and labor duration can be reduced by actively managing labor. It will lead to successful delivery without having adverse maternal and fetal consequences.\(^6\) There has been several randomized clinical trials done on safety of active management of labor, involving thousands of women.\(^5\) Numerous studies reported that shorter duration of labor from time of admission with active management protocols can yield good results.\(^6\)\(^,\)\(^8\) There is a number of smooth muscle relaxants that are being used in labor. The purpose of which is mainly augmenting relaxation and dilatation of cervix. Drotaverine has significant muscle relaxing activity and lacks addictive nature, as it lacks opioid analgesic and narcotic effects.\(^5\) Its mechanism of action is mainly inhibition of phosphodiesterase enzyme. It causes increase in cAMP levels which results in inhibition of smooth muscle contraction which leads to muscle relaxation. It also inhibits selected PDE isoenzyme PDE-IV (rolipram sensitive). Hence its side effects are less. It has more potent action in those tissues which are rich in PDE-IV isoenzyme.\(^9\)

Drotaverine causes significant increase in cervical dilatation in primigravida.\(^10\)\(^ - \)\(^13\) It has no effect on 2\textsuperscript{nd} and 3\textsuperscript{rd} stages of labor in primigravida and also in multigravida.\(^13\)\(^ - \)\(^17\) It does not affect the mode of delivery when used in labor, it only shortens the duration of labour.\(^12\)\(^,\)\(^14\)
A study conducted by Sharma, concluded that duration of first stage of labour and rate of cervical dilatation in Drotaverine group was 194±57.04 minutes and 2.04±0.68 cm per hour and in our study it was 191.25±76.89 minutes and 2.48 cm per hour respectively, so results are comparable with other studies.

In our study mean age of the patients was 25.72 years which was ranged from 2428 years. Most of the pregnant patients presented in this age group. The average gestational age of our patients was 37.26 weeks which is comparable to other studies findings. The gestational age of majority of patients was 36-39 weeks. The average duration of 1st stage of labour was 3.51±0.54 hours. It was followed by 0.50±0.12 hours in second stage while shortest in 3rd stage of labour which was 0.13±0.03 hours.

In our study, 4.12 hour ± 0.551SD was the mean duration of first labor using Drotaverine hydrochloride. Our results were comparable with a same sort of study carried out by Anju Huria et al. In that study they used Drotaverine and Valethamate, both of which significantly reduced the duration of first stage of labour. These drugs caused significant reduction in duration of first stage of labor as compared to control in nulliparous and multiparous both.

A study done by Kaur D and colleagues, Mishra SL and other authors and Sharma JB with his colleagues concluded that Drotaverine is more potent as compared to valethamate in shortening the duration of labour. A study of 535 patients by Gupta and friends was done by using Drotaverine injections during labor. They concluded that Drotaverine has more effective decreasing the time duration of labour. It does it so by inhibiting cervical muscles contractions during labour. This drug has more potency during membrane rupture.

A study by Thapa M et al concluded that duration of labor was significantly reduced after using Drotaverine intravenously. The mean duration from injection to delivery was 196.9 in primigravida and 196.9 in multigravida patients. This decrease in duration of labor is caused by using Drotaverine injection that results in acceleration of first of labor. Yuel et al reported that Drotaverine is more potent than other smooth muscle relaxants (epidosin or buscopan) in cervical dilatation. A study done by Majumder S et.al showed that their mean duration of first stage of labor was 176.67±9.169 min after using Drotaverine hydrochloride injection during labor.

In a study done by Tewari K, they compared the effects of valethamate bromide with hyoscine butylbromide. They gave buscopan 20min apart in two divided doses and found that duration of labor was reduced by 5 hrs. and 12 minz.

Samuels LA included 129 patients in his study out of which 69 received placebo and 60 received hyoscine butylbromide the mean time of duration of labor was 156 minutes in the drug group and 228 in placebo group. It showed significant decrease in duration of labor by 31.7%.

A nonrandomized controlled study was done by Sirohiwal D, on 200 laboring patients. 100 patients at 3cm or more of cervical dilation, received antispasmodic agent and 100 patients didn’t receive any drug. He concluded that duration of first stage of labor was 123.86 minz ±68.89 in first group and 368.05 minz ±133.0 in the controlled group. These findings were significant statistically.

Our results are comparable with the studies done other colleagues in various institutes. We observed no peri-labor mortality or morbidity. All of our patients delivered normally with no progress to caesarian section or forceps assisted delivery.

CONCLUSION

We found from the results of our re-search that using Drotaverine hydrochloride injection in early stage of labor in primigravida patients decreases the duration of labor significantly. It also decreases the incidence of tears in cervical muscles that occur during labor. Its use can result in good maternal and fetal outcome.

However, more research is required specially randomized control trials on a larger sample that will yield the exact dosage and definitive outcome of using Drotaverine in accelerating the labor.

Author's Contribution:
Concept & Design of Study: Seema Gul Salman
Drafting: Maria Rafiq, Sania Hafeez
Data Analysis: Isma Rafiq Khan, Zartaj
Revisiting Critically: Seema Gul Salman, Maria Rafiq
Final Approval of version: Seema Gul Salman

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

REFERENCES

3. Palii SB, Akkupalli VL, Maddi S. The Comparative Study of Drotaverine Hydrochloride and Valethamate Bromide in First Stage
Screening of Thalassemia Major or Intermedia on Routine Complete Blood Count in an Outpatient Setting

Nadeem Nusrat¹, Mohammed Rizwan¹, Mohammed Salman Zafar², Imran Bakar², Iram Nazir¹ and Mohammed Usman¹

ABSTRACT

Objective: To find out the relationship between Red cell distribution width (RDW-CV) and level of fetal hemoglobin on HPLC.

Study Design: Prospective, observational cross-sectional study

Place and Duration of Study: This study was conducted at the Institute of Hematology, Baqai Medical University from September 2018 till March 2019 or a period of six months.

Materials and Methods: Patients were seen in Baqai Institute of hematology and their blood samples were sent to Hematology laboratory of Dow university Ojha complex, Karachi. A total of 394 consecutive blood samples aged 8 months to 5 years were analyzed for Hb. HPLC. Complete blood count was done immediately on fully automatic hematology analyzer while Hb. HPLC was done the same day on automatic Adam’s Arkray HPLC analyzer.

Results: On the basis of RDW-CV, two groups were created as Group 1 & 2 having RDW-CV less than 30.9 and more than 30.9 respectively. Mean RDW and Hb-F levels for group 1 (n = 248) and 2 (n = 146) were 18.5, 1.32 % and 35.62 and 65 % respectively.

Conclusion: Very high RDW-CV on routine CBC has significant relation to high values of Hb-F which is characteristic laboratory feature of the disease.

Key Words: Thalassemia, Anemia, (RDW) Red cell distribution width, failure to thrive, Hb-HPLC, Globin chains, anisocytosis


INTRODUCTION

Hemoglobin (Hb) found in red blood cells is vital for oxygen transport in body. In a normal individual about seven different types of hemoglobins are synthesized different stages of life. Four of them are transient (Hb Gower 1&2 and Hb. Portland 1&2), seen only during the embryonic period while fetal Hb (Hb-F) is predominant Hb in fetal life and makes a major proportion at birth. In normal children and adults Hb-A, comprises a major portion (96-97%) with small amounts of Hb-A2 (2-3.3%) and Hb-F (0.2-1.0 %). Each molecule of Hb i.e. A, A2 and F consists of two alpha globin chains paired respectively with two beta, delta and gamma globin chains attached to one heme.

¹ Department of Pathology, Baqai Medical University, Karachi.
² Department of Pathology, Hamdard College of Medicine & Dentistry, Karachi.

Correspondence: Dr. Nadeem Nusrat. Associate Professor of Hematology, Baqai Medical University,
Contact No: 0333 2907020
Email: nadeem.nusrat@yahoo.com

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continues with a limited capacity as it tries to compensate for the absent or decreased production of Hb A. The net result is severe isolated anemia with variation is size and shape of red cells (anisopoikilocytosis) along with hypochromic microcytic red cells in the peripheral blood. There is little or no Hb A with a relative increased proportion of Hb-F on a background of severe anemia. This is due to ineffective & dyserthropoietic erythropoiesis by the bone (9). Bone marrow expands to compensate this anemia but again is ineffective. This results in various complications of disease like expansion of bone marrow cavity at the expense of thinning of bone cortex and bony deformities, extramedullary erythropoiesis resulting in Hepatosplenomegaly. The child suffers from failure to thrive unless treated. In the severe forms of BTM/I, the Hb level ranges between 2-8 g/dl. Mean corpuscular volume (MCV) and mean corpuscular Hb (MCH) are significantly low, but, unlike thalassemia trait, thalassemia major is associated with a markedly elevated red cell distribution width (RDW), reflecting the extreme anisocytosis. The white blood count is usually elevated and this is due, in part to miscounting circulating nucleated red blood cells as leukocytes. Platelet count is usually normal, unless the spleen is markedly enlarged. Hb electrophoresis usually reveals an elevated Hb F fraction, which is distributed heterogeneously in the RBCs of patients with β thalassemia. The disease is diagnosed by Hb electrophoresis or HPLC (high performance liquid chromatography), which is expensive and not easily available in rural areas. If left untreated, the patient dies within few months due to severe failure to thrive and various disease complications. In order to save the life of child, regular blood transfusion is started to maintain the hemoglobin level at adequate level followed by iron chelation therapy due to anticipated iron overload (11). This treatment continues lifelong or until cure is achieved by allogenic bone marrow transplant. Another treatment which has gained popularity nowadays is the use of Hydroxyurea in these patients. Hydroxyurea (HU), is a ribonucleotide reductase inhibitor, acts by increasing Hb-F production and partially correcting α and non-α globin chains imbalance, thus ameliorating the hemolytic symptoms of these patients. Is a chemotherapeutic agent and has been used since a long time in the treatment of various malignancies especially in the treatment of chronic myelocytic leukemia before the introduction of tyrosine kinase inhibitors. This drug is beneficial in certain types of mutations of the disease and the blood requirement of the patient decreases significantly. It is said that hydroxyurea initiates the formation of Hb-F by stimulating its gene and so the level of hemoglobin don’t fall to very low levels requiring blood transfusion. But these modalities do not offer cure. Up till now allogenic bone marrow or stem cell transplantation is the only means of acquiring a cure is HLA matched sibling is present but is highly expensive, available only in specialized centers and has high risk of morbidities and mortalities. The outcome of stem cell depends upon the age of patient and the number of blood transfusion he has received. The older the age and more the number of transfusions may lower a better outcome of this disease. So, it is important to diagnose it an early stage so that the patient may have received lesser transfusions. Major proportion of Pakistan is underdeveloped and many people living under poverty line along with scarcity of medical and diagnostic facilities, these patients remain undiagnosed for quite some time and are therefore more prone to develop various complications of the disease. This mounts the importance of early diagnosis and treatment of the disease by a screening investigation which should be easily available with a low cost. CBC is the first diagnostic investigation done for any disease and most of the time is the prime investigation that a physician requests for the patient. In our observation RDW parameter in a routine CBC closely parallels with anisocytosis of red cells in peripheral blood. In cases of severe anisocytosis, this parameter reaches very high values which are usually not seen in simple clinical conditions. This variation in size of red cells is called anisocytosis.

RDW value is directly proportional to the degree of anisocytosis (13). RDW can be reported statistically as coefficient of variation (CV), the term which will be used in this article or standard deviation (SD) (14). RDW-SD is expressed in femtolitres & actually measures the width of the RBC size distribution histogram and is measured by calculating the width (in fL) at the 20% height level of the RBC size distribution histogram (Image1) thus making it independent from MCV while RDW-CV (expressed in %) is calculated from a formula which is SD & and MCV:RDW-CV (%) = 1 SD of RBC volume/MCV x 100%, as RDW-CV and is mathematically derived from MCV, it is therefore affected by the average RBC size (MCV). The reference range for RDW-SD is 39-46 fL while for RDW is 11.6-14.6%. Reference ranges may vary depending on the individual laboratory and patient's age (15).

Aim of the study was to use this inexpensive routine CBC parameter for the screening of the beta thalassemia major or Intermedia, so that definite diagnostic investigations and treatment can be initiated early. In this study we plan to correlate high value of RDW-CV on routine CBC with the Hb-F OR fetal hemoglobin concentration on Hb. HPLC.

MATERIALS AND METHODS

This prospective descriptive study was conducted in Institute of hematology, Baqai medical college 16th September 2018 till 16th March 2019 for a period of six
months. Inclusion criteria were age limit from 8 months to five years of age of both genders irrespective of their transfusion status. Sample size was calculated from online Rao Soft Sample size calculator by adjusting the margin of error (d) at 5%, confidence level at 95%, with response distribution at 50%. The recommended sample size was 377 but we took it as 394. Samples were received from all over Karachi and interior of Sindh province. About 2 ml of whole blood sample was taken from a good peripheral vein in EDTA purple top with a vacutainer and CBC was performed within three hours of sample collection on Cell Dyne Sapphire automatic hematology analyzer which incorporates MAPSS (Multi angle polarized scatter separation technology). Quality control is our daily routine three times a day and checked on Levy Jennings chart and accepted only if it did not have any violation of Westgard rules. Remaining sample was run for Hb. HPLC fully automatic Adam’s Arkay analyzer the same day which has the ability to run analysis any time and even individually.

A Total of 394 samples were analyzed for CBC and Hb. HPLC of patients less than five years of age. The demographic data along with results were entered in the computer. The results were computed by SPSS version 20 and mean, median, standard deviation was obtained. The data was analyzed forming two groups of RDW-CV i.e. 30.9% or above as group one (GP I) and 30.8% or below as group 2 (GP II) 30.9 and subjected to student t test in order to obtain P value. A p value of less than 0.05 was considered significant.

RESULTS
As seen in table 1, the total numbers of cases were 394. All were below five years of age. Females were n 184 (46.7%) while Males were n 210 (53%). Comparison of Age, Hemoglobin, RDW-CV and Hb. F value of two groups is shown in table 1. Group I (n 248, 62%, M:F of 130:118) had median age of 2.2 years while group II (n146, 37%, M:F 80:66) had 12 years. Mean Hb levels and Hb-F % in group I and II were 8.14gm/dl, 5.12 gm/dl, 1.03 and 65 % respectively while for RDW-CV it was 18.5 and 35.62. When RDW &Hb-F % of group I&II were compared by t test, the value obtained was highly significant (less than 0.05).

Table No. 1: Comparison of Age, RDW & Hemoglobin & Hb. F values among both groups

<table>
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<th>Group I n248 (M 130 F 118)</th>
<th>Group II n146 (M 80 F 66)</th>
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<td>Group 1 Group 2</td>
<td>Group 1 Group 2</td>
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<tr>
<td>Minimum</td>
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<td>0.8</td>
<td>11.4</td>
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<tr>
<td>Maximum</td>
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<td>5</td>
<td>30.9</td>
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<td>Mean</td>
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<td>16.9</td>
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<td>2.02</td>
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DISCUSSION
As far as our knowledge is concerned, we have not come across any study till date which has related Hb-F levels with RDW in beta thalasemia major/intermedia. The normal value or RDW-CV is less than 14.5 and is raised at the most from 14 to 29 in other cases like iron deficiency but values above this are usually seen in few conditions like beta thalassemia syndromes and rare disorders of congenital dyserythropoietic anemias,(10). The results of our study regarding relation of anisocytosis with RDW-CV correlates very well with the study of T. Jameel et al, In which they tried to differentiate BMT with iron deficiency anemia on the basis of anisocytosis by utilizing RDW-CV on a sample size of 620 patients having hypochromic microcytic conditions by performing Serum ferritin and Hb electrophoresis. The patients with iron deficiency had an increased RDW-CV then those of Beta thalassemia minor diagnosed by an elevated Hb-A2(17). Our finding of very high RDW-CV in beta thalassemia major were also found in a study in Turkey in which the RDW-CV was significantly higher in Delta beta thalassemia than iron deficiency or other hypochromic anemias study showed significant elevation of RDW-CV which was not seen in individuals without Beta thalassemia major (18). Our study was also independent of the transfusion status of the patient and it was seen that transfusion had a minor significant effect on the other group with high RDW-CV. This shows that regular transfusions to maintain peak and trough Hb levels to 12 and 8gms/dl had no significant effect on RDW-CV value. This may suggest that bone marrow is still active in these patients producing the abnormal red
cells. Our explanation for the unusual rise of RDW-CV in beta thalassemia major is due to anisopoikilocytosis (combination of anisocytosis and abnormal shapes of red cells). Our finding and explanation are encouraged by a review of Needs T et al in a review from Stat Pearls Publishing in 2018 stating that due to increased anisopoikilocytosis the RDW is raised as compared to other hypochromic anemias like beta thalassemia trait, iron deficiency anemia or a mixture of both.

CONCLUSION

RDW-CV is an important routine parameter on routine CBC without any extra cost. It can be used in an outpatient setting for the screening of beta thalassemia major / intermedia. This study may be helpful in patients who are not yet diagnosed but had received blood transfusions.

Author’s Contribution:
Concept & Design of Study: Nadeem Nusrat
Drafting: Mohammed Rizwan, Mohammed Salman Zafar
Data Analysis: Imran Bakar, Iram Nazir and Mohammed Usman
Revisiting Critically: Nadeem Nusrat, Mohammed Rizwan
Final Approval of version: Nadeem Nusrat

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

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Stent Thrombosis in Patients Treated with Ticagrelor in Acute Coronary Syndrome (ACS) Among Pakistani Population

Faisal Ahmed, Rubina Khan, Gul Naz, Chander Parkash, Muhammad Nawaz Khan and Ali Nasir

ABSTRACT

Objective: To observe the stent thrombosis with Ticagrelor and to assess the frequency of main cardiovascular (CV) events (CV death, MI and Stroke) in patients treated with Ticagrelor after PCI (Stenting) during 24 weeks.

Study Design: Observational study

Place and Duration of Study: This study was conducted at the department of Cardiology, Liaquat National Hospital, Karachi from March, 2020 to September, 2020.

Materials and Methods: A total of 320 patients between the age of 18-75 year, presenting with acute coronary syndrome were included for this study. Demographic variables like age and gender were recorded. BMI, clinical features and history of previous diseases were also noted. Ticagrelor (Anplag®) 90 mg bd was prescribed to the patients and was followed for 6 months for the occurrence of stent thrombosis, major cardiovascular events and adverse effects of Ticagrelor.

Results: The outcomes of present study showed that there were total 4(1.2%) cases of stent thrombosis. The result in the present study also showed that overall there were 12(3.75%) deaths due to all causes of mortality. The most common adverse effect after taking Ticagrelor within 24 weeks was nausea found in 37(11.6%) and the least common side effect was bleeding in 4(1.3%) cases. The other side effects including dyspnea and dizziness were also observed in 29(9.1%) and 32(10%) cases respectively.

Conclusion: This study concludes that stent thrombosis is uncommon in a patient who receives anti-platelet therapy with Ticagrelor (Anplag®) 90 mg bd. A major prospective of Ticagrelor is the extra ordinary reduction in death among acute coronary syndrome patients.

Key Words: Stent thrombosis, Ticagrelor, Acute Coronary Syndromes

INTRODUCTION

Acute Coronary Syndrome (ACS) has developed as a valuable operational term that can be defined as a group of conditions compatible with acute myocardial ischemia and/or infarction that are developed due to an immediate decline in coronary blood flow. Globally, the frequency and occurrence of cardiovascular diseases vary depending upon several factors that are socioeconomic status, health care systems, etc. Among cardiovascular diseases, ACS is one of the major reasons of morbidity and mortality.

Recent guiding principles recommend that the patients, who present with ACS, particularly ST segment elevation myocardial infarction (STEMI), must undergo primary percutaneous coronary intervention (PCI) in emergency in order to overcome both mortality and morbidity. Primary PCI has its own complications like other interventional procedures and stent thrombosis is the most important one in which stented vessel becomes occluded completely. Stent thrombosis is described as an occlusion of a coronary stent by a thrombus. It is associated with stent placement in percutaneous coronary intervention (PCI). High rates of morbidity and mortality occurs due to stent thrombosis, frequently leading to events of cardiac death or nonfatal myocardial infarction (MI). The aim of this study was to access the stent thrombosis with Ticagrelor in terms of, acute (<24 hours), sub-acute (24 hours–30 days) and late (>30 days up to 24 weeks) thrombosis and also to evaluate the incidence of major cardiovascular (CV) events (CV death, MI and Stroke) and adverse effects in patients pretreated with Ticagrelor after PCI (Stenting) during 24 weeks.
MATERIALS AND METHODS

This observational study by using non-probability convenient sampling technique was carried out at Liaquat National Hospital, Karachi. The ethical approval for the study was taken from Institutional Research and Ethical Committee (Ref:0510-2020-LNH-ERC). Duration of the study was 6 months from 15-03-20 to 15-09-20.

In this study, 320 patients presenting with ACS between the ages of 18-75 years, evidence of CAD, a previous history of MI, or previous revascularization with successful percutaneous coronary intervention with a stent after taking Ticagrelor (Anplag®, Pharm Evo Pvt Ltd, Karachi, Pakistan) 90 mg bd were enrolled for this study. Patients were followed for 6 months for the occurrence of stent thrombosis, major cardiovascular events and adverse effects of Ticagrelor. Exclusion criteria for this study were hypersensitivity to any component of Ticagrelor or contraindication for Ticagrelor, congestive heart failure, age ≥ 75 or < 18, pregnancy and breast feeding, limited life expectancy, bad prognosis due to another co-existing disease e.g. malignancy, liver failure or greater than 50% mortality in next 6 months and having cardiogenic shock. Demographic variables like age and gender were recorded. BMI, clinical features and history of previous diseases were also noted.

The Academic Research Consortium (ARC) guiding principle were published in 2008, described the classifications of stent thrombosis (6). These classifications were based on the type of underlying placement of stent and timing after initial placement of stent viz; acute, sub-acute and late. Early stent thrombosis can be acute or subacute: If thrombosis occurs within 24 hours of initial placement termed as acute. Sub-acute thrombosis occurs between 24 hours to 30 days after initial placement of stent. Furthermore, late stent thrombosis occurs between 30 days till 24th week of initial placement of stent.

Stent thrombosis can be classified into definite, probable, and possible stent thrombosis. Possible stent thrombosis, regarded as with unexplained reason of death in 30 days or later after stent placement. Probable stent thrombosis, regarded as mysterious death within 30 days of stent placement. Definite stent thrombosis in which angiography confirms the presence of stent thrombosis (within the existing stent or within 5 mm proximal or distal to the stent). Ticagrelor, which is classified as the anti-platelet medication, was given to patients with dosage of 90 mg bd.

Data was analyzed by using IBM-SPSS version 23.0. Counts with percentages given for baseline characteristics of studied samples, mean with standard deviation reported for quantitative measurements of samples. Outcomes on stent thrombosis, its risk factors, and major cardiovascular events were also reported with their count and percentages. Descriptive on adverse effects after taking Ticagrelor within 24-week, and compliance of medication were also reported in the tables. Pie diagram was given for graphical presentation of stent thrombosis.

RESULTS

Total 320 patients were included in the study after following the inclusion criteria. Table-1 shows the baseline characteristics of the patients. The mean age of samples was 58.41±10.43 years, mean systolic blood pressure was 125.5±17.66mmHg, mean diastolic blood pressure was 75.42±11.05 mmHg.

Table-II shows the co-morbid and clinical features of the patients, 233(72.8%) found with complain of chest pain, or discomfort, which may involve pressure, tightness or fullness, 202(63.1%) found with complain of discomfort in one or both arms, the jaw, neck, back or stomach, 136(42.5%) found with complain of shortness of breath, 19(5.9%) found with feelings of dizziness or lightheaded, 32(10%) found with Nausea, and 31(9.7%) with sweating. There were 224(70%) patients found with hypertension, 165(51.6%) with diabetes, 97(30.3%) with family history of IHD, 116(36.3%) with hyperlipidemia, 197(61.6%) with obesity and 16(5%) with chronic renal failure.

Table No.1: Baseline Characteristics of the patients (n= 320)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean±SD n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td></td>
</tr>
<tr>
<td>&lt;50 years</td>
<td>54(16.9%)</td>
</tr>
<tr>
<td>51 - 60 years</td>
<td>135(42.2%)</td>
</tr>
<tr>
<td>61 - 70 years</td>
<td>94(29.4%)</td>
</tr>
<tr>
<td>&gt;70 Years</td>
<td>37(11.6%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>218(68.1%)</td>
</tr>
<tr>
<td>Female</td>
<td>102(31.9%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>49(15.3%)</td>
</tr>
<tr>
<td>No</td>
<td>271(84.7%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.41±10.43</td>
</tr>
<tr>
<td>Systolic (mmHg)</td>
<td>125.5±17.66</td>
</tr>
<tr>
<td>Diastolic (mmHg)</td>
<td>75.42±11.05</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>70.28±11.062</td>
</tr>
<tr>
<td>Height (m²)</td>
<td>1.67±0.11</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.61±4.83</td>
</tr>
<tr>
<td>Heart rate (b/min)</td>
<td>78.50±11.91</td>
</tr>
</tbody>
</table>

Table 3 reported the frequency of major cardiovascular events in patients treated with Ticagrelor after PCI (stenting) during 24-weeks, incidence of MI was observed in 6(1.9%), and stroke was found in 3(0.9%). In the present study, overall there were 12(3.75%) deaths due to all causes of mortality. Out of them, 3(0.9%) were due to stent thrombosis and 9(2.8%) were due to unknown etiology. The adverse effects after taking Ticagrelor within 24-weeks were 4(1.3%) with bleeding, 29(9.1%) with dyspnea, 32(10%) with dizziness, and 37(11.6%) patients with nausea.
Figure I shows the frequency of stent thrombosis. There were total 4 cases of stent thrombosis, with only one case, (0.3%) of acute stent thrombosis classified into definite category, 2 (0.6%) cases of sub-acute stent thrombosis classified into probable category, and 1 (0.3%) case of late stent thrombosis classified into probable category.

Table No.2: Co-morbidities and Clinical features of patients (n=320)

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain or discomfort, which may involve pressure, tightness or fullness</td>
<td>233</td>
<td>72.8</td>
</tr>
<tr>
<td>Pain or discomfort in one or both arms, the jaw, neck, back or stomach</td>
<td>202</td>
<td>63.1</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>136</td>
<td>42.5</td>
</tr>
<tr>
<td>Feeling dizzy or light-headed</td>
<td>19</td>
<td>5.9</td>
</tr>
<tr>
<td>Nausea</td>
<td>32</td>
<td>10.0</td>
</tr>
<tr>
<td>Sweating</td>
<td>31</td>
<td>9.7</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>224</td>
<td>70.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>165</td>
<td>51.6</td>
</tr>
<tr>
<td>Family history of ihd</td>
<td>97</td>
<td>30.3</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>116</td>
<td>36.3</td>
</tr>
<tr>
<td>Obesity</td>
<td>197</td>
<td>61.6</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>16</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Table No.3: Frequency of Major Cardiovascular (CV) Events and adverse effects in Patients treated with Ticagrelor after PCI (Stenting) during 24 Weeks

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mi</td>
<td>6</td>
<td>1.9</td>
</tr>
<tr>
<td>Stroke</td>
<td>3</td>
<td>0.9</td>
</tr>
<tr>
<td>Adverse effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>4</td>
<td>1.3</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>29</td>
<td>9.1</td>
</tr>
<tr>
<td>Dizziness</td>
<td>32</td>
<td>10.0</td>
</tr>
<tr>
<td>Nausea</td>
<td>37</td>
<td>11.6</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Total deaths</td>
<td>12</td>
</tr>
</tbody>
</table>

DISCUSSION

Primary Percutaneous Coronary Intervention (PPCI) is a successful procedure for patients who are suffering from ACS. It decreases the chances of myocardial injury because the infarcted arteries are perfused without any delay. Hence, it reduces the mortality rate and results in better quality of life. A patient of ACS gets advantage from a good pre-treatment before PPCI. The typical analysis is that pre-treated with Ticagrelor can decrease the chances of thrombus formation in ACS patients undergoing PPCI, so resulting in considerably decreased all-cause mortality (8-11).

In our study, the frequency of major adverse events such as MI was 1.9% in patients with coronary artery syndrome. In a research by KimWJ et al. (12) the frequency of major adverse effects was 2% in patients with ischemic heart disease that were vascularized with eluting stents. In another study by Jensen LO et al. (13) the rate of incidence of major adverse events was 10.3% in patients pretreated with eluting stents. These findings were inconsistent with our result due to the pretreated with Ticagrelor that shows overall 3.75% deaths. Myocardial infarction occurred at rate of 1.9% in our observation. In study by Jensen LO et al. the frequency of myocardial infarction in patients with ischemic heart disease already treated with eluting stents was 1.9%. In another research by Kalesan B et al. (14) in which patients with acute coronary syndrome vascularized with eluting stents were studied, the frequency of myocardial infarction was 2.1%. In our study 3.75% patients showed CV death, 1.9% shows MI and 0.6% suffered from stroke. Repetition of ischemic condition at follow up is an important incident that needs revascularization of targeted lesion and vessels. In study by KimWJ et al. (12) recurrence of ischemia after revascularization with eluting stents needs to target vessel for revascularization was 0.7%. In similar study by Jensen LO et al. (13) recurrence of ischemia needing targeted vessel revascularization was 3.1%.

Stent thrombosis is an important reason of morbidity and mortality in patients vascularized with drug eluting stents. In study by KimWJ et al. the rate of occurrence of stent thrombosis including acute, sub-acute and late stent thrombosis was 0.7%. In another study Park D Wet al. (15) the frequency of stent thrombosis in patients revascularized with eluting stents was 0.7%. In another study in which patients with acute coronary syndrome were observed, it was 3.8%. In our study it was 1.2% pretreated with Ticagrelor which is almost similar to first two studies.

In another study that has reported the rate of early stent thrombosis (acute or sub-acute) after primary PCI was found to be 5.8%, of which 0.5% was acute and 5.3% were sub-acute (16). But our study showed that the rate of early stent thrombosis (acute or sub-acute) after primary PCI was found to be 0.9%, of which 0.3% was acute and 0.6% was sub-acute and in late stent thrombosis it was 0.3% which was relatively low.

In our study, dyspnea and nausea were more common adverse effects following treatment with Ticagrelor in 9.1% and 11.6% respectively. But occasionally, discontinuation of therapy decreases the persistent
adverse effects. Most observed cases of dyspnea were mild-to-moderate, occurred previously and lasted for few days with Ticagrelor therapy. However, most of the dyspnea-related cases in the study resolved after discontinuation of therapy shows that Ticagrelor-related dyspnea does not cause chronic pulmonary changes.

Finally, our study demonstrated that in 320 patients admitted for ACS, treated with Ticagrelor for 24 weeks resulted in fewer deaths. Moreover, it had proved that treatment with Ticagrelor helps in preventing CV death, MI or stroke\(^{(17)}\).

When the effectiveness of Ticagrelor therapy was checked across geographic regions, it had proved that the greater benefits may be achieved with Ticagrelor therapy among various categories of ACS patients. The Ticagrelor benefits remained considerably important as the reduction in the frequency of bleeding was observed in Ticagrelor-treated patients \(^{(18)}\).

In fact, different studies proved that clopidogrel, which is a pro-drug with a short-lived active metabolite, had a low potency and a slow onset of action in its biological effects. These limitations were responsible for the adverse effects of ischemic events that is stent thrombosis \(^{(19)}\). Hence, Ticagrelor is a faster and more potent P2Y\(_{12}\) inhibitor that showed an important clinical benefit in comparison with other drugs like clopidogrel in ACS because there is no need of hepatic biotransformation in order to become active. It is therefore, suggested as a first-line agent in ACS and it can be used safely in high-risk PCI patients with stable angina.

However, the study might not be immune from observer and selection bias. Further studies with larger sample size and probability sampling technique might be helpful to generalize the results in larger population.

**CONCLUSION**

Our study has predicted that the stent thrombosis is a major complication that is connected with stent placement in percutaneous coronary intervention, which can be reduced if pretreated with Ticagrelor (Anplag\(^{®}\)). Ticagrelor is an effective adjunctive pharmacotherapy in both early invasive as well as long-term management of a broad spectrum of Acute Coronary Syndrome patients by reducing the cases of all-cause mortality, stent thrombosis and myocardial infarction without a considerable difference in bleeding events in comparison with other anti-platelet therapy.

**Author’s Contribution:**

<table>
<thead>
<tr>
<th>Concept &amp; Design of Study:</th>
<th>Faisal Ahmed</th>
</tr>
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<tbody>
<tr>
<td>Drafting:</td>
<td>Rubina Khan, Gul Naz</td>
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<td>Data Analysis:</td>
<td>Chander Parkash, Muhammad Nawaz, Khan and Ali Nasir</td>
</tr>
<tr>
<td>Revisiting Critically:</td>
<td>Faisal Ahmed, Rubina Khan</td>
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</tbody>
</table>

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

**REFERENCES**

Effect of Zinc Supplementation on Heat Induced Gross Changes in Testes of Adult Mice

Mushtaq Ahmad¹, Bilal Hassan¹, Saif Abbass¹, Nauman Idris Butt², M Sabir² and Liaqat Ali²

ABSTRACT

Objective: To compare the effects of Zinc supplementation on heat induced gross changes in testes of adult mice with placebo.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Anatomy Department ANMC Islamabad and Anatomy Department Sialkot Medical College, Sialkot in collaboration with (N.I.H) Islamabad from January 2016 to May 2017.

Materials and Methods: Fifty-four adult male BALB/c mice were divided into two main groups. Control group of 18 mice and Experimental group of 36 mice. Control group was further divided into Normal control group of 9 mice and Experimental control group of 9 mice. Normal control group was given neither heat nor given any drug or placebo and were sacrificed on day 0 of the experiment. Experimental control group was given limited body heat and then sacrificed after 48 hours of heat exposure. Experimental group was further divided into two groups, Group C and Group D. Group C was further subdivided into C1, C2, C3.C1 was given limited body heat then placebo (Normal Saline) for 15 days, C2 for 30 days and C3 for 60 days. Group D was further subdivided into subgroups D1, D2, and D3. D1 was given limited body heat then ZnSO₄ for 15 days, D2 for 30 days and D3 for 60 days. 6 mice from group C were sacrificed on 15, 30 and 60 days each. 6 mice from group D were sacrificed on 15, 30 and 60 days each. Testes were dissected out for gross examination.

Results: Consistency was firm after heat exposure, weight was reduced but it regained after drug treatment.

Conclusion: Zinc supplementation completely reverses the gross changes produced by limited heat in testes of adult mice.

Key Words: Normal Saline, placebo, Testes, Zinc supplementation, ZnSO₄


INTRODUCTION

The testes are paired organs that are present in scrotum in the lower part of anterior abdominal wall. Each testis is divided into lobules by incomplete connective tissue septa that project from capsule¹. Each lobule of testis consists of seminiferous tubules which are highly convoluted. These seminiferous tubules contain Spermatogenic cells and sertoli cells. The Spermatogenic cells are derived from primordial germ cells which originate in yolk sac during early development of testis². Sperms are produced in these tubules. In the interstitial spaces between seminiferous tubules are present Leydig cells, these Leydig cells secrete testosterone under effect of anterior pituitary gland³.

In humans testis develop in abdominal region and at 26th week of gestation descend into scrotum. During descent from abdomen to scrotum testes carry with them the blood vessels, nerves, lymphatics, ductus deferens and an extension of abdominal peritoneum called tunica vaginalis². Within scrotum temperature is 2c to 8c low than core body temperature⁴. This lower body temperature is essential for spermatogenesis but low temperature is not required for steroidogenesis⁵.

Thermoregulation in testis is very important as slight increase in temperature can cause disruption of spermatogenesis and ultimately problems with fertility. With the exception of elephants and whales most mammals have a scrotum and scrotal temperature is always lower than that of abdomen⁶. The tone of dartos muscle in scrotum and countercurrent heat exchange between testicular artery & pampiniform plexus play their role in maintaining testicular temperature at low⁷.
Occupational exposure to high temperatures in men impairs testicular function. Depending on period of arrest it leads to partial or complete Spermatogenic arrest in these workers. After heat stress increased metabolism in testes may not be met with sufficient increase in blood flow and testes become hypoxic. Hypoxia then results in cell cycle arrest and apoptosis. Although testes require Zinc for spermatogenesis, sperm viability and motility, and its deficiency compromise fertility in men. Intracellular zinc functions to improve sperm oxygen uptake, sperm capacitation and in vitro fertilizing ability of spermatozoa, yet insufficient work has been done to see the reversal effects of Zinc on heat induced changes on testes in our country. Therefore, current study has been done to observe the effects of zinc supplementation on heat induced gross changes in testes of adult mice.

MATERIALS AND METHODS
This experimental study was performed at Anatomy Department Al-Nafees Medical College and Hospital Islamabad, in collaboration with National Institute of Health (N.I.H) Islamabad from January 2016 to May 2017 after approval from IRBC (letter number F.2/IUIC-ANMC/EC-86/2015). 54 adult male BALB/c mice, with age of 50-100 days were procured from NIH Islamabad. The mice were segregated by simple random selection and then divided into control and experimental groups. The mice of group A (Normal Control Group) were neither given heat nor were they given any drug or placebo. The mice were sacrificed by cervical dislocation at the start of experiment on day 0. Testes were dissected out, gross features were noted. The mice of group B (Experimental Control Group) were anesthetized by giving ketamine 100mg/kg and xylazine 10mg/kg. Then mice of this group were exposed to limited heat by submerging the hind legs, scrotal area and tail in a water bath which was maintained at temperature 43˚C for 15 minutes on the day 0 of the experiment. They were sacrificed by cervical dislocation 48 hours after heat exposure. Testes were dissected out, gross features were noted. The mice of group C were anesthetized by giving ketamine 100mg/kg and xylazine 10mg/kg. Then mice of this group were exposed to limited heat by submerging the hind legs, scrotal area and tail in a water bath which was maintained at temperature 43˚C for 15 minutes on the day 0 of the experiment. They were divided into subgroups C1, C2 and C3. Mice of subgroup C1 were given 0.2ml orally 0.9%NaCl for 15 days. Mice of subgroup C2 were given 0.2ml orally 0.9%NaCl for 30 days. Mice of subgroup C3 were given 0.2ml orally 0.9%NaCl for 60 days.

The mice of group D were anesthetized by giving ketamine 100mg/kg and xylazine 10mg/kg. Then mice of this group were exposed to limited heat for 15 minutes by submerging the hind legs, scrotal area and tail in a water bath which was maintained at temperature 43˚C on the day 0 of the experiment. Then they were divided into subgroups D1, D2 and D3. Mice of subgroup D1 were given ZnSO₄ orally for 15 days, Mice of subgroup D2 were given ZnSO₄ orally for 30 days. Mice of subgroup D3 were given ZnSO₄ orally for 60 days, testes were dissected out, gross features were noted, consistency was noted using gloved hands and weight was measured using an electronic weight machine. %ages of mice were calculated for consistency, while weight was measured in mg for testes, mean ±SD were calculated.

Data Analysis: Data were analyzed using SPSS version 20. Student’s t-test was applied and results with p values ≤ 0.05 were taken as statistically significant.

RESULTS
Consistency of testes: Consistency was firm in group B (100%), in subgroup C1 83.33% was soft and 16.67% was firm, subgroup C2 83.33% was soft and 16.67% was firm, subgroup C3 100% was soft. In subgroup D1 83.33% was soft and 16.67% was firm, in subgroups D2 and D3 consistency was soft 100% which shows that limited body heat changed the consistency of testes from soft to firm (Group B). After placebo (Normal Saline) given consistency returned to soft after 60 days (group C) and after ZnSO₄ treatment consistency of testes returned to soft form in 15 to 30 days.

Weight of testes: On comparison of weight of experimental control group B with subgroups of group C and D, statistically significant results were achieved. Limited body heat decreased the weight of testes (Group B). by giving placebo (Normal Saline) weight of testes returned towards normal in 60 days (Group C) and by giving ZnSO₄ the weight of testes returned to normal in 15 days.

Table No.1: Comparison of Mean Weight of Testes in mg ± SD

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean weight in mg ± SD</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.2133±0.13</td>
<td>0.01*</td>
</tr>
<tr>
<td>B</td>
<td>0.210±0.01</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.196±0.13</td>
<td>0.01*</td>
</tr>
<tr>
<td>C1</td>
<td>0.196±0.13</td>
<td>0.03*</td>
</tr>
<tr>
<td>C2</td>
<td>0.196±0.13</td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>0.211±0.01</td>
<td>0.02*</td>
</tr>
<tr>
<td>D</td>
<td>0.210±0.01</td>
<td></td>
</tr>
<tr>
<td>D1</td>
<td>0.211±0.01</td>
<td>0.04*</td>
</tr>
<tr>
<td>D2</td>
<td>0.212±0.01</td>
<td>0.03*</td>
</tr>
<tr>
<td>D3</td>
<td>0.213±0.01</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

F.2/IUIC/ANMC/EC-86/2015.54 adult male BALB/c mice, with age of 50-100 days were procured from NIH Islamabad, in collaboration with National Institute of Health (N.I.H) Islamabad from January 2016 to May 2017 after approval from IRBC (letter number F.2/IUIC-ANMC/EC-86/2015).
Table No.2: Comparison of Consistency of Testes in Control and Experimental Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Consistency</th>
<th>Soft</th>
<th>Firm</th>
<th>Firm to Hard</th>
<th>Hard</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>18 / 18 = 100%</td>
<td>0 / 18</td>
<td>0 / 18</td>
<td>0 / 18</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td>0 / 18</td>
<td>18 / 18 = 100%</td>
<td>0 / 18</td>
<td>0 / 18</td>
</tr>
<tr>
<td>C1</td>
<td></td>
<td>10 / 12 = 83.33%</td>
<td>2 / 12 = 16.67%</td>
<td>0 / 12</td>
<td>0 / 12</td>
</tr>
<tr>
<td>C2</td>
<td></td>
<td>10 / 12 = 83.33%</td>
<td>2 / 12 = 16.67%</td>
<td>0 / 12</td>
<td>0 / 12</td>
</tr>
<tr>
<td>C3</td>
<td></td>
<td>12 / 12 = 100%</td>
<td>0 / 12</td>
<td>0 / 12</td>
<td>0 / 12</td>
</tr>
<tr>
<td>D1</td>
<td></td>
<td>10 / 12 = 83.33%</td>
<td>2 / 12 = 16.67%</td>
<td>0 / 12</td>
<td>0 / 12</td>
</tr>
<tr>
<td>D2</td>
<td></td>
<td>12 / 12 = 100%</td>
<td>0 / 12</td>
<td>0 / 12</td>
<td>0 / 12</td>
</tr>
<tr>
<td>D3</td>
<td></td>
<td>12 / 12 = 100%</td>
<td>0 / 12</td>
<td>0 / 12</td>
<td>0 / 12</td>
</tr>
</tbody>
</table>

DISCUSSION

This study is of experimental type. This study highlights the significance of zinc supplementation for treatment of infertility especially in subjects working in extremes of temperature. Out of various techniques used in past for germ cell apoptosis, we used technique of submerging hind legs, tail and scrotal areas of mice in a water bath maintained at 43°C for 15 minutes after anesthetizing animals. Zinc has its well defined role in spermatogenesis, sperm viability and motility yet sufficient work was not done in our country to see the effects of zinc on heat induced changes in testes of mice. Therefore, current study has been done to see effects of zinc supplementation on heat induced changes in testes of mice. Our study shows that limited body heat to testes reduces weight. A similar study done by Kanter M. et al in 2013 showed decrease in weight of rat testes by 40% after local heat of 43°C for 30 minutes. Another study done by Mura M. et al in 2002 showed decrease in testicular weight by 50-60% after 14 days of scrotal heat. Still another study done in 2008 by Paul C. et al showed reduction in weight of testes by 40% and 60% after 7 and 14 days post heat exposure to testes respectively. The weight of testes is reduced after exposure to heat due to increase in loss of germ cells.

In a study done on rat testes by Yetertopcu et al. in 2009 Carnitine was used as antioxidant after apoptosis was done by irradiation. At 21, 44 and 70 days post irradiation the rat testes showed significant increase in weight as compared to controls. Carnitine has antioxidative activity and it protects cellular DNA and membranes against free radical injury.

Future recommendations for our study are that electron microscopic studies should be done on testes of mice after limited body heat. In this way the cellular changes can be evaluated for decrease in weight of testes and change of consistency of testes to firm after heat exposure. And after treatment with zinc how these cellular changes are reversed so that weight of testes increases back to normal weight of testes and consistency of testes changes back to soft after zinc treatment.

CONCLUSION

Our study showed that zinc supplementation completely reversed the heat induced gross changes in testes of adult mice and on comparing its effect with placebo, zinc supplementation performs its function more rapidly and early.

Author’s Contribution:
Concept & Design of Study: Mushtaq Ahmad
Drafting: Bilal Hassan, Saif Abbass
Data Analysis: Nauman Idris Butt, M Sabir, Liaquat Ali
Revisiting Critically: Mushtaq Ahmad, Bilal Hassan
Final Approval of version: Mushtaq Ahmad

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

REFERENCES

ABSTRACT

Objective: This study evaluated the frequency of vaginal candidiasis among pregnant women.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Antenatal Care Clinic Sheikh Zaid Hospital Larkana from February 2019 to June 2020.

Materials and Methods: A total of 384 pregnant women were included in the study at High vaginal swabs were taken from these women for gram staining and culture to diagnosis the candidiasis.

Results: A total of 384 samples of pregnant women were examined, 216 were positive, the frequency of vaginal candidiasis showed 56.2%. The age group 21 to 30 years showing the highest number 133(61.6%) of positive candidiasis. Multigravida 188(87%) was more commonly affected than primigravida 28(13%) and commonly seen in the third trimester 136(63.0%).

Conclusion: In the study, a very high frequency of vaginal candidiasis was observed among women, so there is a keen need for related health education programs for awareness, besides effective antenatal care system for early diagnosis/screening as well as prompt treatment of vagina candidiasis in pregnant women.

Key Words: Frequency, Vaginal, Candidiasis, Women, Clinic

INTRODUCTION

Vaginal candidiasis is characterized by vaginal discharge (like curd) and itching and is linked with a lot of trouble for the patient. Increased incidence in pregnancy and can cause complications such as miscarriage, preterm childbirth, Candida chorioamnionitis, and others.¹ Vaginal candidiasis typically called "yeast infection", commonly occur during pregnancy,² so more than 20 species of Candida yeast that can cause infections in humans, such as pruritus, soreness, burning sensation, and irritation, sometimes accompanied by dysuria.³,⁴ Numerous species are innocuous commensals or endoosimbians of the host; including humans. In any case, when the mucosal protection is upset or there is a weak immune response, after antibiotics, and

usually during pregnancy.⁵,⁶ Estimated prevalence of vaginal candidiasis up to 75%, and mostly occur in 20-30 years age group.⁷,⁸,¹²,¹³ In developing countries, there are scanty data regarding the frequency of vaginal candidiasis. According to our best knowledge, some studies had examined the frequency of vaginal candidiasis among pregnant women in Pakistan, which was between 26.9 and 48 percent.⁹,¹⁰,¹⁵ Currently, studies showed that the frequencies of vaginal candidiasis during pregnancy in different countries such as in a lebanian study conducted on 258 pregnant women showed 39%¹¹, another Ghana study showed 30.7% prevalence conducted, on 176 sample size.¹² During pregnancy, enhance the levels of progesterone as well as estrogen hormones.⁷ Due to progesterone, reduction in the power of neutrophils to fight the Candida while estrogen disturbs the defense of epithelial cells of the vagina against the infectious agent like yeast. and reduces the immunoglobin in genital secretion. During pregnancy, these problems remain continuous, lend themselves to various recurrence.¹³ During pregnancy, vaginal candidiasis may be prolonged and more severe symptoms, and for these solutions usually of long-term treatment is required.¹⁴ Therefore, in this scenario, such studies can improve the clinical condition of women and newborns by early examination, early diagnosis, and proper treatment.
MATERIALS AND METHODS

A cross-sectional (observational) study was carried out among 384 pregnant women who were attending the care unit of SZ hospital Larkana. During antenatal visits consented pregnant women’s sociodemographic, clinical data were taken, as well as screening samples were taken for pathological analysis.

**Sampling technique**: Convenience (non-randomized) sampling technique.

**Sample Size**:
The Sample size was calculated according to formula⁷ and the assuming frequency of vaginal candidiasis 48%, so the sample size is calculated as under:
Sample size= \( \frac{Z^2 \times p \times (1-p)}{C^2} \)
Sample size= \( 3.8416 \times 0.48 \times 0.52 \div 0.0025 \)
Sample size= 383.53
therefore, the sample size of 383.53 subjects of the study were calculated.

**Sampling criteria**

- **Inclusion criterion**:
  - Known pregnant woman,
  - During any period of pregnancy (All 03 trimesters)
  - Vaginal discharge history

- **Exclusion criterion**:
  - Unmarried women
  - Menstruation history
  - Pregnant women with known secondary diseases such as chronic disease e.g: Diabetes, HIV, TB, on immunosuppressive therapy,
  - Use of antibiotics during the last week

**Data analysis**: SPSS version 16 was applied for data analysis. The mean and SD were applied for quantitative variables such as age and a t-test was applied. Ratio and proportion were calculated for qualitative data etc and chi-square tests were applied. P-value <0.05 was consider significant.

RESULTS

The cross-sectional (observational) study, comprised 384 pregnant women of all trimester who participated at antenatal care clinic SZ hospital CMC/SMBB Medical University Larkana. All the subjects were analyzed regarding their age, residency, parity, trimester of pregnancy, sign and symptoms like vaginal discharge, smell, itching, redress, dysuria, use of antibiotics and others, etc

Upon analysis of the entire data, out of the 384 pregnant women examined, 216 were Candida positive, thus indicating a frequency level of vaginal candidiasis 56.2 percentages in the study population. Fig: 1
In frequency data, other variables showed the mean age of pregnant women was 27.4297 ±0.203 years and the range between 15-39 years was recorded. According to the age group (21 to 30 years) seemed more presentation 249(64.8%) in study as compared to 31 to 40 years 94(24.5%) and very low in <20 years 41(10.7%) age group while above 41 years no any case respectively.

Table 1. Pregnant women, during third trimester 227(59.1%) seemed more frequent as compared to the 2nd and 1st trimester. Analysis of parity distribution showed that the majority of women were recorded in multigravida 321(83.6%) and only 63(16.4%) were in primigravida, furthermore in residency, urban women 234(60.9%) seemed more than rural resident 150(39.1%).

<table>
<thead>
<tr>
<th>Table No.1: Frequencies Data Sociodemographic and Other Variables</th>
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</thead>
<tbody>
<tr>
<td>Frequency Data Of Demographic &amp; Other Variables</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>&lt;20 years</td>
</tr>
<tr>
<td>21-30 years</td>
</tr>
<tr>
<td>31-40 years</td>
</tr>
<tr>
<td>&gt;41 years</td>
</tr>
<tr>
<td><strong>Residence</strong></td>
</tr>
<tr>
<td>Urban</td>
</tr>
<tr>
<td>Rural</td>
</tr>
<tr>
<td><strong>Gestation</strong></td>
</tr>
<tr>
<td>First trimester</td>
</tr>
<tr>
<td>Second trimester</td>
</tr>
<tr>
<td>Third trimester</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
</tr>
<tr>
<td>Primigravida</td>
</tr>
<tr>
<td>Multigravida</td>
</tr>
<tr>
<td><strong>Vaginal Itching</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Vaginal redness</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Dysuria</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Discharge smell</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Use of antibiotic</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Vaginal Candidia</strong></td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Positive</td>
</tr>
</tbody>
</table>
The main signs and symptoms frequencies were observed in pregnant women were vaginal itching 310(80.7%), redness 239(62.2%), dysuria 156 (40.6%) and smell 142(37.0%). In the laboratory, for diagnosis of candidiasis species, a high frequency of candidiasis species 216(56.2%) was observed in culture, while wet mount preparation and gram’s stain showed 324(84.4%) and 336 (87.5%) respectively.

On the bivariate analysis between the frequency of vaginal candidiasis with other variables like age showed a high prevalence of vaginal candidiasis was observed in 21 to 30 years age group 133(61.6%); but relatively very low below the ages of 20 years 19(8.8%), significant associated(p=0.019). Table 2. Table 2 A very high significant prevalence rate of vaginal candidiasis was observed in the 3rd trimester136(63%) of pregnancy as compared to a rate of 58(26.9%) and 22(10.2%) in the 2nd and 1st trimesters, respectively (p=0.038), as shown Table 2.

Table No.2: Summarized Data Analysis Vaginal candidiasis with variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 years</td>
<td>19</td>
<td>0.019</td>
</tr>
<tr>
<td>21-30 years</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>31-40 years</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td>0.255</td>
</tr>
<tr>
<td>Urban</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Gestation</td>
<td></td>
<td>0.038</td>
</tr>
<tr>
<td>First trimester</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Second trimester</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Third trimester</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td>0.027</td>
</tr>
<tr>
<td>Primigravida</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Multigravida</td>
<td>188</td>
<td></td>
</tr>
<tr>
<td>Vaginal Itching</td>
<td></td>
<td>0.036</td>
</tr>
<tr>
<td>Yes</td>
<td>167</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Redness</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Dysuria</td>
<td></td>
<td>0.020</td>
</tr>
<tr>
<td>Yes</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>118</td>
<td></td>
</tr>
<tr>
<td>Discharge smell</td>
<td></td>
<td>0.060</td>
</tr>
<tr>
<td>Yes</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>163</td>
<td></td>
</tr>
<tr>
<td>Use of antibiotic</td>
<td></td>
<td>0.383</td>
</tr>
<tr>
<td>Yes</td>
<td>02</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>214</td>
<td></td>
</tr>
</tbody>
</table>

The high parity distribution showed among multigravida women that 188(87.0%) while 28(13%) were prim gravidae. significant relationship (p=0.027) Distribution of clinical presentation among vaginal candidiasis showed significant association vaginal itching 167(77.3%), redness 150(69.4%), and dysuria 98(45.4%), whereas residency, vaginal smell, use of antibiotic showed no significant association.

**DISCUSSION**

The study showed a high frequency (56.2%) of vaginal candidiasis during pregnancy as compared to other studies previously observed in the state. To my best knowledge, in Pakistan, mostly the frequency rate of vaginal candidiasis in pregnancy ranges between 26.9% to 48% was observed in different regions. Furthermore many current studies like Nigerian, Indian, and many studies revealed the current studies. Table 1. vaginal candidiasis is more prevalent among pregnant women within the 21 to 30 years age group 133(61.6%) and declines after the age between 31-40 years (29.6%), which is statistically significant (p<0.05).

Infection, in this group seemed more frequent than other group may be due to increased sexual activity and it is certainty that in this age group may possibly increase the use of contraceptives and use of drugs to prevent the pregnancy. Many studied that revealed the current study.
The high-frequency rate of vaginal candidiasis was observed in the third trimester 136(63.0%), which is more than double and after that second trimester 58(26.9%) and showed statistically significant (p=0.038) as well as corresponding with previous studies.9,16,12

The explanation behind this is that during pregnancy, generally in the third trimester, high glycogen collects in the vagina because of elevated levels of estrogen, and good provision of carbon, which help the multiply of Candida species. Additionally, estrogen hormone enhances the candidias’ affinity for the yeast cytosol receptor in epithelial cells of vaginal.24

The reason for this is that during pregnancy, mostly in the third trimester, high glycogen accumulates in the vagina as a result of high levels of estrogen, and provides a good source of carbon, which supports the spread of Candida species. Also, estrogen hormone enhances the affinity of Candida for the yeast cytosol receptor in vaginal epithelial cells.24

On analysis of parity distribution showed significantly more in multigravida 188(87%), whereas 28 (13. %) were in prim gravidae. Similar results were generated in another study.1,7,16,23

The study showed that vagina candidiasis developed more in multigravida women, due to longer sex history and increase number of pregnancies than the prim gravidae who have less sexual exposure.9

Vaginal candidiasis is usually diagnosed on clinical presentations alone, while as many as half of these women may have other conditions with similar symptoms.12 In the present study mostly the clinical presentation seemed in vaginal candidiasis such as vaginal discharge 216(100%), itching 167(77.3%), redness 150(62.2%), dysuria 98(45.4%) and smell 53(24.5%). Shailaja S. D et al and A Maleeha et al founded similar presentation of vaginal candidiasis in pregnant women.20,7

CONCLUSION

In this study, vaginal candidiasis infection is observed more frequent among pregnant women, represent a major health concern. In this scenario, a great need of to improve the antenatal care, proper routine examination, early diagnostic screening, treatment and health education of vaginal candidiasis. Therefore, further studies and to assess the potential factors that prevents and reduce burden of disease.

Author’s Contribution:
Concept & Design of Study: Lubna Naz
Drafting: Shabnam Naz, Vijia Kumar Gennani
Data Analysis: Kanwal Gul, Sarmad Jamal Siddiqui, Pritiya
Revisiting Critically: Lubna Naz, Shabnam Naz

Final Approval of version: Lubna Naz

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

REFERENCES


23. A prevalence study of vaginal candidiasis among pregnant women Pooja Sutaria1*, Meera Cholera2, Shilpa B. Donga3

Association of Maternal Renal Artery Resistive Index with Serum Uric Acid in Gestational Hypertension

Kevin Joseph Jerome Borges¹, Syed Nudrat Nawaid Shah¹, Madeeha Sadiq¹, Shazia Hashmat², Nuzhat Hassan¹ and Syed Tousif Ahmed²

ABSTRACT

Objective: To quantitatively study the correlation between maternal renal artery resistive index (RARI) and levels of serum UA in Pregnancy Induced Hypertension.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Ziauddin Hospital from June-2017 to May-2018.

Materials and Methods: 90 females with PIH were included after ruling out conditions affecting renal artery flow other than PIH. Doppler ultrasound examinations were carried out at 36 weeks’ gestation and maternal RARI and serum UA was noted. Regression analysis and Pearson’s correlation were done to determine the relation of RARI and UA with each other.

Results: A highly significant (p=0.001) moderate (r=0.52) positive correlation between RARI and serum UA was observed.

Conclusion: We demonstrated that as RARI increases, so does the plasma level of UA. This can be directly attributed to decrease in blood flow to the renal arteries in PIH which has an inverse relation to RARI. This is the first study to our knowledge to quantify the relation of serum uric acid to RARI. We conclude that RARI could be a useful non-invasive and cost-effective tool in assessing the severity of PIH.

Key Words: Resistive Index, Uric Acid, Pregnancy Induced Hypertension

INTRODUCTION

Gestational hypertension for some reason has been increasing in incidence worldwide. It increases the risk of maternal as well as neonatal morbidity and mortality.¹ Its prevalence varies in different parts of the world with an average worldwide prevalence of 7.8%.² Different factors have been considered to be culprits developing GH at different points in time. Some of these factors are include hypoxia, diet, prostacyclin/thromboxane ratio imbalance, intravascular volume contraction, endothelial injury and genetic predisposition.³⁴ Whatever the underlying cause, at the core of the changes occurring in these conditions lies a defective trophoblast invasion.⁵

Altered supply of blood to the placenta causes release of certain factors in maternal circulation causing altered metabolic pathways. All this ends up in increasing the maternal blood pressure.⁶ Studies have also shown that due to hypoxia, soluble fms-like tyrosine kinase (sFlt-1) is released in greater amounts. This antagonizes vascular endothelial growth factor (VEGF) and placental growth factor (PIGF). Both of these are vasodilators as well as inducers of angiogenesis.⁷ As these factors are antagonized, the trophoblast finds it difficult to invade the spiral arteries of the uterus, thus resulting in decreased fetoplacental circulation. Relationship between the rising levels of soluble endoglin and ratios of sFlt1: PIGF, and the onset of preeclampsia has also been demonstrated.⁸ Elevated uric acid and diminished prostacyclin levels are also known to be related to hypertensive pregnancies. As a matter of fact, uric acid has been proven to be as important as proteinuria in identifying fetal outcomes in PIH.⁹ Placental morphometric differences have been seen between normal and hypertensive pregnancies. Uric acid is produce breakdown of purine nucleotides. About 70% of uric acid in the body is excreted via urine. So any change in glomerular filtration rate (GFR) should directly influence the plasma uric acid level.¹⁰,¹¹,¹²

The gold standard tool till date to pick variations in circulation is Doppler Ultrasound.¹³,¹⁴,¹⁵ Studies done previously have proven that Doppler waveforms are important predictors of pregnancy outcome. The
Resistive Index (RI) specifically shows the resistance to flow of blood through an artery. Studies have shown higher values of RI in abnormal pregnancies as compared to normal and Doppler Indices overall have been shown to be a good tool in prediction of pregnancy outcome. The study was a cross-sectional study. Written consent was taken from all participants. 90 patients were recruited. Blood pressure readings of equal to or greater than 140/90mmHg at two separate points in time at least two weeks apart was defined as PIH.

MATERIALS AND METHODS
The study was a cross-sectional study. Written consent was taken from all participants. 90 patients were recruited. Blood pressure readings of equal to or greater than 140/90mmHg at two separate points in time at least two weeks apart was defined as PIH.

Inclusion Criteria:
- Parity 1 to 3
- Confirmed gestational age (LMP + Ultrasound)
- Women registered at any campus of Ziauddin University Hospital before eighteenth week gestation
- Normotensive till twentieth week

Exclusion Criteria:
- Essential Hypertension
- Twin, Triplet or more pregnancy
- Any surgery of uterus previously
- Placenta Praevia
- Leiomyoma
- Congenital uterine anomaly
- Abnormal vaginal discharge or bleeding
- Vascular Disorders
- Diabetes (Mellitus or Gestational)
- Fetus with congenital anomaly
- Previous delivery before term
- Use of any addictive drug

A single operator carried out Doppler ultrasound examinations noting down maternal Renal Artery Resistive Index. A mean of three values was recorded. The study was approved by the Ethical Review Committee, Ziauddin University, Karachi.

Statistical Analysis: Data was fed and analyzed on SPSS ver20.0. General characteristics such as age, gestational age and weight are given as mean and standard deviation. Regression analysis and Pearson’s correlation has been used to evaluate the correlation between renal artery resistive index and uric acid levels. In all analysis, a p-value <0.05 was considered as significant.

RESULTS
Table-1 shows the general characteristics of the subjects included in the study. Table-2 shows a highly significant moderate positive correlation between RI and UA

Figure 1 graphically depicts the highly significant moderate positive correlation between renal artery RI and serum UA.

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
</tr>
<tr>
<td>1 (Constant)</td>
<td>.406</td>
<td>.869</td>
</tr>
<tr>
<td>RI</td>
<td>4.580</td>
<td>1.358</td>
</tr>
</tbody>
</table>

DISCUSSION
Numerous physiologic changes occur in the maternal body during pregnancy which include increase in blood volume with increased renal blood flow resulting in increased glomerular filtration rate. All these changes eventually decrease the uric acid concentration in serum. Similarly, uricosuric effect of estrogen also contributes significantly to the decline in UA levels in normal pregnancy.
However, in gestational hypertension there is a reduction in renal blood flow and in glomerular filtration rate which is known to increase the levels of urea in serum.\textsuperscript{24,25}

Our study demonstrates this effect using a non-invasive parameter called renal artery resistive index (RI). As the renal artery RI increases, so does the plasma level of UA. This can be directly attributed to the decrease in blood flow to the renal arteries in gestational hypertension which in our case is being represented by an increase in renal artery RI. As the flow to the kidneys decreases, the clearance of UA also decreases leading to its accumulation in blood. Similarly, there have been associations found in diseases with affect renal blood flow and serum uric acid but, none to our knowledge have been able to quantify it with relation to renal artery RI.\textsuperscript{26}

Studies done in the past have shown an association of these parameters with hypertension.\textsuperscript{27} Increased levels of UA have been shown to activate the renin-angiotensin-aldosterone system (RAAS). UA achieves this due to increased oxidative stress by increasing the levels of reactive oxygen species within certain cells like adipocytes. This in turn causes overexpression of the RAAS gene which ultimately leads to systemic hypertension.\textsuperscript{28}

Gestational hypertension is also associated with placental ischemia.\textsuperscript{29} Also reported in literature is that tissue ischemia results in increased conversion of adenosine triphosphate to adenosine and xanthine. Levels of xanthine oxidase are also increased in the ischemic tissue which further enhances the conversion of xanthine into uric acid and production of super oxide anions.\textsuperscript{30,31,32}

The two mechanism stated above lead to a chicken and egg dilemma but none the less start a vicious cycle which contributes to the many complications associated with gestational hypertension.

These findings could prove UA to be a useful tool assessing the severity of gestational hypertension in a non-invasive manner ultimately helping in prevention of end organ damage.

**CONCLUSION**

The study shows that in women with gestational hypertension, the blood flow to the kidneys decreases, hence forth affecting the clearance of uric acid resulting in its accumulation in blood. The accumulated uric acid activates the rennin angiotensin system causing further hypertension. This starts a vicious cycle which, if not controlled can lead to further complications.

**Author’s Contribution:**

Concept & Design of Study: Kevin Joseph Jerome Borges
Drafting: Syed Nudrat Nawaid Shah, Madeeha Sadiq Hassan Hashmat, Nuzhat Hassan, Syed Tousif Ahmed

Revisiting Critically: Kevin Joseph Jerome Borges, Syed Nudrat Nawaid Shah

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

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Comparison of Early Versus Delayed Laparoscopic Cholecystectomy in Acute Cholelithiasis

Liaqat Ali Zia, Muhammad Khalid, Mudassir Rasool, Imran Amin, Muhammad Ansar Aslam and Hafiz Muhammad Khizar Nawaz Cheema

ABSTRACT

Objective: To compare the early versus delayed laparoscopic cholecystectomy in acute cholelithiasis.

Study Design: Descriptive Study

Place and Duration of Study: This study was conducted at the DHQ Teaching Hospital Gujranwala during May 2019 till October 2019.

Materials and Methods: This study was conducted with the permission of ethical committee of hospitals. There were 50 patients that were included in this study. All patients were subjected to laparoscopic cholecystectomy.

Results: The data was collected from 50 patients. The data was divided into two groups, one was early group and one was delayed group. Both groups contain 25 patients. The data of these two groups were compared in terms of age, pathological parameters and ultrasound findings.

Conclusion: It is concluded that both methods of laparoscopic cholecystectomies are reasonable and safe in acute cholecystitis patients.

Key Words: Biliary, LC, Patients, Randomized

INTRODUCTION

Biliary diseases are a disorder of major portion of digestive tract. Among these is cholelithiasis, which causes general medical affliction, and henceforth requires careful intercession for all out fix. Gallstone disease is multiple times more normal in women than men1. Acute cholecystitis is a significant intricacy of gallstones. In the previous a very long while, research has been conducted along a few roads to develop less obtrusive, less agonizing, and more affordable methods of gallstone treatment. Such methods like oral desaturation agents, contact dissolution agents, and extracorporeal stun wave lithotripsy, are limited by stone substance, size, and number2.

In addition, they leave a flawless gallbladder already known to hold lithogenic bile. In this way, these nonoperative methods are inadequate for an enormous extent of gallstone patients and can't guarantee a lasting fix from gallstone disease3.

Henceforth, cholecystectomy remains the treatment of decision for gallstone disease. Open cholecystectomy remains the criterion for suggestive cholelithiasis for longer than a century. Nonetheless, in the most recent decade, the introduction of LS strategy to perform cholecystectomy has revolutionized this procedure4.

Two methodologies are accessible for the treatment of acute cholecystitis; the main methodology is ahead of schedule (inside 7 days of beginning of manifestations)5,6 laparoscopic cholecystectomy (LC) as definitive therapy subsequent to setting up diagnosis and careful wellness of the patient in a similar emergency clinic admission. The other methodology is moderate treatment which is effective in 90% of the cases and then delayed cholecystectomy is performed in the hospital admission after a time frame 10 weeks7. The decision of approach depends upon clinic framework, careful ability, and patient's condition.

The main objective of the study is to compare the early laparoscopic delayed laparoscopic cholecystectomy in acute cholelithiasis.

MATERIALS AND METHODS

This descriptive study was conducted in DHQ Teaching Hospital Gujranwala during May 2019 till October 2019. This study was conducted with the permission of ethical committee of hospitals. There were 50 patients that were included in this study.

Data Collection: The data was collected from acute cholecystitis patients and they randomly assigned to receive either early laparoscopic cholecystectomy...
within 72 hours of admission or initial conservative treatment followed by delayed interval surgery 5-10 weeks later. On admission, a detailed history was taken. Intensive general physical assessment and foundational assessment was done for each patient. Important investigations were done, which included total hemogram, pee assessment, urea, creatinine, blood sugar, serum electrolytes, LFT’s, serum amylase, and lipase where indicated, besides X-beam chest, electrocardiogram, and USG abdomen. Postoperatively, the patients were allowed oral admission 5-10 hrs after medical procedure in the event that they had no sickness or spewing. Help with discomfort was obtained by intramuscular diclofenac infusion, which was changed to oral once quiet was allowed orally.

The data was collected from 50 patients. The data was divided into two groups, one was early group (Group A) and one was delayed group (Group B). Both groups contain 25 patients. The data of these two groups were compared in terms of age, pathological parameters and ultrasound findings.

In our study, conversion to open cholecystectomy was done in 4 patients due to dense adhesions. The early LC was done in 19 patients and delayed LC was done in 21 patients. Conversion rate of OC was 15% in early group and 9% in delayed group.

RESULTS

Table No.1: USG findings in Group A and Group B

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distended GB</td>
<td>6 (24.7%)</td>
<td>6 (24.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>Thickened GB</td>
<td>12 (47.3%)</td>
<td>13 (51.3%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Murphy's sign</td>
<td>2 (8%)</td>
<td>3 (12%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Gall stones</td>
<td>3 (12%)</td>
<td>2 (8%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Pericholecystic fluid</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Table No.2: Comparison of conversion to open cholecystectomy in both groups

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Early</th>
<th>Delayed</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic cholecystectomy</td>
<td>19</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Conversion to open cholecystectomy</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Conversion rate</td>
<td>15%</td>
<td>9%</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Table No.3: Comparison of early and delayed LC

<table>
<thead>
<tr>
<th>Groups</th>
<th>Early</th>
<th>Delayed</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46.381 ± 13.57</td>
<td>51.26 ± 10.05</td>
<td>0.32</td>
</tr>
<tr>
<td>Sex</td>
<td>9 : 16</td>
<td>7 : 18</td>
<td>0.999</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>34.64 ± 22.01</td>
<td>37.1 ± 22.30</td>
<td>0.21</td>
</tr>
<tr>
<td>TLC</td>
<td>10710 (6500–23200)</td>
<td>12100 (6600–18100)</td>
<td>0.341</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.86 (0.5–1.03)</td>
<td>1.9 (0.7–2.6)</td>
<td>0.05</td>
</tr>
<tr>
<td>SGOT</td>
<td>35 (15–94)</td>
<td>76 (14–99)</td>
<td>0.06</td>
</tr>
<tr>
<td>SGPT</td>
<td>38 (12–55)</td>
<td>98 (12–92)</td>
<td>0.09</td>
</tr>
<tr>
<td>Thickened GB</td>
<td>12 (47.3%)</td>
<td>13 (51.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Distened GB</td>
<td>6 (24.7%)</td>
<td>6 (24.7)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

DISCUSSION

Laparoscopic cholecystectomy was started in 1987 for the treatment of indicative cholelithiasis and was additionally used for acute cholecystitis as more experience was gained in the method [8]. Notwithstanding, some ongoing reports have suggested that LC is possible and safe procedure for acute cholecystitis additionally, in spite of the fact that the difficulties and change rates are variable. Nonetheless, more studies are required for convincing outcomes [9]. The specialized contrast of LC is identified with usable discoveries during early medical procedure. An ailing GB containing tainted bile is regularly found in intense cholecystitis. We accept that few specialized central issues must be remembered while performing lap medical procedure for intense cholecystitis. For a decent presentation of Calot’s triangle, an extra port can be helpful. Decompression of GB permits better getting a handle on of GB by grasper. In the event that accessible, ultrasonic dissector and coagulator ought to be utilized for adhesionolysis. In spite of the fact that there are not a few studies which compared the difference in the blood misfortune, more blood misfortune in early gathering is due to profoundly vascular adhesions around incendiary GB [10].

With the expanded involvement with laparoscopy, specialists began to endeavor early laparoscopic cholecystectomy for intense cholecystitis. Be that as it may, early laparoscopic cholecystectomy is still performed by just a minority of specialists. Moreover, the specific planning, expected advantages, and cost-
viability of LC in the treatment of intensely aggravated gallbladder have not been unmistakably settled and keep on being disputable. Despite the fact that activity inside 72 hrs from the beginning of manifestations has been suggested, such an early medical procedure isn't generally conceivable in clinical practice in view of strategic difficulties in working such patients on a crisis premise.

**CONCLUSION**

It is concluded both methods of laparoscopic cholecystectomies are reasonable and safe in acute cholecystitis patients. Delayed LC is associated with lower change rate as compared to early LC and early avoids the issue of failed moderate management and repetitive side effects which required crisis medical procedure.

**Author’s Contribution:**
- Concept & Design of Study: Liaqat Ali Zia
- Drafting: Muhammad Khalid, Mudassir Rasool
- Data Analysis: Imran Amin, Muhammad Ansar Aslam and Hafiz Muhammad Khizar Nawaz Cheema
- Revisiting Critically: Liaqat Ali Zia, Muhammad Khalid
- Final Approval of version: Liaqat Ali Zia

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

**REFERENCES**

Association of Vitamin D Deficiency with Ischemic Cardiomyopathy

Imran Waheed¹, Zeeshan Hassan¹ and Aamir Siddique²

ABSTRACT

Objective: The basic aim of this study is to analyze the association of vitamin D deficiency with ischemic cardiomyopathy.

Study Design: Cross-Sectional study

Place and Duration of Study: This study was conducted at the Government Khawaja Muhammad Safdar Medical College Sialkot during June 2019 till December 2019.

Materials and Methods: All study participants underwent physical examinations, blood analysis, and echocardiographic evaluation. Venous blood samples were collected in the first part of the day after a short-term quick (10 to 12 hours). Afterwards, the serum was separated through centrifugation and immediately transported to the research facility for biochemical investigation.

Results: The data was collected from 50 patients. There were no differences in age, gender, body mass index, and sun exposure within the groups. Biochemical parameters were not significantly different in all study participants except that patients with ICMP had low calcium levels than the control group. The mean 25(OH) D3 levels were significantly lower and NT-proBNP levels were significantly greater in patients with ICMP than controls.

Conclusion: It is concluded that patients with ICMP had lower Vitamin D levels than controls, and Vitamin D deficiency had a significant relationship with cardiac function.

Key Words:

INTRODUCTION

Vitamin D plays an important role in maintaining balanced serum calcium and phosphate levels for bone mineralization and skeletal health. Recent literature, in any case, has indicated a lot broader part of Vitamin D than just the guideline of calcium digestion as Vitamin D receptors (VDRs) are found in an assortment of cells and tissues¹. These include harmful bosom, colon, and prostate cells and typical cells of the safe framework, kidney, heart, and vasculature². Vitamin D probably gives physiologically pertinent pleiotropic capacities that include cardio protective and immunomodulatory impacts just as improves antimicrobial capacity and its deficiency could lead to increased danger of cardiovascular disease and malignancy³.

1. Department of Cardiology, Government Khawaja Muhammad Safdar Medical College Sialkot.
2. Department of Cardiology, Wazirabad Institute of Cardiology, Gujranwala.

Correspondence: Dr. Imran Waheed, Associate Professor of Cardiology at Government Khawaja Muhammad Safdar Medical College, Sialkot.
Contact No: 0303-4939333 (umar)
Email: cardiovascularpic@gmail.com

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The instances of vitamin D inadequacy are regular both in the North American and in the European nations. Vitamin D, a steroid hormone, is additionally notable for its important function in calcium balance and musculoskeletal digestion⁴. Nonetheless, there is a developing body of evidence indicating that there might be a connection between vitamin D deficiency and cardiovascular diseases⁵. Vitamin D receptors present wide distribution all through the cardiovascular framework including vascular smooth muscle, endothelium, and cardiomyocytes⁶. Late studies reported that low vitamin D level is exceptionally regular in the patients with cardiovascular breakdown and it is linked with helpless guess among these patients. Chen and associates have likewise demonstrated that vitamin D-vitamin D receptor flagging framework has a direct antihypertrophic impact on cardio myocytes. Additionally, past studies indicate that there is a connection between vitamin D and left ventricular calculation⁷.

Vitamin D deficiency is associated in different ways with the human body e.g DM, low HDL cholesterol, weight, older age and skin problems⁸. The heart is especially imperative in that plasma 25-hydroxyvitamin D3 [25(OH) D3] levels have been appeared to associate contrarily with the incidence of an assortment of cardiac disorders including ischemic coronary illness and cardiovascular breakdown⁹. Part of Vitamin D in myocardial contractility was demonstrated in a network study of 870 elderly patients without coronary illness during which higher circling Vitamin D levels were
found to connect with better left ventricular (LV) systolic capacity and litter LV end-systolic diameter. The basic aim of this study is to analyze the association of vitamin D deficiency with ischemic cardiomyopathy.

MATERIALS AND METHODS

This cross sectional study was conducted in Government Khawaja Muhammad Safdar Medical College Sialkot during June 2019 till December 2019. This study was done with the permission of ethical committee of hospitals. All study participants underwent physical examinations, blood analysis, and echocardiographic evaluation. Venous blood samples were collected in the first part of the day after a short-term quick (10 to 12 hours). Afterwards, the serum was separated through centrifugation and immediately transported to the research facility for biochemical investigation. Serum complete cholesterol, hs-CRP, glucose, phosphorus, calcium and egg whites focuses were measured by standard research facility methods. The serum convergence of 25OHD3 was measured by radioimmunoassay. The serum PTH concentration was assessed by immunoassay method.

Statistical Analysis: All statistical were carried out with the Statistical Package for Social Science for Windows form 21.0 (SPSS Inc., Chicago, IL)

RESULTS

The data was collected from 50 patients. There were no differences in age, gender, body mass index, and sun exposure within the groups. Biochemical parameters were not significantly different in all study participants except that patients with ICMP had low calcium levels than the control group. The mean 25(OH) D3 levels were significantly lower (14.5 ± 7.4 ng/ml vs. 28.2 ± 12 ng/ml, P = 0.001), whereas PTH (90.5 ± 28.5 pg/ml vs. 57 ± 20.2 pg/ml, P = 0.02) and NT-proBNP levels were significantly greater in patients with ICMP than controls.

Table No.1: Biochemical parameters of patients with ischemic cardiomyopathy and controls

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with ICMP</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>104±18.2</td>
<td>96±12.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>186±25.6</td>
<td>178±22.6</td>
<td>0.56</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>116±18</td>
<td>112±12</td>
<td>0.06</td>
</tr>
<tr>
<td>Hemoglobin (mg/dl)</td>
<td>9.2±1.8</td>
<td>11.2±2.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.9±0.03</td>
<td>0.82±0.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Albumin (mg/dl)</td>
<td>3.4±1.2</td>
<td>4.2±1.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>8.2±1.4</td>
<td>9.6±0.8</td>
<td>0.01</td>
</tr>
<tr>
<td>25(OH) D3 (ng/ml)</td>
<td>14.5±7.4</td>
<td>28.2±12</td>
<td>0.001</td>
</tr>
<tr>
<td>Parathyroid hormone (pg/ml)</td>
<td>90.5±28.5</td>
<td>57±20.2</td>
<td>0.02</td>
</tr>
</tbody>
</table>

DISCUSSION

Vitamin D decreases inflammation by means of a few pathways, for example, restraint of prostaglandin and cyclooxygenase pathways. Vitamin D deficiency animates foundational and vascular irritation, empowering atherogenesis. Then again, as already mentioned, hypertension is likewise associated with absence of vitamin D, due to enactment of the RAA framework, empowering endothelial dysfunction, the initial phase in plaque development.

In the current study, it was observed that 25(OH) D3 levels were lower than typical in both the gatherings and altogether low in patients with DCMP than controls who were likewise the patients with other medical diseases. There was a negative relationship between's 25(OH) D3 and LV dimensions in DCMP patients. This perception was in concordance with Ameri et al. who likewise reported that 25(OH) D3 level had reverse connection with LVESD and LV volume in patients with cardiovascular breakdown.

A few studies have demonstrated associations of low Vitamin D focuses with cardiovascular occasions including sudden cardiac death and mortality with cardiovascular breakdown patients. In a study drawn from the NHANES III database, Vitamin D inadequacy was associated with cardiovascular breakdown. In another study of patients, Vitamin D levels were contrarily correlated with NT-proBNP, a marker of cardiac dysfunction and disappointment, and adversely correlated with NYHA. After rectification for cardiovascular danger factors, the hazard proportion for death due to cardiovascular breakdown was fundamentally higher when Vitamin D deficient patients. Strikingly, an ongoing report linked a useful polymorphism in the 1-(OH) ase quality, the rate-restricting advance in the combination of dynamic 1,25(OH) 2 with increased danger for cardiovascular breakdown.

ICMP is the third most basic reason for cardiovascular breakdown with a wide scope of etiologies, for
example, hereditary, irresistible, immune system, poisonous, metabolic, wholesome, endocrine, mitochondrial. Notwithstanding, now and again the specific etiology stays hazy. Hypocalcaemia is one of the inconsistent and reversible reasons for the DCMP. Some case reports indicated that the DCMP can be associated with hypocalcaemia and vitamin D deficiency in the pediatric populace. Generally, these cases were effectively treated with calcium and vitamin D substitution treatment, at that point cardiac dysfunction and dilatation totally resolve inside months.

CONCLUSION

It is concluded that patients with ICMP had lower Vitamin D levels than controls, and Vitamin D deficiency had a significant relationship with cardiac function. In this way, screening for Vitamin D deficiency alongside brief treatment is recommended in patients with ICM.

Author’s Contribution:
Concept & Design of Study: Imran Waheed
Drafting: Zeeshan Hassan
Data Analysis: Aamir Siddique
Revisiting Critically: Imran Waheed, Zeeshan Hassan
Final Approval of version: Imran Waheed

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

REFERENCES

Effect of Perioperative Dexamethasone on Postoperative Mean Pain Score

Zahid Hanif¹, Umar Iqbal³, Ahsan Khan¹, Nighat Parveen², Aqeel Moazzam⁵ and Muhammad Saqib¹

ABSTRACT

Objective: To evaluate the analgesic effect of perioperative single dose of dexamethasone with control in patients undergoing surgery under general anesthesia.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Anaesthesia, Arif Memorial Teaching Hospital associated with Rashid Latif Medical College and Lahore General Hospital, Lahore from July 2019 to December 2019.

Materials and Methods: One hundred and forty patients, aged 18-60 years, undergoing surgery under general anesthesia. They were split into two groups, Control (Group C) and Dexamethasone (Group D). The patients in control group were given injection nalbuphine 6-10mg with placebo while those in study group were given injection dexamethasone 0.1mg/kg along with injection nalbuphine 6-10mg. The technique for general anesthesia was standard for both groups. After 12 and 24 hours patients were evaluated for post-operative pain by using visual analogue score (VAS).

Results: Mean pain score with dexamethasone was significantly low compared to the placebo group i.e. Dexamethasone: 1.41 vs. Placebo: 2.96, p-value=0.000. Patients were stratified according to age i.e.<40 and ≥40 years, Sex i.e., male and female patients, BMI i.e., normal, overweight & obese and the mean pain score was notably reduced with Dexamethasone as compared to placebo group across all groups.

Conclusion: Dexamethasone at dose of 0.1 mg/kg, is efficacious in minimizing postoperative pain.

Key Words: Control, Dexamethasone, General anesthesia, Pain score, Single dose

INTRODUCTION

Immediate postoperative pain is an unpleasant consequence that slows down functional recovery of patients, prolong hospital stay and reduce patient satisfaction. Multimodal analgesic technique has been an important strategy to manage postoperative pain. Glucocorticoids have pain-relieving, anti-inflammatory and anti-emetic effects. Several randomized controlled trials have evaluated responses associated with a single perioperative dose of glucocorticoids in various major and minor surgical procedures. Dexamethasone has been conventionally used as peri-operative corticosteroid to lower the incidence of nausea and vomiting after surgery, and assumed to have a significant role as an analgesic in the immediate post-operative period.¹,² Studies have shown that preoperative administration of dexamethasone reduces the post-operative pain significantly. It inhibits peripheral phospholipase, which reduces the pain-enhancing agents from the cyclooxygenase and lipoxygenase pathways. Additionally, corticosteroids inhibit expression of cytokine gene and hinders the release of pro-inflammatory enzymes, bradykinin, and neuropeptides from damaged nerve terminals, key factors in precipitating pain.³,⁴ Previous studies have evaluated the potential analgesic effect of single perioperative intravenous dose of dexamethasone for several surgical procedures. Waldron et al. conducted a systemic review to investigate effect of a single intravenous dose of dexamethasone on postoperative pain and side effects related to it. A single intravenous perioperative dose of dexamethasone less but statistically significant benefits.⁵,⁶ A literature review by Moore SG concluded that a minimum dose of at least 0.1 mg/kg of dexamethasone will be effective in reducing the pain scores and opioid requirements.⁷

¹ Department of Anaesthesia / Gynecol & Obstet², Lahore General Hospital, Lahore.
² Department of Anaesthesia / Surgery¹ / Orthopaedics³, Rashid Latif Medical College Lahore.

Correspondence: Dr. Umar Iqbal, Associate Professor of Anaesthesiology, Rashid Latif Medical College Lahore.
Contact No: 0321-4243093
Email: umer8808@gmail.com

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A meta-analysis carried out by De Oliveira et al. (2011) concluded that medium dose dexamethasone (0.11 to 0.2 mg/kg) is a potent post-operative pain control strategy without having any significant harmful effects and better controlled achieved with preoperative drug administration. The rationale of the study is to compare the mean pain score with perioperative single dose of dexamethasone versus placebo in patients undergoing surgery under general anaesthesia. Literature review of some studies show that the addition of dexamethasone during surgery under general anaesthesia has no use as there was no difference in post-operative pain. In contrary some data showed that dexamethasone is highly effective in controlling post-operative pain. No such data is available for our local population. So we conducted this study to conclude whether to implement the use of dexamethasone in general anesthesia surgeries and if not effective, then additional dexamethasone could be restricted. This will help in reducing harmful effects of pain, patient sufferings, on the other hand, reducing burden on staff.

MATERIALS AND METHODS

This randomized controlled trial was performed in the Department of Anaesthesia, Arif Memorial Teaching Hospital associated with Rashid Latif Medical College and Lahore General Hospital, Lahore from 1st July 2019 to 31st December 2019. One forty patients in the age range of 18-60 years were registered in this study after written informed consent. Patients undergoing gynecological procedures, orthopedic and general surgeries under general anaesthesia were included in this study. Patients with hepatic and renal insufficiency, diabetes mellitus, history of corticosteroid hypersensitivity, prior gastric ulcer, already on corticosteroids or immunosuppressive drugs, analgesics and opioids were excluded. Patients were randomly divided into two groups, Group C (control) and D (dexamethasone) by using lottery method. After baseline blood pressure, oxygen saturation, capnography, electrocardiographic evaluation, and hydration with 10 mL/Kg of crystalloids in all patients, general anesthesia was induced with propofol and atracurium 0.5mg/kg. In both groups inj. Nalbuphine 0.1mg/kg was given as premedication prior to induction and 30 mg inj. Ketorolac intraoperatively. The patients in control group (C) were given 2ml normal saline after induction while in group D (dexamethasone), 0.1 mg/kg inj. Dexamethasone was given. After surgery patients were shifted to post anesthesia care units and postoperative pain was assessed by using VAS at 12 and 24 hours. The range of this score is from 0 to 10. ‘0’ was considered as no pain while ‘10’ was considered as worst bearable pain. 0.1 mg/kg of nalbuphine was given as rescue analgesia at VAS score greater than 3. The data was analyzed using SPSS version 21. Student ‘t’-test was applied for the comparison of the mean pain score in both groups. p-value ≤0.05 was considered as significant.

RESULTS

Mean age of patients in dexamethasone and in placebo group was 36.93±12.24 and 40.87±12.03 with age range between 18 and 60 years (Table 1). In dexamethasone group 51.4%(n=36) patients were male and 48.6% (n=34) patients were female while in placebo group there were 44.3% (n=31) male and 55.7% (n=39) female patients (Table 2). Mean BMI of patients in Dexamethasone and in Placebo was 24.07±2.87 and 25.21±2.57 (Table 3). Mean pain score was significantly higher in placebo group at 12 and 24 hours. The Mean pain score at 12 hours was 2.37±1.00 in dexamethasone group vs 3.07±1.01 in placebo group (p=0.009). It was 1.41±1.05 in dexamethasone group at 24 hours while in placebo group it was 2.96±1.31 [p=0.000] (Table 4).

DISCUSSION

Postoperative pain is one of the main reasons of delayed recovery and unanticipated hospital admission in day care anesthesia. The intensity of postoperative pain differs from individual to individual and is mediated by following factors: age, sex, psychological and emotional factors, site and type of surgery, pain threshold and anesthetic agents. Glucocorticoids have been investigated for their role in reducing inflammation, anodyne effects and immune modulatory actions. Several studies have been conducted to evaluate the effect of a perioperative single
glucocorticoid dose administration.\textsuperscript{2,3} The pain lowering effects of glucocorticoids are primarily mediated by the peripheral inhibition of phospholipase enzyme, thus reducing the products of the cyclooxygenase and lipoxygenase pathways hindering inflammatory reactions. Besides anti-inflammatory effects, steroids are presumed to reduce the amount of substance P released at dorsal root ganglion which may be additive to its pain reducing actions.\textsuperscript{3}

The recommended analgesic dose of dexamethasone for this purpose is variable. Our study concluded that one dose of 8mg dexamethasone was efficacious in reducing postoperative pain after general anaesthesia. Similar findings were seen with dexamethasone (8mg) on VRS pain scores at 24 hours in patients having total knee replacement by Samona et al. Dexamethasone group (4.57) had lower pain score than the control group (6.077) (P = 0.003).\textsuperscript{2}

The results of our study were also comparable with that of Szucs et al who concluded a significant improvement in postoperative analgesia with a single dose of 0.1mg/kg intravenous dexamethasone given prior to operative fixation of fractured neck of femur. Pain scores 6h post-surgery were less in the dexamethasone group in comparison to group which received placebo [0.8±1.3 vs. 3.9±2.9] (p = 0.0004).\textsuperscript{9}

Sharma et al also evaluated the effects of preoperative injection dexamethasone on intra and immediate post-operative pain for procedures on lumbar spine and reported similar observations. They found that a dose of 8 mg intravenous dexamethasone to be efficacious when compared to placebo. (p<0.001).\textsuperscript{5}

In accordance to our study, Shahlu et al have seen significant reduction in VAS scores at 12 and 24 hours postoperatively with administration of intravenous dexamethasone (8mg) in elective caesarian section under spinal anaesthesia (p<0.001).\textsuperscript{10} Our study is also in line with a study done by Melese et al in Ethiopia on the analgesic effect of Intravenous Dexamethasone Prior to Spinal Anesthesia Among Parturient Undergoing Cesarean Section. They found statistically significant decrements in NRS score both at rest and voluntary coughing in dexamethasone group at 12 and 24 hours (p=0.0001).\textsuperscript{11}

Kadur et al investigated the effect of intravenous dexamethasone 0.1mg/kg on postoperative pain, nausea and vomiting after spinal anesthesia with pethidine and bupivacaine in lower limb orthopedic surgery. They also found significant reduction in VAS scores with dexamethasone at 12 hours (4.12±1.59 vs 5.11±1.57) and 24 hours (1.61±0.74 vs 2.30±1.81) as compared to control group (p=0.000).\textsuperscript{12}

Similarity was seen in results of study by Harr et al. They had shown that one 8 mg dose of intravenous dexamethasone given at least an hour before surgery was effectual to control post-operative pain at 12 hours in comparison with placebo (2.8±1.3 vs 4.2±2.4). Inconsistent with our study results, no significant difference was seen at 24 hours. (p>0.05).\textsuperscript{13}

In contrast, Jain et al did not find significant reduction in pain scores with 8mg dexamethasone at 24 hours during infraumbilical surgeries under spinal anaesthesia (p=0.08). This difference could be due to variation in methodology as they had given study drug preoperatively.\textsuperscript{1}

One of the limitations of our study was that we did not measure the total consumption of rescue analgesia. Another limitation was that we did not evaluate postoperative side effects in terms of delayed wound healing, nausea and vomiting. Also serum concentration of dexamethasone was not measured. Future studies can be done regarding these along with different dexamethasone doses at different times.

**CONCLUSION**

The single perioperative dose of intravenous dexamethasone is effective in decreasing postoperative pain.

**Author’s Contribution:**

Concept & Design of Study: Zahid Hanif

Drafting: Umar Iqbal, Ahsan Khan

Data Analysis: Nighat Parveen, Aqeel Moazzam, Muhammad Saqib

Revisiting Critically: Zahid Hanif, Umar Iqbal

Final Approval of version: Zahid Hanif

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

**REFERENCES**


Anti-Inflammatory Effect of Local Application of Curcuma Gel in Patients of Chronic Periodontitis

Iqra Amin¹, Asrar Ahmed², Amna Amanat², Faiqua Yasser³, Muhammad Dilshad¹ and Muhammad Sharjeel Ilyas⁴

ABSTRACT

Objective: To determine the anti-inflammatory effects of oral curcuma gel on salivary calprotectin level in patients of chronic periodontitis.

Study Design: Randomized controlled clinical trial study.

Place and Duration of Study: This study was conducted at the Department of Periodontology, de’ Montmorency College of Dentistry (Punjab Dental Hospital) Lahore from February 2019 to August 2019.

Materials and Methods: In this experimental study 15 patients were selected having chronic periodontitis and pocket depth 3-7mm. Subgingival ultrasonic scaling was done of patients at day 0 after collection of saliva and Pocket depth (PD) measurement. Patients were instructed to apply curcuma oral gel (each gram containing 10 mg of curcuma longa extract and glycerol is used as a vehicle), twice a day for three weeks after brushing. Pocket depth (PD) measured and saliva was collected 3 times during the study – Day 0, Day 10 and at day 21 with ±2 days of arrival. The calprotectin levels will be measured in saliva and compared each time by ELISA technique according to manufacturer’s instructions.

Results: In this study, curcuma oral gel treatment proves to be effective in terms of PD measured and calprotectin levels in saliva. Marked reduction in PD from 5.27±0.78 at day 0 to 3.17±0.41 at day 21 has been measured having p-value < 0.001. Mean calprotectin level at day 0 is 3.75±0.64 and at day 21 is 1.67±0.32.

Conclusion: This study shows effectiveness of curcumin in curing periodontitis by reducing proteomes present in saliva. The anti-inflammatory action of Curcuma gel topical application is proved clinically by the values of PD measured and biochemically by reduction in salivary calprotectin level.

Key Words: Saliva, Calprotectin level, Periodontitis, Curcuma gel

INTRODUCTION

The periodontium means supporting tissues of teeth and inflammation of these tissues is called periodontitis.¹ Periodontitis is a bacterially induced inflammation of periodontal tissues which leads to shrinkage of gums and loosening of teeth.²

1. Department of Oral and Maxillofacial Surgery, Punjab Dental Hospital, Lahore.
2. Department of Oral Biology, de’Montmorency College of Dentistry, Lahore.
3. Department of Oral Pathology, Institute of Dentistry, CMH, Lahore Medical College, Lahore.
4. Department of Anatomy, Postgraduate Medical Institute, Lahore.

Correspondence: Dr. Iqra Amin, Postgraduate Resident Oral and Maxillofacial Surgery, Punjab Dental Hospital, Lahore.
Contact No: 0332-4717510
Email: iqraamin726@gmail.com

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Chronic periodontitis (CP) is the most common periodontal disease consisting of chronic inflammation of periodontal tissues. It leads to the destruction of connective tissue (gingivae, periodontal ligaments) and loss of the adjacent supporting bone.³ Clinical attachment loss (CAL) of ≥5 mm is characterized as severe chronic periodontitis (SP).⁴

The major categories of saliva available are whole saliva and cell free saliva.⁵ Whole saliva can be stimulated or unstimulated. The salivary flow of unstimulated saliva ranges from 0.3 to 0.4 mL/min.⁶ Saliva is said as “the mirror image of blood” for diagnosing various diseases.⁷ Numerous studies have emphasized on role of salivary biomarkers for diagnosing and foretelling periodontal disease advancement.⁸ ⁹ ¹⁰

The proteome is the protein complement of the genome, and proteomics is the study of its analysis.¹⁰ Calprotectin is a 36-kDa glycoprotein of lipocalin family. Heterodimercal protect in is formed by S100A8 and S100A9.¹¹ Calprotectin is found in the cytoplasm of neutrophils (representing 60% of cytosolic proteins) and macrophages,¹² and is a protein secreted from neutrophils during cell death and is linked with...
innumerable autoimmune and inflammatory diseases like periodontitis. Turmeric (haldi) is a rhizome of Curcuma longa. Curcuminoids are a leading chemical element of turmeric including bisdemethoxycurcumin, demethoxycurcumin, and CUR. Curcumin has prominent pleiotropic effects e.g. anti-inflammatory, anti-oxidation, and anti-tumor effects. Curcumin is analogous to phenylbutazone, a well-known anti-inflammatory agent. Curcumin causes inhibition of COX-1 and COX-2 to prevent production of prostaglandin E2 and 5-Hydroxyeicosatetraenoic acid (5-HETE).

In 1937, first article was published on the use of curcumin in human disease. The acceptable daily intake of curcuminoids by WHO and food and drug administration (FDA) is 0-3 mg/kg. Turmeric has wide span of pharmacological actions such as antioxidant, anti-protozoal, anti-venom activities, anti-microbial, anti-fungal, anti-malarial, anti-viral, wound healing, anti-inflammatory, anti-proliferative, anti-dysenteric for children, anti-angiogenic, anti-tumor and anti-aging properties.

Curcumin solution has a role as a sub gingival irrigation, as an ointment for oral sub mucous fibrosis, leukoplakia, and lichen planus. Turmeric extract along with polymerizable resin can be applied as a pit and fissure sealant. Turmeric in mouthwash form was used by Bhandari and Shankwalkar, 1980. Antimicrobial activity of turmeric was observed by Hamedet al. and Munet al.

The purpose of this study is to investigate the anti-inflammatory effect of oral curcuma gel in patients of chronic periodontitis by focusing on (MRP)8/14 (calprotectin) as an inflammatory marker and to correlate the change in the level of this marker and that of PD (a known inflammatory clinical indicator).

MATERIALS AND METHODS

In this randomized controlled clinical trial was carried out at Department of Periodontology, de’ Montmorency College of Dentistry (Punjab Dental Hospital) Lahore from 2nd February 2019 to 5th August 2019. A total of 15 subjects of either sex with age range 20-40 years were selected.

Pre-treatment assessment: Patients were examined using a mouth mirror, explorer, William’s graduated periodontal probe, tweezers and the related data was recorded in a patient Performa sheet. At day 0 before starting ultrasonic scaling whole unstimulated salivary sample was collected in 15 ml test tube from both study and control groups. Subjects were asked not to eat, drink or smoke for at least 1 hour before saliva collection. Salivary calprotectin levels were measured by enzyme-linked-immunosorbent using a commercial Cal ELISA kit of GLORY Science USA. The ELISA procedure was performed according to the manufacturer’s instructions. After undergoing ultrasonic scaling at day 0, patients were instructed to apply oral curcuma gel (each gram containing 10 mg of curcuma longa extract) with cotton buds on their gingivae in the whole oral cavity, twice a day for three weeks after brushing. They were asked to leave the gel in place for at least 10 minutes and then rinse with water. Saliva was processed and PD was measured by William’s graduated periodontal probe 3 times during the study – Day 0, Day 10 and at day 21 with ±2 days of arrival. The calprotectin levels were measured and compared each time by ELISA technique according to manufacturer’s instructions.

Post-treatment assessment: Patients were examined using a mouth mirror and William’s graduated periodontal probe to record PD at day 10 and day 21 in department of Periodontology, Punjab Dental Hospital Lahore. About 5ml of unstimulated saliva sample was collected in test tubes for assessment of salivary calprotectin level by ELISA technique (Figs. 1-2). The data was entered and analyzed through SPSS-22.

RESULTS

Repeated measures analysis of variance test revealed that mean Calprotectin levels differed statistically significant among different days (Table 1). Post hoc test using Bonferroni correction showed that the mean Calprotectin level at day 0 was significantly higher as compared to day 10 and 21. Similarly there was significant difference between day 10 and 21 levels (Table 2).

Table No.1: Comparison of Calprotectin levels (µg/L) among different days

<table>
<thead>
<tr>
<th>Day</th>
<th>Mean±SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3.75±0.64</td>
<td>2.47</td>
<td>4.72</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>10</td>
<td>2.18±0.41</td>
<td>1.53</td>
<td>2.90</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>1.67±0.32</td>
<td>1.17</td>
<td>2.15</td>
<td></td>
</tr>
</tbody>
</table>

*Repeated measures ANOVA

Table No.2: Pair wise comparison among days

<table>
<thead>
<tr>
<th>Days</th>
<th>Mean difference (µg/L)</th>
<th>Std. Error</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
<td>1.577*</td>
<td>0.139</td>
</tr>
<tr>
<td>21</td>
<td>10</td>
<td>2.081*</td>
<td>0.145</td>
</tr>
<tr>
<td>21</td>
<td>10</td>
<td>0.504*</td>
<td>0.087</td>
</tr>
</tbody>
</table>

*Repeated measures ANOVA

Table No.3: Showing comparison of the pocket depth levels among different days

<table>
<thead>
<tr>
<th>Day</th>
<th>Mean±SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.27±0.78</td>
<td>4.00</td>
<td>6.50</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>10</td>
<td>4.30±0.59</td>
<td>3.50</td>
<td>5.00</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>3.17±0.41</td>
<td>2.50</td>
<td>4.00</td>
<td></td>
</tr>
</tbody>
</table>

*Repeated measures ANOVA
Repeated measures analysis of variance test revealed that mean pocket depth differed statistically significant among different days, $p < 0.05$ (Table 3). The results showed statistically significant reduction in pocket depths at day 10 and 21 compared to baseline values at day 0 ($p < 0.05$). There was also significant improvement in pocket depths at day 21 compared to day 10 ($p < 0.05$) [Table 4]. Table 5 shows correlation of Calprotectin with pocket depth. The correlation between Calprotectin levels and pocket depth was strong positive at day 0 and day 21 and they were significant.

**DISCUSSION**

The current study was a multi-center, randomized, controlled clinical study. The results depicted the effects of curcumin on inflammatory marker (Calprotectin) and clinical marker (PD) in chronic periodontitis patients. Study by Panov et al.\textsuperscript{13} reported that salivary calprotectin level and gingival inflammation both were decreased after azithromycin treatment 500mg/day for 4 days in chronic periodontitis patients. In the present study significant reduction in calprotectin level from 3.75±0.64 at day 0 to 1.67±0.32 at day 21 (Table 1) was observed after application of curcuma gel for 21 days consecutively.

Ravi Shankar et al.\textsuperscript{25} compared topical application of curcuma gel and reduction in PD (3.35±0.70 mm) to ornidazole group (5.07±1.00 mm). Curcumin has both antimicrobial and anti-inflammatory effects. It is in accordance with the present study where there is marked reduction in PD from 0 to 21 days i.e. 5.27 to 3.17 mm after curcuma gel therapy (Table 3).

Behal et al.\textsuperscript{26} evaluated the effects of LDD system containing 2% turmeric gel as an adjunct to scaling and root planning in chronic periodontitis. The study concluded that investigational drug used along with SRP was effective in removing the local irritants, reducing gingival inflammation, reducing PD and gain in clinical attachment level. PD was reduced from 5.72 at day 0 to 4.317 mm at day 45. Similar study conducted by Farjana et al.\textsuperscript{24} to evaluate the anti-inflammatory effects of topical application of curcuma gel in gingivitis management. There was reported significant reduction in bleeding on probing on day 21. In the present study that reduction in inflammation was recorded as reduction in calprotectin levels in saliva. The salivary calprotectin level lowered and PD reduced as inflammation was reduced by application of oral curcuma gel (Table 5).

In the study by Kido et al.\textsuperscript{27} there is a marked correlation in the GCF calprotectin levels and the concentrations of other biochemical markers (IL-1b and PGE2). Calprotectin was also found related with clinical indicators of periodontal inflammation. It was reported that calprotectin is present in dental calculus and inflammatory exudate of chronic periodontitis patients.\textsuperscript{28} Porphyromonas gingival lipopolysaccharide is found to encourage the release of calprotectin from neutrophils and monocytes.\textsuperscript{29} Currently we are investigating calprotectin as a marker of extent and progression of disease activity in patients of chronic periodontitis.

**CONCLUSION**

This study shows effectiveness of curcumin in curing periodontitis by reducing proteomes present in saliva. The anti-inflammatory action of Curcuma gel topical application is proved clinically by the values of PD measured and biochemically by reduction in salivary calprotectin level. The use of curcumin topical application could be beneficial in the treatment of chronic periodontitis patients. Further long term clinical trials are needed to evaluate the effect of curcumin on periodontitis patients.

**Author’s Contribution:**

Concept & Design of Study: Iqra Amin

Drafting: Asrar Ahmed, Amna Amanat

Data Analysis: Faiqua Yasser, Muhammad Dilshad, Muhammad Sharjeel Ilyas

Revisiting Critically: Iqra Amin, Asrar Ahmed

Final Approval of version: Iqra Amin

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

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Evaluation of Resection Margin at 0.5 and 1 cm to Estimate the Adequacy of Resection in the Treatment of Multicystic Ameloblastoma

Sartaj Khan¹, Tahirullah Khan³, Waqar-Un-Nisa², Saif-Ullah¹, Shandana Khan¹ and Ahmed Khan¹

ABSTRACT

Objective: To determine the tumor cell infiltration and estimate a safe resection margin in the treatment of multicystic ameloblastoma.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Oral & Maxillofacial Surgery, Mardan Medical Complex, Bacha Khan Medical College, Mardan Pakistan from January 2013 to June 2020.

Materials and Methods: Thirty patients with histopathologically and radiographically diagnosed as multicystic ameloblastoma were selected. Tumor resection including margin of 1cm adjacent to apparently normal bone was performed. The specimens were then assessed at two levels labelled as A and B, representing 0.5 cm and 1 cm margin respectively for histopathological evaluation.

Results: Mean age of the patients was 40.8±10.07 years. The most common age groups were second and third group. There were 17 males (56.6 %) and 13 females (43.4%). Twenty-two cases (73.3%) involved posterior mandible in body and ramus area. All patients were treated surgically depending upon the extent of the tumor. Among these 30 cases, marginal resection was carried out in 2 cases (6.7%), segmental resection in 13 cases (43.3%) and composite resection in 15 (50%) cases. Histopathology of resection margins were positive in 12 patients at 0.5 cm and negative in 18 patients, while margin was negative in all these 30 cases at 1 cm margin.

Conclusion: The tumor cells can infiltrate 0.5 cm deep into the adjacent clinically normal bone. Hence resection with a 1 cm safe margin of spongy bone may be an adequately conservative treatment for multicystic ameloblastoma.

Key Words: Resection margins, Tumor margins, Ameloblastoma


INTRODUCTION

Ameloblastoma is common benign but locally invasive odontogenic polymorphic tumor of the jaws.³ It may arise from odontogenic cyst epithelium and residual epithelial rests.² It usually affects children and adolescents, more often involving mandible than maxilla and occurring more commonly in males as compared to females.³

Ameloblastoma has various sub types among which multicystic variant is more common than others and is usually encountered in third to seventh decade of life.⁴ About 85% of multicystic ameloblastoma occur in mandible and 15 % occur in maxilla.⁵ Radiographically multicystic ameloblastoma present as multilocular radiolucent lesion and may present as “soap bubble” or “honeycombed” appearance.⁵ Multicystic ameloblastoma can be histologically classified as plexiform (55.3%), follicular (37.6%), basaloid (3.5%), acanatomatosous (1.4%), granular cells (1.4%), and desmoplastic (0.8%).⁵,⁶ The multicystic ameloblastoma frequently infiltrate the cancellous bone but invasion of cortical bone is infrequent.⁷ Solid ameloblastoma is more aggressive in nature with high recurrence rate.⁸,⁹ It may damage adjacent organs like eye and nose leading to functional disability and in addition to this local destruction of jaw bones, the tumour can also metastasize to lungs and kidneys and may even transform into ameloblastic carcinoma.¹⁰,¹¹

¹ Department of Oral & Maxillofacial Surgery / Oral Pathology², Bacha Khan Medical College, Mardan.
³ Department of Oral & Maxillofacial Surgery, Lady Reading Hospital, Medical Teaching Institute Peshawar.

Correspondence: Dr. Tahir Ullah Khan, Assistant Professor of Oral & Maxillofacial Surgery, 2nd Floor ENT/Eye Building, Lady Reading Hospital Peshawar.
Contact No: 0333-9736279
Email: dr.tahir786@hotmail.com

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Because of its recurrent nature, conservative approach advocated by some has lost ground in favor of more radical surgical approach and the treatment modalities like curettage, chemical cauterization of the walls of lesion or electro-cauterization are now only of historical importance.\textsuperscript{12} Overall recurrence rate varies from 7.1\% to 45.5\%.\textsuperscript{13} In radical surgery lesion is excised with a margin of “normal bone”.\textsuperscript{14} Several studies have been conducted regarding the removal of lesion along with uninvolved bone with various suggested resection margins of 5mm, 1cm, 1.5cm and even up to 2 cm.\textsuperscript{15-17} Extensive resection is always undesirable as it can lead to functional impairment and esthetic defects in regards to facial region that are difficult to reconstruct.

The purpose of this study was to determine the tumor cell infiltration at 0.5cm and 1cm on the histopathological examination to estimate a safe resection margin for multicystic ameloblastoma.

**MATERIALS AND METHODS**

This study was conducted in Department of Oral & Maxillofacial Surgery, Mardan Medical Complex, Bacha Khan Medical College, Mardan Pakistan from 1\textsuperscript{st}January 2013 to 30\textsuperscript{th}June 2020. Patients of any age group and either gender with histopathologically and radiographically proven as multicystic ameloblastoma were selected in this study. Lesion involving the maxilla and vital structures like base of skull were excluded from the study. The confounding variables like age, sex and site of the tumor were adjusted by stratification. Investigations included; routine investigations and special investigations like orthopantomogram (OPG), x-ray posteroanterior (PA) face, 3D CT scan, and histopathological examination. An informed consent was obtained from the patients or their parents/guardians. The whole mass of the tumor was either directly removed with 1cm safe margin or curettage of the lesion was performed first followed by resection with 1 cm margin of adjacent apparently normal bone. The whole specimen was then examined at two levels i.e. 0.5 cm and 1 cm margin labelled as level A and B respectively. The histopathological result achieved, were then reviewed. The collected data was entered in SPSS version 22 and analyzed.

**RESULTS**

Mean age of the patients was 40.8±10.07 years. The most common age groups were second and third group. There were 17 males (56.6\%) and 13 females (43.4\%). Multicystic ameloblastoma was more common in posterior mandible as compared to anterior part. In all these patients only 8 cases (26.6\%) were observed in anterior part while the rest 22 cases (73.3\%) involved posterior mandible in body and ramus area. All patients were treated surgically depending upon the extent of the tumor. Among these 30 cases, marginal resection was carried out in 2 cases (6.7\%), segmental resection in 13 cases (43.3\%) and composite resection in 15 (50\%) cases (Table 1). Histopathology of the resection margin of 1 cm was carried out at two levels i.e. 0.5 cm (level A) and 1cm (level B) in all 30 cases of multicystic ameloblastoma. Resection margins were positive in 12 patients at 0.5 cm and negative in 18 patients, while margin were negative in all these 30 cases at 1 cm (Table 2).

**Table No.1: Demographic information of the patients (n=30)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>5</td>
<td>16.7</td>
</tr>
<tr>
<td>31-40</td>
<td>11</td>
<td>36.7</td>
</tr>
<tr>
<td>41-50</td>
<td>11</td>
<td>36.7</td>
</tr>
<tr>
<td>51-60</td>
<td>3</td>
<td>10.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>56.6</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>43.3</td>
</tr>
<tr>
<td>Site of multicystic ameloblastoma in mandible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior mandible</td>
<td>8</td>
<td>26.6</td>
</tr>
<tr>
<td>Posterior body/Ramus</td>
<td>22</td>
<td>73.3</td>
</tr>
</tbody>
</table>

**Table No.2: Histopathological result of specimen**

<table>
<thead>
<tr>
<th>Histopathology result</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 0.5 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>12</td>
<td>40.0</td>
</tr>
<tr>
<td>Negative</td>
<td>18</td>
<td>60.0</td>
</tr>
<tr>
<td>At 1 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Negative</td>
<td>30</td>
<td>100.0</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The most common age of patients observed in our study was between 3\textsuperscript{rd} to 5\textsuperscript{th} decades of life. The mean age being 40.8 years, which is comparable with previous studies by Di Cosola et al\textsuperscript{18}, who have shown mean age of such patients with multicystic ameloblastoma to be 39.6 years. Zhang et al\textsuperscript{19} studied odontogenic tumors in Chinese population and Adebiyi et al\textsuperscript{20} conducted a similar study in Nigerian population both confirming these tumors to occurring more frequently in 4\textsuperscript{th} decade of life. In contrast to these studies the patients presented to us showed increased frequency in 5\textsuperscript{th} decade of life. Male to female ratio in our study was 1.3:1, which is more or less similar to previous studies conducted worldwide, as no significant predominance between genders.\textsuperscript{18-20} The multicystic ameloblastoma is more common in the posterior parts of the jaws as reported by various studies conducted around the world. This was confirmed in our study as in 22 cases tumor has involved body and ramus of mandible.\textsuperscript{21,22} We found that the tumor cells can infiltrate up to 0.5 cm of adjacent clinically healthy bone, which strongly contradicts the conservative management of
ameloblastoma propagated by some researchers. All resection margins at 1cm distance from lesion were free of tumor cells. Curettage involves eradication of macroscopically visible mass of tumor by scraping procedure. Similarly Carnoy’s solution has been used by some authorities in the treatment of conventional multicystic ameloblastoma as adjunct to curettage. Sehdev reported 90% recurrence rate mandibular ameloblastomas after curettage. Subsequent resection could control 80% of recurrences. D’Agostino et al observed 28.57% recurrence following enucleation and curettage while 0% seen in wide bone resection. He suggested conservative surgical treatment should be considered only in unicystic lesions when extraosseous spread has not yet occurred. In multicystic the most appropriate therapeutic approach appears to be an ‘extended surgical resection’ of the tumor. The conservative’ treatment has poor outcome as compared to radical treatment. Literature regarding the surgical safe margin is much confusing because of conflicting ideas of many researchers. Majority of the studies suggested surgical margins based on the assumptions of tumor behavior rather than on histological reviews of tumor histopathological margins. In this study, the infiltration of tumor into the adjacent cancellous bone was investigated, and the appropriate resection margin was suggested based on histopathology rather than merely on assumptions. Gortzak et al stated that ameloblastoma has invasive growth pattern in the cancellous bone, with smaller tumor nests present at a depth of 5 mm from tumor with extensive and infiltrative invasion of the Haversian canals. They recommended resection of tumor with 1 cm safe margin similar to our study. Marx et al reported that ameloblastoma extend 2.3–8 mm beyond the radiographic margin and because of this microscopic infiltration they advocated resection of 1 cm of normal appearing bone. The invasive borders of ameloblastoma have been reported to be diffuse, and some authors have suggested resection with a 1.5-3cm margin of normal bone. It is worth mentioning here that the removal of 2-3 cm of adjacent bone at times may create a continuity defect or other functional and esthetic deformity that some clinician may wish to preclude in treatment of a benign nevertheless a locally aggressive pathology that needs to be treated adequately but still conservatively.

CONCLUSION

Multicystic ameloblastoma is predominant in 3rd and 4th decade of life and involve mostly the posterior part of mandible. The tumor cells can infiltrate 0.5 cm but rarely up to 1cm deep into the adjacent clinically normal bone. Hence resection with a 1 cm safe margin of spongy bone may be an adequate treatment for multicystic ameloblastoma.


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

REFERENCES

Clinical and Histopathological Evaluation of Odontomes

Waqar-Un-Nisa¹, Sabreen Hassan⁴, Mussarat Hussain², Sertaj Khan³, Ahmad Shah⁵ and Sofia Haider Durrani⁶

ABSTRACT

Objective: To evaluate the epidemiological features, assess clinical manifestations and histopathological features of odontomes.

Study Design: Descriptive case series

Place and Duration of Study: This study was conducted at the Department of Oral Pathology, Bacha Khan Medical College Mardan from November 2015 to June 2020.

Materials and Methods: Seventeen patients of odontomes were observed. Patients detail medical and dental history, clinical features, radiographic findings on the panoramic radiographs and pathological reports were investigated.

Results: 52.9 percent patients were males. Majority of the patients were males with age range 13-17 years. The common chief complaint was bony and soft tissue swelling and 41.2% of the cases the odontomes were associated with unerupted tooth. Anterior maxilla was involved in 35.3% cases followed by posterior mandible which was involved in 17.6% cases. Radiographically 70.6% odontoma appeared as a tooth like structures surrounded by a narrow radiolucent zone and histopathologically diagnosed as compound odontomes.

Conclusion: Odontomes are rare tumors comprising of various dental tissues. The most common form diagnosed is compound odontomes both radiographically and histopathologically. It predominantly involves young males, presenting as swelling in anterior maxilla and most commonly associated with unerupted tooth.

Key Words: Epidemiological features, Clinical manifestations, Histopathological features, Odontomes

INTRODUCTION

Odontomas are considered to be developmental anomalies resulting from the growth of differentiated epithelial and mesenchymal cells. Odontomas are the most common odontogenic tumors, in which all structures that form dental tissues are represented.¹ Odontomes are divided in two forma complex and compound. In Complex odontoma the tissues are well formed with disordered pattern and in compound form the dental structures are arranged in more orderly pattern.²

Odontomas are mostly associated with permanent teeth, and they are rarely associated with deciduous teeth.³ The etiology of odontomas remains unknown, although local trauma, infection, and genetic factors have been suggested. Their growth is typically slow and asymptomatic. Therefore, odontomas are generally diagnosed by routine radiological examination in the second and third decades of the life.⁴ Histologically, they are composed of different dental tissues, including enamel, dentine, and cementum and, in some cases, pulp tissue.⁵ Radiographically, the complex odontoma appears as a more or less amorphous, solitary mass of calcified material, and in compound odontoma it reveals tooth-like radiopaque structures.⁶ Odontomas should be removed by conservative surgery because they have very low growth potential and enucleation or surgical excision is curative. Recurrence is unusual.⁷

The present study was therefore designed to evaluate the epidemiological features of odontomas, i.e., age and gender distribution, and location, and to assess clinical manifestations and histopathological evaluation, with the purpose of offering more reliable information for diagnosing these tumors.

MATERIALS AND METHODS

This descriptive case series was conducted in Bacha Khan Medical College, Mardan from 1st November 2015 to 30th June 2020. A total of 17 patients of
Odontomes were observed retrospectively from OPD Department of Oral and Maxillofacial Surgery, Mardan Medical Complex and Bacha Khan College of Dentistry, Mardan. Patients detail medical and dental history, clinical features, radiographic findings on the panoramic radiographs and pathological reports were investigated. The data was entered and analyzed through SPSS-22.

RESULTS

23.5% patients were in age range 8-12 years. 35.3% patients were in age range 13-17 years, 17.6% lied in the age range of 18-22 years, 17.6% were in between 23-27 years and 5.9% were in age range 28-32 years. The odontomas were diagnosed most frequently at 13-17 years of age. 52.9% patients were males and 47.1% patients were females with male to female of 2:1. Bony and soft tissue oral swelling was the chief presenting complaint and was found in 17.6% and 11.8% of cases while pain was the presenting complaint in only 5.9% of cases. 11.8% cases the odontomes were found on routine radiographic examination. It was interesting to note that in 41.2% of the cases the odontomes were associated with unerupted tooth (Table 1).

Anterior maxilla was involved in 35.3% cases followed by posterior mandible which was involved in 17.6% cases. Beside from these two sites, posterior maxilla and anterior mandible were less frequently involved (Table 2). Radiographically, 70.6% odontoma appeared as a tooth like structures surrounded by a narrow radiolucent zone while 29.4% appeared as an amorphous, solitary mass of calcified material. This lesion was of considerable size and was associated to the permanent tooth which had failed to erupt in the dental arch. Histologically 70.6 percent odontomas were compound while 29.4 percent were complex type (Table 3).

Table 1: Demographic information of the patients (n=17)

<table>
<thead>
<tr>
<th>Variable</th>
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<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-12</td>
<td>4</td>
<td>23.5</td>
</tr>
<tr>
<td>13-17</td>
<td>6</td>
<td>35.3</td>
</tr>
<tr>
<td>18-22</td>
<td>3</td>
<td>17.6</td>
</tr>
<tr>
<td>23-27</td>
<td>3</td>
<td>17.6</td>
</tr>
<tr>
<td>28-32</td>
<td>1</td>
<td>5.9</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>47.1</td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>52.9</td>
</tr>
<tr>
<td>Complaints</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bony swelling</td>
<td>3</td>
<td>17.6</td>
</tr>
<tr>
<td>Pain</td>
<td>1</td>
<td>5.9</td>
</tr>
<tr>
<td>Soft tissue swelling</td>
<td>2</td>
<td>11.8</td>
</tr>
<tr>
<td>Routine radiograph examination</td>
<td>3</td>
<td>11.8</td>
</tr>
<tr>
<td>Underlying erupting tooth</td>
<td>8</td>
<td>41.2</td>
</tr>
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</table>

Table 2: Site of distribution of odontomas (n=17)

<table>
<thead>
<tr>
<th>Site of odontoma</th>
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<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MandLT-3,4</td>
<td>1</td>
<td>5.9</td>
</tr>
<tr>
<td>MandLT-5,6</td>
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<td>11.8</td>
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<tr>
<td>MandLT-7,8</td>
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<td>5.9</td>
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<tr>
<td>MandRT-5,6</td>
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<td>MandRT-7,8</td>
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<td>17.6</td>
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<td>6</td>
<td>35.3</td>
</tr>
<tr>
<td>MaxRT-5,6</td>
<td>1</td>
<td>5.9</td>
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</table>

Table No. 3: Radiographic and histologic findings of odontomas (n=17)

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<thead>
<tr>
<th>Findings</th>
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<td>Radiographic appearance</td>
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<td></td>
</tr>
<tr>
<td>Amorphous, solitary mass of</td>
<td>5</td>
<td>29.4</td>
</tr>
<tr>
<td>calcified material</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiolucent with tooth like</td>
<td>12</td>
<td>70.6</td>
</tr>
<tr>
<td>structures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histologic diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex</td>
<td>5</td>
<td>29.4</td>
</tr>
<tr>
<td>Compound</td>
<td>12</td>
<td>70.6</td>
</tr>
</tbody>
</table>

DISCUSSION

Odontogenic tumours constitute an important aspect of jaw pathology that shows variation of frequency in different populations of the world. This study describes their relative frequency and appearance of tumors in our population and their clinicopathological spectrum in comparison with other studies conducted on various populations of the world. Regarding patient age most odontomas can be identified in the first two decades of life in coincidence with our own observations. Tekkesin et al7 found that out of 160 odontomas, 80 were male (50%) and 80 were female (50%). In the present study, 52.9% patients were males and 47.1% patients were females. Philipsen, et al8 also showed more males are involved as compared to females (1.2:1).

According to our result the commonest site for odontomas was anterior maxilla (47.1% cases) followed by posterior mandible (23.4% cases). Beside from these two sites, middle mandible involved 17.7% cases and only 5.9% of the cases were present in anterior mandible and middle maxilla each. While in a study carried out by Sanchez et al14 stated that most of the lesions (56%) were located in the upper maxilla, with 44% in the mandible differentiating the series in an anterior zone (region of the incisors and canines), middle zone (premolars) and posterior zone (molars). Among the lesions found in the upper maxilla, 72.8% were located in the anterior region, 18.3% in the posterior region, and 8.9% in the middle zone. In the mandible, 44.4% were located in the anterior region, 40.6% in the posterior region, and 15% in the middle
sector. Khan et al\textsuperscript{13} found that posterior mandible was the predominant site for odontomes of the jaw. Our study revealed that total number of cases were 53% in maxilla while 47% in mandible with was in contrary to study done by Tekkesin et al\textsuperscript{9} showing that mandible was more commonly involved than the maxilla with all odontomas. Similarly, another study by Lee et al\textsuperscript{15} revealed that of all the odontomas 45% were located in the mandible and 55% in the maxilla.

In the present study bony tissue oral swelling was the chief presenting complaint and was found in 17.6% cases while soft tissue swelling account for 11.8%. Pain was the presenting complaint in only 5.9% of cases. 11.8% cases the odontomes were found on routine radiographic examination. It was interesting to note that in 41.2% of the cases the odontomes were associated with unerupted tooth. Khan et al\textsuperscript{13} reported that the most frequent presenting complaint was extra or intra oral swelling which was noted in 47.37% of the cases. While in 26.32% of the cases, pain was the presenting complaint of patients and 21.05% of the cases odontomes were a chance finding on radiographic examination. Similar presenting complaints were reported by Hidalgo-Sánchez\textsuperscript{7}, Haishima et al\textsuperscript{6} and Owens et al\textsuperscript{17}.

In this study radiograph revealed 29.4% compound odontoma appeared as a tooth like structures surrounded by a narrow radiolucent zone while 70.6% appeared as an amorphous, solitary mass of calcified material with varying levels of radiodensity. This lesion was of considerable size and was associated to the permanent tooth which had failed to erupt in the dental arch. Lee and Park\textsuperscript{15} in their study revealed that radiographically compound odontomes appear with unilocular and multiple radio opaque mini teeth surrounded by defined radiolucency whereas complex odontoma showed unilocular undistinguished radiopaque mass surrounded by radiolucent zone and a distinct radiopaque border.

In the present study among the two histological types of odontomes, compound odontomes were more common i.e. 70.6% while 29.4% were complex odontomes. These findings match with the findings of the study done by de Andrade Santos et al\textsuperscript{9} revealing that 62.5% were compound and 37.5% were complex. Hidalgo-Sánchez et al\textsuperscript{14} observed the same clear predominance of compound odontomes over complex odontomes. The opposite was reported by Khan et al\textsuperscript{13} showed that complex odontomes were more common accounting for 58% while 42% were compound odontomes. In a study carried out by Tekkesin et al\textsuperscript{9} also showed that out of 160 cases, 99 were complex, 57 were compound and 4 were mixed odontomas.

**CONCLUSION**

Odontomes are rare benign tumours and its occurrence varies from region to region. Majority of the patients in this were males with age range 13-17 years. The common radiologically and histopathologically diagnosed form of tumour presented was compound form. The common chief complaint was bony and soft tissue swelling. The tumour appeared more commonly in anterior maxilla. Interestingly most of the cases were associated with unerupted tooth. Therefore, diagnosis of odontomes requires thorough clinical and radiographical examination with histopathological evaluation as the gold standard. Routine findings if missed may complicate the treatment plan.

**Author’s Contribution:**

Concept & Design of Study: Waqar-Un-Nisa

Drafting: Sabreen Hassan, Mussarat Hussain

Data Analysis: Sertaj Khan, Ahmad Shah, Sofia Haider Durrani

Revisiting Critically: Waqar-Un-Nisa, Sabreen Hassan

Final Approval of version: Waqar-Un-Nisa

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

**REFERENCES**


15. Lee CH, Park GJ. Complex and compound odontomas are clinicopathological entities. Basic Appl Pathol 2008;11:30-33.
Glycemic Control among Type-2 Diabetes Mellitus Patients: A Large Samples Hospital Based Study
Shabina Saifullah¹, Muhammad Abbas², Noor Muhammad² and Akhtar Zarin¹

ABSTRACT

Objective: To find out the sugar control among type 2 diabetic patients assessed on glycosylated hemoglobin (HbA1C) test.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Pathology Department, Kuwait Teaching Hospital, Peshawar from January 2017 to December 2018.

Materials and Methods: A total of 2654 participants were in the study. The inclusion criteria were type 2 diabetic cases, Pakistani nationals, both genders, and age above 18 years. Freshly diagnosed type 2 diabetes, secondary diabetes, type 1 diabetes, pregnancy associated diabetes, unknown type of diabetic cases or endocrine disorders were excluded. The recorded data were age, gender, and HbA1C. Poor glycemic patients were those cases having above 7% HbA1C level.

Results: The mean age of the participants of the study was 51.96±13.84 years and mean glycosylated hemoglobin 8.52±3.060. The females (n=1608, 60.6%) were more than males (n=1046, 39.4%). Of total sample 2654 the poor glycemic control (>7% HbA1C) was in 1705(64.2%) patients while in 949(35.8%) the glycemic control was good (<7% HbA1C). Glycemic control was different among the age groups very highly statistically significantly (P<0.001). With increasing age the glycemic control become poorer.

Conclusion: About two third type 2 diabetic patients have poor sugar control in our population. These results should be considered in future interventional research aiming to improve glycemic control in type 2 diabetes mellitus patients.

Key Words: Endocrine disorder, Glycemic control, HbA1C, Type 2 diabetes mellitus

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INTRODUCTION

Diabetes mellitus (DM) is not a single disease but it is comprised of a group of some other metabolic diseases or disorders that are manifested by chronic hyperglycemia which arise from either insulin poor action, defect in someplace in insulin secretion or both.¹² Diabetes mellitus is divided into following general categories: type I diabetes which resulted from autoimmune elimination/damage of beta-cell which in turn causes insufficient production of insulin; type II diabetes which is caused by a gradual or progressive loss of insulin secretion from beta-cell; gestational diabetes mellitus which is usually detected in the second or third trimester of gestation; and other special kinds of diabetes which are due to some other causes e.g. neonatal diabetes, maturity-onset diabetes of the young, diseases of exocrine pancreas and drug induced diabetes.³ According to survey done in 2014 by world health organization, the world wide prevalence of diabetes mellitus was 9% among people aged 18 years or above.⁴ It is estimated that by the year 2035, 592 million people will be affected by diabetes.⁵ According to American Diabetes Association (2014) 29.1 million American, or 9.33% of the total US population had diabetes mellitus.⁶ In North Africa & Middle East, 10% of the total population is diabetic i.e. >37 million people are diabetic, which is estimated to rise to 68 million by the year 2035. Saudi Arabia has 3.8 million diagnosed cases of diabetes.⁷ Pakistan is located in South Asia and is the ⁶⁸th most popular country and 36th largest country of the world.⁸ Majority of Pakistani population lives in rural areas but growing urbanization has led to high calorie diet, eating more but consuming less, sedentary life style and the stressful condition increase the prevalence of diabetes mellitus in Pakistan.⁹ International Diabetic Federation (IDF) reported in 2015, that 415 million population of
the world has diabetes and will increase to 642 million by the year 2040 and in Pakistan the figure will reach to 14.4 million. Province wise prevalence of diabetes in Pakistan shows that 16.2% men and 11.70% women in Sindh; 12.14% men and 9.83% women in Punjab, where’s in Balochistan and in Khyber Pakhtunkhwa the mean prevalence is 13.3% men and 8.9% women, 9.2% in males and 11.6% in females respectively. Comparing urban and rural areas, type II diabetes affecting more urban than rural areas i.e. 14.81% in urban and 10.34% in rural areas. Glycated hemoglobin provides us the evidence of glucose level in blood for last three months, which is the approximated half-life of red blood cells (RBCs). Glycated hemoglobin is nowadays suggested as a standard diagnostic tool to test and monitor diabetes type II. Koenig et al first proposed the use of HbA1c as a biomarker for monitoring the levels of blood sugar in patients of DM. On HbA1C diabetes is diagnosed at equal to 6.5% or higher. The sensitivity and specificity of HbA1c is good for the diagnosis of DM of type II in comparison to other tests. This test shows sugar control of the last three months. In a research conducted in China on glycemic control showed that above 50% patient’s glycemic control (HbA1C >7%) was poor. This study was retrospective database at a tertiary care diabetes centre. Other studies reported that in type 2 diabetes the poor sugar control was 15 to 68% . This is of prime importance to know the glycemic control of our population on large sample in order to avoid or stop the complications of type 2 diabetes like nephropathy, retinopathy, vasculopathy, ketoacidosis and diabetic foot. Most of the studies conducted in our country are on prevalence of diabetes and not on glycemic control of type 2 diabetes. This study can help the clinicians to know the burden of uncontrolled diabetes.

MATERIALS AND METHODS

This retrospective study was carried out at Pathology Department, Kuwait Teaching Hospital, Peshawar from 1st January 2017 to 31st December 2018 on Khyber Pakhtunkhwa (KP) residents and comprised of 2654 participants. The inclusion criteria were type 2 diabetic cases, Pakistani nationals, both genders, and age above 18 years. Freshly diagnosed type 2 diabetes, type 1 diabetes, secondary diabetes, gestational diabetes, unknown type of diabetic cases or endocrine disorders for instance Cushing syndrome or hyperthyroidism were excluded because of high sugar level. The recorded data were age, gender, and HbA1C. Poor glycemic control patients were those cases having above 7% HbA1C. The data was examined in SPSS-22. Chi-square test was applied and P≤0.05 was the significance level.

RESULTS

The mean age of the study was 51.96±13.84 years and mean glycosylated hemoglobin was 8.52±3.060 (Table I). The females (n=1608, 60.6%) were more than males (n=1046, 39.4%). The most common age category was 40 to 60 years which had 1626(61.3%) participants followed by above 60 years (n=605, 15.9%) and least was 18 to 39 years [n=423, 15.9%] (Table 2). Of total sample 2654 the poor glycemic control (>7% HbA1C) was in 1705(64.2%) subjects while in 949(35.8%) the glycemic control was good [<7% HbA1C] (Fig. 1). Glycemic control among genders was not different statistically significantly [P=0.677] (Table 3). Glycemic control was different among the various age groups very highly statistically significantly (P<0.001). With increasing age the glycemic control become poorer. Above 40 years, the number of diabetic patients with bad sugar control was more than good glycemic control, and age 40 to 60 years 496(30.50%) had good glycemic control while 1130(69.50%) had poor glycemic control. Similar results were found for above 60 years age (Table 4).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.96±13.84</td>
<td>18-105</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>8.52±3.060</td>
<td>0-17.26</td>
</tr>
</tbody>
</table>

Table 2: Frequency of gender and age groups (n=2654)

<table>
<thead>
<tr>
<th>Gender</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1046</td>
<td>39.4</td>
</tr>
<tr>
<td>Female</td>
<td>1608</td>
<td>60.6</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-39</td>
<td>423</td>
<td>15.9</td>
</tr>
<tr>
<td>40-60</td>
<td>1626</td>
<td>61.3</td>
</tr>
<tr>
<td>&gt;60</td>
<td>605</td>
<td>22.8</td>
</tr>
</tbody>
</table>

Figure No.1: Glycemic control of the study
DICUSION

The research was done to find out the control levels of glucose among the patients of type 2 DM. The study findings showed that in 64.2% had poor glycemic control (>7% HbA1C). With increasing age the glycemic control become poorer. As far as the control of blood sugar level in patients with DM type 2 is concerned, the tertiary care hospitals typically carry out realistic estimate comparative to primary and secondary healthcare levels due to large number of cases available.17

Our research found that 64.2% patients had poor control of blood glucose level. Liu et al16 conducted a nationwide multicenter study in China. They reported that 65% type 2 diabetic patients had poor sugar control. Ji et al18 investigated the sugar control among type 2 diabetics in China receiving oral hypoglycemics drugs or injectable insulin. They included 238,639 patients in their survey. They reported that 68% type 2 diabetic patients had bad sugar control. These results are in consistent with our study. Another cross sectional, multicenter study conducted in Lahore, Pakistan on glucose levels of DM type 2 on elderly subjects. They reported that only two third (32.3%) had good glycemic control19 and results were found similar to the present study.

However another two studies conducted on blood sugar level among type 2 diabetic subjects reported that 51% and 52% had poor glycemic control respectively.15,20 The difference in results can be attributed to awareness among patients, educational level of patients, and availability of physicians.

Our results showed that with increasing age the glycemic control become poorer. Similar results were found by Li et al4 in China and Atif et al19 in Pakistan. There has an established positive association between prolong duration of type 2 diabetes poor glycemic control.18,21 As type 2 diabetes is progressive disease, as the time passes the functional and volumetric capacity of β-cells steadily decreases.14 In order to attain strict glycemic control systemic approach is recommended for type 2 diabetic patients. These include modification in lifestyle like diet and physical activity, use of oral hypoglycemics and insulin as suggested by endocrinologist.22

The current study showed that the glycemic control among genders was not statistically significant. Similar findings were shown in retrospective study in China by Li et al.14

Our study has some strong and some weak points also but this is the first study of such a large sample to explore the glycemic control among type 2 diabetics in a teaching and tertiary care hospital of Peshawar. We used HbA1C test which gold standard for glycemic control for monitoring over past 3 months. However, our study was retrospective design and single center. So, multi centre and prospective design studies are recommended to further explore this area.

CONCLUSION

About two third diabetic patients have very bad sugar control in our population. These results should be considered in future interventional research aiming to make better the sugar control in diabetic patients.

REFERENCES

Efficacy of Tramadol Nebulization in Reducing Post-Operative Sore Throat

Umar Iqbal1, Ahsan Khan2, Aqeel Moazzam3, Muhammad Saqib4, Asghar Ali4 and Zahid Hanif4

ABSTRACT

Objective: To compare the efficacy of preoperative tramadol nebulization versus placebo in reducing postoperative sore throat.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Departments of Anesthesiology, Lahore General Hospital, Lahore and Arif Memorial Teaching affiliated with Rashid Latif Medical College Lahore from January 2018 to June 2018.

Materials and Methods: One hundred and sixty-four patients, aged 20-50 years undergoing general anesthesia. Group A was given pre-operative tramadol nebulization 1mg/kg in 3ml normal saline while Group B was given normal saline nebulization. Nalbuphine 0.1 mg per kg was used for intraoperative analgesia. After application of standard monitoring, induction was done with Propofol 2mg/kg and tracheal intubation with atracurium 0.5mg/kg. Maintenance of anesthesia was done with oxygen, nitrous and isoflurane 1.2% with IPPV. After extubation all patients were assessed after 12 hours for sore throat, hoarseness and pain (VRS score).

Results: The mean age of the patients was 38.65 ± 8.37 years in the tramadol group and 37.03±9.66 years in the placebo group (P-value = 0.311). 71.9% patients achieved efficacy of the drug in the tramadol group and 51.6% attained in the placebo group in terms of no or mild post-operative sore throat (p = 0.018).80.8% males in the tramadol group had no or mild sore throat as compared to65.8%) females.

Conclusion: Pre-operative tramadol nebulization can significantly reduce the incidence of POST as compared to placebo.

Key Words: Efficacy, Placebo, POST, Sore throat, Tramadol

INTRODUCTION

Postoperative sore throat is an accepted phenomenon following general anesthesia with a reported incidence of 21-66%.1,3 Postoperative sore throat (POST) is experienced by 30% to 65% of the patients after general anesthesia despite being perceived as a trivial problem.1 POST is a major cause of patient annoyance and physical discomfort during the recovery phase and post hospital discharge and thus should be prevented.2,5,6 Symptoms of sore throat manifests as dysphagia, dysphonia, hoarseness, continuous throat pain and pharyngeal dryness.3

It is attributed to various perioperative conditions, including local irritation and inflammation of airway, mucosal injury in the trachea, oropharyngeal suctioning, intra cuff pressure, use of throat pack, size of the endotracheal tube, duration of surgery and multiple attempts of intubation.2 Female sex, pre-existing pulmonary disease, anesthesia time and staining of blood on tracheal tube on extubation are all related to the greatest risk of postoperative sore throat.7 The peak of sore throat is in the initial period after surgery, 2 to 6 hours after extubation, but the incidence decreases quickly with time.3 Several techniques have been evaluated to reduce POST like drug-free interventions such as relatively small sized endotracheal tubes, reducing intracuff pressure to less than 18cm H2O, lubrication of the endotracheal tube with water-soluble jelly, gentle airway handling, intubation with maximum muscle relaxation and extubation after full deflation of tracheal cuff.8 Pharmacological measures such as clonidine, betamethasone gel, benzylamine hydrochloride, NSAIDs, local anaesthetics, ketamine gargles and chamomile extract spray have been used to reduce POST with variable responses.1 Simple, safe, and inexpensive therapies to reduce or eliminate POST would be helpful and could improve patient satisfaction significantly.

1. Department of Anaesthesiology / Surgery2 / Orthopedics3, Rashid Latif Medical College, Lahore.
2. Department of Anaesthesia, Lahore General Hospital, Lahore.

Correspondence: Dr Umar Iqbal, Associate Professor of Anaesthesiology, Rashid Latif Medical College Lahore.
Contact No: 03214243093
Email: umer8808@gmail.com

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Experimental studies have shown that NMDA (N-methyl-D-aspartate) receptor antagonists when intravenously administered have anodyne and anti-inflammatory effects and were effective in reducing POST.\(^2\) Tramadol hydrochloride is a synthetic analogue of codeine, an opioid receptors agonist and a NMDA receptor antagonist. It hampers reabsorption of monoamines (noradrenaline and serotonin) and has some local anesthetic effect as well.\(^2\) It acts on peripheral nerve endings in the pharyngeal mucosa and can reduce the incidence of sore throat.\(^2\) The positive effects of tramadol on reducing sore throat have been seen in early research. In a study conducted by Lee CP et al, preoperative gargling with tramadol comforted pain in early POST.\(^5\) Rashwan et al\(^6\) in his study found the occurrence of postoperative sore throat to be remarkably low with preoperative tramadol gargles in comparison to placebo.

**MATERIALS AND METHODS**

It is a randomized controlled trial conducted at the Departments of Anesthesiology, Lahore General Hospital, Lahore and Arif Memorial Teaching affiliated with Rashid Latif Medical College Lahore from 1\(^{st}\) January 2018 to 30\(^{th}\) June 2018. A total of 164 patients were enrolled. All patients undergoing elective general anesthesia with an age range of 20 to 50 years, including both genders belonging to ASAII and ASAII were included. Approval was seeked from hospital ethical committee and informed consent was obtained from each patient. Group A was given pre-operative tramadol nebulization 1mg/kg in 3ml normal saline (treatment group) while Group B was given normal saline nebulization (placebo group). No other preoperative sedative premedication was used. Nalbuphine 0.1 mg per kg was used for intraoperative analgesia. After application of standard monitoring, induction was done with Propofol 2mg/kg and tracheal intubation with atracurium 0.5mg/kg. Oxygen, nitrous and isoflurane 1.2% with IPPV were used for maintenance of anesthesia. At the end of surgery reversal was given and patient extubated. All patients were assessed after 12 hours for sore throat, hoarseness and pain (VRS score).

Data was analyzed by SPSS 20. Descriptive statistics were calculated for outcome variables. T-test for continuous and Chi-square test for categorical was applied to check the significance among groups. \(P\)-value \(0.05\) was considered as significant.

**RESULTS**

The mean age of the patients in tramadol group was \(38.65 \pm 8.37\) years and \(37.03 \pm 9.66\) in the placebo group (Table 1). Baseline body mass index among patients of both groups was comparable and calculated to be \(25.47 \pm 2.82\) vs \(25.71 \pm 3.10\) kg/m\(^2\) in tramadol versus placebo group respectively (Table 2). The mean verbal rating scale score was calculated to be \(2.64 \pm 1.66\) in tramadol group versus \(3.89 \pm 2.39\) in the placebo group. Significant difference was detected for the VRS score among both groups with \(P\)-value = 0.001 (Table 3). In the tramadol group patients, the efficacy (in terms of no or mild post-operative sore throat) was observed in \(46/64\) (71.9%) and \(33/64\) (51.6%) in placebo group. Significant difference was seen in the occurrence of sore throat among the groups (p=0.018). The percentage of efficacy was better in the tramadol group (Table 4).

<table>
<thead>
<tr>
<th>Table No.1: Comparison of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>Group A (Tramadol)</td>
</tr>
<tr>
<td>Group B (Placebo)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No.2: Comparison of body mass index (kg/m(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>Group A (Tramadol)</td>
</tr>
<tr>
<td>Group B (Placebo)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No.3: Comparison of verbal rating scale</th>
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</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>Group A (Tramadol)</td>
</tr>
<tr>
<td>Group B (Placebo)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No.4: Comparison of efficacy of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
</tr>
<tr>
<td>Count</td>
</tr>
<tr>
<td>% within Groups of the patients</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>Count</td>
</tr>
<tr>
<td>% within Groups of the patients</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No.5: Comparison of operative time according to efficacy of the drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time (min)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>≤60</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>&gt;60 to ≤120</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>&gt;120 to ≤180</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

No significant difference was found among the groups with duration of surgery less than 120 minutes (p value=0.315). In surgical procedures lasting for more than 120 minutes, significant difference was seen among the groups. In tramadol group 69.2% (9/13)
patients versus 33.3% (7/21) in placebo group did not complain of sore throat (p value=0.042) (Table 5). When data was stratified with respect to gender it revealed that 21/26 (80.8%) males in the tramadol group had no or mild sore throat as compared to females 25/38 (65.8%) in the tramadol group which demonstrate that the highest efficacy was achieved in males with statistically significant difference between the groups [p = 0.015] (Table 6).

Table No.6: Comparison of gender according to groups

<table>
<thead>
<tr>
<th>Gender</th>
<th>Tramadol</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>26</td>
<td>32</td>
<td>58</td>
</tr>
<tr>
<td>% within Groups of the patients</td>
<td>40.6%</td>
<td>50%</td>
<td>45.3%</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>38</td>
<td>32</td>
<td>70</td>
</tr>
<tr>
<td>% within Groups of the patients</td>
<td>59.4%</td>
<td>50%</td>
<td>54.7%</td>
</tr>
</tbody>
</table>

DISCUSSION

Postoperative sore throat has a complex etiology, and multiple factors contribute to POST include age, sex, type of surgery, mode of anesthesia, dimensions and cuff pressure of endotracheal tube, pharyngolaryngeal mucosal trauma from laryngoscopy, injury while insertion of airway, suctioning, and procedural handling of the airway and surrounding tissue.1,3 It indicated that irritation of pharynx, larynx, or trachea leading to inflammation may be the causes for POST.3 There are various pharmacological methods for prevention of POST and include steroid both in intravenous and topical preparation, topical benzydamine hydrochloride, topical magnesium, ketamine gargles and topical liquorice.3 According to study by Subedi et al4 dexamethasone lowered the incidence of POST. Ahuja et al12 concluded that ketamine nebulization markedly reduced the prevalence and intensity of POST, especially in the immediate post-operative period with no harmful outcomes. Similar results were observed by Aimingad and Jayaram13 who found ketamine nebulization to be effective in attenuating POST. Although previous studies have been done with different drugs by nebulization but data is sparse with tramadol use for POST. Pneumatic nebulization generates large sized particles which deposit in the mouth and throat during nebulization rendering low frequency and severity of post-operative sore throat.4 The current study showed that tramadol nebulization 1mg/kg in 3ml normal saline administered pre-operatively reduced POST, at 12 hours after surgery, post general anesthesia with laryngoscopy and or tracheal intubation. Tramadol nebulization showed no side effects in the treatment group. It is suggested that NMDA antagonists significantly reduced the frequency and severity of POST because of their pain relieving and anti-inflammatory effects.14

The efficacy in our study results was achieved in 71.9% of the patients in the tramadol group in comparison to 51.6% in the placebo group however the incidence of postoperative sore throat (regardless of its severity) was notably reduced in tramadol treated group compared to placebo group. Consistent with the results of our study, Yadav and Gopinath compared the effect of Ketamine, tramadol, 1.5% saline and normal saline gargles on postoperative sore throat and found decrease in incidence of sore throat with ketamine and tramadol after 2.4 and 24 hours (p < 0.05). They did not find any marked difference in incidence of sore throat in association with gender which was different from our study.8

Similar to the current study results, the work done by Kudva and Hegde found preoperative Tramadol gargle to be proportional with Ketamine gargle in reducing the frequency and severity of POST at 2.4 and 24 hours postoperatively.2

Lee et al9 compared tramadol and benzydamine gargle in relieving POST after Proseal Laryngeal Mask Airway (PLMA) anesthesia. Similar to our study results they found significantly few patients complaining of sore throat with preoperative tramadol gargling at 30 minutes of removal of PLMA. In contrast to our observation POST was not affected by duration of surgery in their study which could be because of placement of PLMA and not ETT. Comparable to our results, the frequency of postoperative sore throat (regardless of its severity) was significantly lower in tramadol treated group compared to placebo group at 2, 6, 12, and 24 h (p<0.05) in study by Rashwan et al10

Farzam et al15 studied the effects of tramadol and lidocaine gel on complications of orotracheal intubation. Inconsistent with the results of our study they did not find significant effect on reduction of sore throat with 5% tramadol gel and 2% lignocaine gel. The difference in results could be due to use of gel in comparison to our study where we nebulized with tramadol.

The etiology of POST includes exasperation of the mucosa and cuff-induced pressure on the mucosa followed by an aseptic inflammatory process. Tramadol is NMDA receptor antagonist that acts on peripheral nerves of pharyngeal mucosa and thus reduces inflammation.8,14

One limitation of our study was that we did not observe the haemodynamic changes and side effects that could have occurred with tramadol nebulization. Also serum levels of tramadol were not measured. Future studies can be done with different doses of tramadol and measuring the hemodynamic changes and serum levels.
CONCLUSION

Pre-operative tramadol nebulization can significantly reduce the incidence of post-operative sore throat as compared to placebo in patients undergoing elective surgeries utilizing general anesthesia. Thus we can make some practical recommendations in our routine practice guidelines to decrease post-operative sore throat in order to improve the patient’s satisfaction and decrease the morbidity of patients.

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

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

REFERENCES

Objective: To find frequency of asthma chronic obstructive pulmonary disease overlap syndrome in patients with chronic obstructive pulmonary disease.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine, Avicenna Medical & Dental College, Lahore from November 2019 to April 2020.

Materials and Methods: Two hundred patients of both genders presented with chronic obstructive pulmonary disease were taken. The name, age, and gender, contact details and BMI were recorded. Five ml of venous blood was drawn for IgG and CBC and bronchodilator response was assessed on spirometry. All clinical diagnosis and procedures were made by senior consultant.

Results: The mean age of all cases was 51.63±7.17 years with minimum and maximum age as 40 and 64 years. There were 115 (57.5%) male and 85 (42.5%) female cases. The mean weight, height and body mass index were 93.19±18.05, 1.83±0.18 and 27.90±4.10 respectively. A total of 70 (35%) cases were obese and 130 (65%) cases were non-obese in this study. According to operational definition the frequency of ACOS was noted in 39 (19.5%) and 161 (80.5%) cases did not have ACOS. When data was stratified, the frequency of ACOS was statistically same in both age groups, gender, obese and non-obese and regardless of duration of COPD, p-value > 0.05.

Conclusion: The frequency of ACOS was diagnosed 19.5% of cases that is higher percentage. So cases with COPD must be diagnosed ACOS and should be managed by prescribing more appropriate medication such as inhaled corticosteroids early in the course of the disease. Through early intervention we can reduce the related complications and mortality.

Key Words: Obstructive lung diseases, Airway hyper responsiveness, Wheeze, Respiratory function tests, Differential diagnosis, ACOS


INTRODUCTION

The COPD is a chronic respiratory condition with time-limited decreases in lung function followed by respiratory symptoms, mainly dyspnea, cough and sputum. COPD is a highly heterogenenous disease, although the clinical appearance and prediction can vary for all patients with chronic, non-full reversible airflow restrictions. COPD is frequently related to a tobacco history and is the major contributor to chronic lower-respiratory mortality and has been one of the third leading causes of death. The prevalence of COPD varies from 0.2%-37%, but is significantly different across countries and communities and across methods for diagnosing and classifying COPDs. In men and women aged 75 years and older, prevalence and incidence was highest. Furthermore, both chronic conditions are asthma and COPD, which are very common for people in general. These airway obstruction diseases have a persistent inflammatory effect that affects the entire respiratory tract. Obstructions in asthma are normally sporadic and reversible, but are gradual and irreverent in COPD. Asthma and COPD can overlap and converge particularly in older people [Overlap Obstructive Pulmonary Disease Overlap Syndrome (ACOS). Asthma COPD (ACOS) is characterized in association with an incompletely reversible airflow obstruction as symptoms of increased variability of airfield.
A recent study found that the prevalence of ACOS in PDC patients was 15%, whereas the general prevalence of ACOS in PDC patients was reported by another study at approximately 17.4%. ACOS has risen with age in prevalence.

The explanation for the present study is to classify ACOS frequency in COPD Patients as asthma and COPD are often considered to be mutually exclusive diseases primarily due to the inclusion in therapeutic clinical trials only of typical cases of asthma or COPD. However, in a large number of patients, doctors can not differentiate the two disorders, which can be referred to as "asthmatic-COPD overlap syndrome." This agency should be noted because patients with an overlap of asthma-COPD are more symptomatic, lower in quality of life and more exacerbated than those of either asthma or COPD alone.

**MATERIALS AND METHODS**

This cross-sectional study was conducted at hospital Medicine Department of Avicenna Medical & Dental College, Lahore during from 1st November 2019 to 30th April 2020. A total of 200 patients of both genders presented with COPD were taken. The demographical data (name, age, and gender), contact details and BMI were obtained. Patient’s ages were ranging from 40 to 65 years. Patients with severe chronic respiratory disease (cystic fibrosis, pulmonary fibrosis, active neoplasm) on medical record were excluded. Five ml of venous blood was drawn for IgG and CBC and bronchodilator response was assessed on spirometry. ACOS was defined if patients have history of asthma and a bronchodilator response to albuterol higher than 15% and 400 mL, IgE >100 IU, a percentage of blood eosinophils >5%. All clinical diagnosis and procedures was made by senior consultant having more than 5 years of experience to avoid any bias. All data was collected by researcher himself. SPSS version 20 was used to collect and analyze data. Chi-square test was applied considering p-value ≤ 0.05 as significant.

**RESULTS**

There were 115 (57.5%) male and 85 (42.5%) female cases. 125 (62.5%) cases were 40-54 years old and 75 (37.5%) cases were 55-64 years old. Mean BMI was 27.90±4.10. Seventy (35%) cases were obese and 130 (65%) cases were non-obese. Duration of disease was also noted and there were 127 (63.5%) cases had COPD since 6-12 months and 73 (36.5%) cases had COPD from >12 months (Table 1).

In 40-54 years and 55-64 years of age the frequency of ACOS was seen in 27 (21.6%) and 12 (16%) of the cases[\(p > 0.05\)] (Table 2). When we stratified with gender we found that in male and female cases the frequency of ACOS was also statistically same, i.e. 17.4% versus 22.4%. p-value > 0.05. (Table 3).

**DISCUSSION**

Asthma is a disease which frequently develops during infancy but can also be diagnosed during the life of adults. It is characterized by an airway hyper-responsiveness (AHR) which results in an airway obstruction that is intermittent and normally reversible, and COPD is a chronic respiratory disease usually linked to tobacco, which typically occurs in individuals...
over the age of 40 and is characterized by progressive and irreversible airway obstruction. Asthma chronic obstructive pulmonary disease overlap syndrome was recently identified as a condition characterized by persistent airflow restrictions with several features typically associated with asthma and several features typically linked to COPD, as a recent document produced by the scientific committee both of the Global Asthma Initiative (GINAs) and the Global Initiative of Chrons’ Chronic Obstruction Lung Disease (GOLDs). The overlap makes it difficult to distinguish COPD from asthma with persistent airflow limits, particularly among smokers and seniors. The mean age was 51.63±7.17 years in the current study with the minimum and maximum age at the age of 40 and 64. 115 males (57.5%) and 85 (42.5%) female cases occurred. The majority of patients were males (93.0 percent), a mean age 73.5±8.3 years (110) reported a study in 2017. These results are close to our analysis. The occurrence of ACOS in 39 (19.5%) and 161 (80.0%) cases were not reported under operational description. ACOS was not reported in 161 (80.5%). A recent study found that the prevalence of ACOS in PDC patients was 15%, whereas the general prevalence of ACOS in PDC patients was reported by another study at approximately 17.4%. ACOS prevalence is increasing with age. Thus, in the current analysis, the frequency of the ACOS was greater than both. In 2015, a systematic analysis was also performed of a total of nineteen studies, in which it was found that the overlap prevalence of COPD among population-based research populations and clinical trials was 27% (95% CI: 0.16-0.38%, p<0.000) and 28% (95% CI: 0.09-0.47%, p=0.0032). ACOS is therefore a common disorder in a large number of COPD subjects. ACOS is a distinct clinical phenotype with more frequent aggravation, admission, reduced quality of life related to health, and higher health costs than any single disorder. The management and treatment of this syndrome must be better defined.

In various age groups and genders, we found no superiority of ACOS. In a further trial, patients receiving inhaled corticoids (63.2%) with ACOS were mainly male (81.6%) with symptomatic mild to moderate diseases (67%).

CONCLUSION

The frequency of ACOS was diagnosed 19.5% of cases that is higher percentage. So cases with COPD must be diagnosed ACOS and should be managed by prescribing more appropriate medication such as inhaled corticosteroids early in the course of the disease. Through early intervention we can reduce the related complications and mortality.

REFERENCES


Assessment of Oral Hygiene Maintenance among Young Adults
Muhammad Arqam Najmi1, Jawaria Zeeshan2, Waqas Iqbal3, Uzma Tariq3, Morfique Abdull Momen Al Absi4 and Naveed Irfan5

ABSTRACT

Objective: Oral health is essential for general health of the individuals, poor health is related to significant morbidity and it affects the quality of life of the affected person. The objective of the present study was to assess the oral hygiene practices among students of different institutions of Karachi city.

Study Design: Cross Sectional study.

Place and Duration of Study: This study was conducted at different educational institutions of Karachi and Hyderabad (Bahria University of Medical and Dental College University, University Dental College, Hyderabad) from January 2019 to June 2019.

Materials and Methods: It was conducted among 500 subjects who were randomly selected from the different educational institutions of Karachi and Hyderabad. A questionnaire was administered to determine the oral health knowledge and practice in 500 samples from January to June, 2019. The data was analyzed on statistical package for the social sciences (SPSS), version 23.

Results: The present study findings showed that majority of the male students 338 (98.5%) used tooth brush as a cleaning aid followed by miswak 4(1.2%) and Manjan 1(0.3%). Medium bristled tooth brush was more widely used among females as compared to males with a p-value 0.004. The change of tooth brush was observed within 1-3 months with significance of <0.05 p-value.

Conclusion: In this study potential for the improvement in the oral health status and interest in taking modern oral hygiene maintenance measures among students was found significant. However, much emphasize must be taken on a larger scale to implement these measures for general young population.

Key Words: Tooth brush, Oral Hygiene, Brushing teeth, Awareness

INTRODUCTION

Oral hygiene has been recognized as important as general health. It plays an important role in the pathogenesis of dental decay and periodontal disease therefore, maintaining a good oral hygiene is imperative for oral health. Regular cleaning of the teeth and routine dental check-up is mandatory for good oral hygiene maintenance.

Research has shown that in developing countries, the oral hygiene practice has been ignored due to lack of oral health knowledge and low socioeconomic status.

According to World Health Organization (WHO), about 60% to 90% school going children and nearly every adult around the globe has dental caries. Dental caries is the highly prevalent dental problem in most of the world. Studies have shown that 90% of the students have experienced dental cavities which lead to tooth loss at a young age.

The practice of brushing teeth varies in different parts of the world. A study conducted in Jordan, illustrates that female students brushed their teeth more frequently than male students. Almas conducted a study in Gulf country which demonstrated that 50% of dental patients brushed their teeth twice daily. This study revealed that knowledge and awareness about oral health care was better in male subjects than female. The aim of this study was to assess the knowledge and perception about oral health care among students of Karachi and Hyderabad cities.

MATERIALS AND METHODS

This cross-sectional and multicenter study was carried out from January to June, 2019 for assessing dental care knowledge and awareness among school going pupils. 500 students participated in this study. For this study the non-probability convenient sampling technique was utilized. A questionnaire was designed to assess their
oral health knowledge comprising of demographic details and questions related to oral health, presented in simple English language. The questionnaire reflected the following variables: frequency of tooth brushing, type of dentifrices used and when to change a tooth brush. The present study was approved by Ethical Board Review Committee. An informed consent was taken prior to initiation of the study. Inclusion and exclusion criteria were strictly followed and only those variables were presented as frequency and percentages. To see the significance between gender with type of instrument used and other variables Chi-Square test was used. P-value of $\leq 0.05$ considered to be statistically significant.

**RESULTS**

A total of 500 students participated in this study. Out of the 500, there were 343 (68.6) males and 157 (31.4) females. The results from this study revealed that the mean age of the participants, was 19.95 and STD±1.62. In present study, the different types of instrument used for tooth brushing were also examined based on gender. As shown in Table 1, a majority of the male participants which was about 255 (51.0%) used tooth brush as a cleaning aid followed by Miswak and Manjan respectively 4(1.2%), 1(0.3%) as shown in Table 1. However, it was also observed that none of the females used Miswak and Manjan so the only cleaning aid used by them was a tooth brush. The gender difference was statistically in significant (p=0.315) when compared with type of instrument used.

**Table No.1:** Different Instrument for Brushing Teeth

<table>
<thead>
<tr>
<th>Type of instrument used for brushing teeth</th>
<th>Gender</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>Miswak</td>
<td>4(1.2%)</td>
<td>0(0.0%)</td>
<td>4(0.8%)</td>
</tr>
<tr>
<td>Tooth brush</td>
<td>338(98.5%)</td>
<td>157(100%)</td>
<td>495(99.0%)</td>
</tr>
<tr>
<td>Manjan</td>
<td>1(0.3%)</td>
<td>0(0.0%)</td>
<td>1(0.2%)</td>
</tr>
<tr>
<td>总计</td>
<td>343(100%)</td>
<td>157(100%)</td>
<td>500(100%)</td>
</tr>
</tbody>
</table>

*Chi-square test was applied, P-value $\leq 0.05$ considered to be statistically significant

**Table No.2:** Distribution of Types of Tooth Brush Bristles Among Gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft</td>
<td>118(34.4%)</td>
<td>66(42%)</td>
<td>184(36.8%)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Medium</td>
<td>206(60.1%)</td>
<td>87(55.4%)</td>
<td>293(58.6%)</td>
<td></td>
</tr>
<tr>
<td>Hard</td>
<td>19(5.5%)</td>
<td>4(2.5%)</td>
<td>23(4.6%)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square test was applied, P-value $\leq 0.05$ considered to be statistically significant

Moreover, 293 (58.6%) of the patients used medium bristled tooth brush, while 184 (36.8%) used soft bristled and 23 (4.6%) used hard bristled. Again, the use of medium bristled tooth brush was more popular in males than in females as shown in Table 2. P-value 0.004 was observed statistically highly significant. Change of tooth brush was cross tabulated with gender, demonstrating that the p-value $\leq 0.000$ was highly significant when comparing gender with change of tooth brush. Present findings showed that the replacement of tooth brush was most commonly seen during the period of 1-3 months in males 266 (77.6%), 102(65.0%) in females and least during 7-9 months, in 14 males (4.1%) and 5 females (3.2%), Table 3.

**Table No.3:** When to Change Tooth Brush (Time Bound)

<table>
<thead>
<tr>
<th>Months</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 months</td>
<td>266 (77.6%)</td>
<td>102(65.0%)</td>
<td>368(73.6)</td>
<td>0.000*</td>
</tr>
<tr>
<td>4-6 months</td>
<td>63 (18.4%)</td>
<td>50(31.8%)</td>
<td>113(22.6%)</td>
<td></td>
</tr>
<tr>
<td>7-9 months</td>
<td>14 (4.1%)</td>
<td>5(3.2%)</td>
<td>19(3.8%)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi Square test was applied to see the significance, P-value $\leq 0.05$ considered to be significant.

It was further observed in the study, that 255 (51.0%) a majority patients brushed their teeth once daily 255 (51.0%). Out of which, 213 (62.1%) were males and 42 (26.8%) were females. However, a slight difference was seen between the two genders who brushed their teeth twice a day as shown in Table 4. Statistically significant P-value was observed to be 0.000.

**Table No.4:** Frequency of Tooth Brushing with Gender

<table>
<thead>
<tr>
<th>Months</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once daily</td>
<td>213(62.1%)</td>
<td>42(26.8%)</td>
<td>255(51.0%)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Twice daily</td>
<td>120(35.0%)</td>
<td>115(73.2%)</td>
<td>235(47%)</td>
<td></td>
</tr>
<tr>
<td>Occasionally</td>
<td>10(2.9%)</td>
<td>0(0.0%)</td>
<td>10(2.0%)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi Square test was applied to see the significance, P-value $\leq 0.05$ considered to be significant

**DISCUSSION**

Dental plaque is considered to be one of the most important factors for dental caries and periodontal diseases. There is a variety dental cleansing materials available in the market to decrease the amount of bacterial growth which later causes dental problems. In present study, we also investigated the different measures that were taken by our subjects to maintain their oral hygiene. A majority of the male subjects used tooth brushes with tooth paste as a cleaning aid followed by Miswak and manjan respectively. However, it was also observed that none of the females used Miswak and Manjan so the only cleaning aid used
by them was tooth brush. Similar results were also observed by Oberoi study in which 83.6% patients used tooth paste with tooth brush as a cleaning aid. A study by Hind Al-Johani reported that approximately, all patients (95.4%) used tooth brushes for cleaning teeth. These studies also support our findings. In contrast, Singh et al reported in their study that approximately 60% of their patients used finger along with white powder for the cleaning of teeth, in rural areas of India.

Research has shown that dental caries mostly seen in school going children. The duration of tooth brushing plays an important role in the efficient removal of plaque and buildup of tartar which prevents bad breath and keeps the teeth whiter. Brushing teeth twice a day keeps the gums healthy and prevents from gum diseases. A study conducted on adults and children in Jakarta, Indonesia by Anton Rahardjo et al showed a larger number of participants brushing their teeth twice daily. A study on Chinese adolescents showed that 67% of the subjects were brushing their teeth twice daily. Similarly, another study by Tsevenjav and colleagues, who compared the dentist with general population, revealed that 81% of dentists brushed their teeth twice daily. This could be due to fact that dentist are health care professionals who are more aware of preventive dentistry as compared to rest of the community. Dentists are considered to be the role models as they maintain a meticulous oral hygiene. A study conducted by Wagle M et al, showed that even a majority (96%) of the dentists brushed their teeth twice daily compared to a layman. These differences could be related to the knowledge and awareness of oral health care, socioeconomic status and eating habits. On the other hand, the current study findings showed a higher incidence among males who brushed their teeth once daily. A study conducted in Central Gujarat showed that majority of the male subjects, (82.1%) brushed their teeth once a day. This study also supported our findings. On the other hand, a meta-analysis data with respect to gender showed that females brushed their teeth significantly more often than males. It is also noticed that both male and female were found to have a similar risk of developing tooth decay.

Abrasion of teeth is ‘pathologic wearing a way of tooth substance through some abnormal mechanical processes. Use of abrasive dentifrices or aggressive teeth brushing with hard type of tooth brush may results in V-shaped or wedge shape defect on the root side of cement enamel junction area. Factors such as brushing technique, force applied, brushing frequency and stiffness of tooth brush play an important role in the etiology of abrasion. In our study, most of the patients 293 (58.6%) used medium bristled tooth brush followed by soft bristled and hard bristled brush.

Change of tooth brush was also investigated in our study. Study conducted on Nigerian dental therapist showed that 98 (40.5%) of them replaced their tooth brush every 3 months. These results are in accordance to our study findings. On the contrary a study conducted on oral health knowledge in rural Indian population showed that the knowledge on frequency of changing tooth brush was found to be poor. This again was due to the lack of awareness and affordability.

CONCLUSION

It is concluded that in the present study there is an improvement in the oral health status and behavior among young students. It is observed that general young population of Karachi and Hyderabad can practice oral hygiene maintenance measures if regular community visits and governmental interests in this regards are held in an organized pattern on a regular basis.

Author’s Contribution:
Concept & Design of Study: Muhammad Arqam Najmi
Drafting: Jawaria Zeeshan, Waqas Iqbal, Uzma Tariq
Data Analysis: Morfique Abdullmomen, Al Absi
Revisiting Critically: Naveed Irfan
Final Approval of version: Muhammad Arqam Najmi

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

REFERENCES
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Objective: To determine the treatment outcomes of simple dilatation procedure for the management of short segment urethral strictures.

Study Design: Retrospective/observational study

Place and Duration of Study: This study was conducted at the Saidu Teaching Hospital Swat and PIMS Hospital Islamabad during from June 2019 to November 2019.

Materials and Methods: Total 104 patients presented with simple short segment urethral strictures were included. Patients detailed demographic including age, sex, clinical presentation and etiology of strictures were recorded after written consent. All patients receive simple urethral dilatation with antibiotics under local anesthesia. Pre and postoperative maximum flow rate on uroflowmetry and post-void residual urine (PVR) were recorded. Follow-up was taken at 4, 12 weeks and at 1 year. Overall improvement and recurrence rate was examined at final follow-up.

Results: The mean age of patients was 38.52±11.46 years. Majority of patients 80 (78.85%) had weak urine stream. 90 (86.54%) patients had iatrogenic strictures and 14 (13.46%) had idiopathic strictures. There is a significant improvement regarding maximum flow rate and PVR at 1, 3 and 6 months postoperatively with p-value 0.0001. At final follow-up, 95 (91.34%) patients showed full improvement. Recurrence found in 9 (8.65%) patients.

Conclusion: Simple dilatation under antibiotics cover is safe and effective treatment modality with fewer complications rate.

Key Words: Shor Segment Urethral Strictures, Urethral Dilatation

INTRODUCTION

Urethral strictures are a common urological and complex disorder. There are currently various operations to treat this condition. However, there is the lack of an appropriate technology in the variety of treatment methods. The urethra, in particular the bulbar tract, which is 46.9 percent, mainly includes the urethra in the developing countries. Moreover, the penile urethra represents 30 percent, with the remainder in a blend of both and panurethra. Strictness also varies from site to location.

The urethral rigidity is unknown anatomy. Outside trauma typically induces partial or complete contact with a urethra which is otherwise intact. Why stringency in other situations is unclear but, for some reason, a scar tends to arise as a result of changes in the urethral epithelium's structure and function and sub-epithelial spongy tissue that cause fibrotic urethra narrowing. Surgical treatment is increasingly emerging for urethral rigorous disease. There are currently several ways in which the urethra can be repaired and nearly all identical for technical ease, related morbidity and consequence. However, it is not clear which one is the best technique. The most popular treatments for urethral stringency diseases are Internal Urethrotomy and urethral dilatation. Laser urethrotomy, intraluminal stents and urethroplasty are other treatment choices. Initial urethrotomy requires cold knife and laser surgery, the most up-to-date procedure for urethral stricture. However, these techniques are flaws of strict repetition and the need for additional surgery. Therefore, some authors have described temporary expansion following internal urethrotomy in order to prevent stricture recurrence. dilatation is one of the most common models used for patients with urethral surgery; urethral dilatation is less invasive and with limited side effects. A randomized study compared internal dilatation and direct vision urethrotomy.
(DVIU) with no difference in healing outcomes between the two modes. However, due to the high recurrence rate, urethral dilution is mostly performed as a palliative manoeuvre and a further urethral reparatory surgery would be needed for the majority of patients. Many past studies have shown simple expansion for short segment urethral strictures to be safe and effective, with significant improvement and a lower rate of complications. The present study analyzed the effects of a simple dilatation procedure in the treatment of urethral short-segment strings.

**MATERIALS AND METHODS**

This prospective study was conducted at Saidu Teaching Hospital Swat and PIMS Hospital Islamabad during from June 2019 to November 2019. There were a total of 104 patients with ages 20 to 60 years who had simple urethral strictures in the short section. After written consent, the patients received comprehensive demographic details, including age, sex, clinical appearance and stricture etiology. Urethrogram retrograde has been completed. The study ruled out patients with unnecessary strictures, complicated and crumbling strictures.

Simple urethral dilatation with antibiotics under local anaesthesia was performed in all patients. Full uroflowmetry and postoperative residual urine (PVR) flow rate pre and postoperative (Qmax) were recorded. Follow-up was taken at 1, 3 and 6 months. At the final follow-up, overall progress and recurrence rates were examined. SPSS 24.0 was used to analyze the results. Student t-test was applied to compare the urine flow rate pre and postoperative (Qmax) were recorded. SPSS 24.0 was used to analyze the results.

**RESULTS**

The mean age of patients was 38.52±11.46. The median stricture length was 0.81 cm.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency No.</th>
<th>%/age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>38.52±11.46</td>
<td>-</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weak Urine Flow</td>
<td>80</td>
<td>78.85</td>
</tr>
<tr>
<td>Refractory UTI</td>
<td>7</td>
<td>6.73</td>
</tr>
<tr>
<td>Interrupted Urine Stream</td>
<td>5</td>
<td>4.81</td>
</tr>
<tr>
<td>Painful Micturition</td>
<td>5</td>
<td>4.81</td>
</tr>
<tr>
<td>Urinary Incontinence</td>
<td>4</td>
<td>3.85</td>
</tr>
<tr>
<td>Urinary Stream Deviation</td>
<td>3</td>
<td>2.88</td>
</tr>
<tr>
<td><strong>Types of Strictures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>90</td>
<td>86.54</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>14</td>
<td>13.46</td>
</tr>
</tbody>
</table>

Majority of patients 80 (78.85%) had weak urine stream, 7 (6.73%) patients had refractory urinary tract infection, 5 (4.81%) patients had interrupted urine stream, 5 (4.81%) patients had painful micturition, 4 (3.85%) patients had urinary incontinence and 3 (2.88%) patient had urine stream deviation. 90 (86.54%) patients had iatrogenic strictures and 14 (13.46%) had idiopathic strictures. Preoperatively median maximum flow rate (Qmax) on uroflowmetry was 5.9 ml/sec. A significant improvement was observed postoperatively at 1, 3 and 6 months with p-value <0.0001. The median post void residual on ultrasonography preoperatively was 70.65ml and a significant decrease in PVR was observed at 1, 3 and 6 months postoperatively with p-value <0.0001. (Table 2).

**DISCUSSION**

Urethral stricture in men is one of the common highly morbid malignant disorders. Most surgical procedures were used to treat urethral strings, but due to their ease and lower rates of complications dilatation is one of the most common surgical techniques for short-range urethral strings. The purpose of the present study was to determine the effects of simple dilation with the addition of antibiotics in short-specific urethral rigidity patients. In this study, 90.38% of patients had no significant complications completely recovered. Found repetition in 5 patients (9.62%). These findings demonstrated the same efficacy with some previous research in 85 to 95 percent repeat patients 0 to 10 percent.

In our study the mean age of patients was 38.52±11.46. The median stricture length was 0.81 cm. Majority of patients 80 (78.85%) had weak urine stream, 7 (6.73%) patients had refractory urinary tract infection, 5 (4.81%) patients had interrupted urine stream, 5 (4.81%) patients had refractory urinary tract infection, 5 (4.81%) patients had interrupted urine stream, 5 (4.81%) patients had refractory urinary tract infection, 5 (4.81%) patients had interrupted urine stream, 5 (4.81%) patients had interrupted urine stream, 5 (4.81%) patients had interrupted urine stream.
patients had painful micturition, 4 (3.85%) patients had urinary incontinence and 3 (2.88%) patient had urine stream deviation. 90 (86.54%) patients had iatrogenic strictures and 14 (13.46%) had idiopathic strictures. These results were comparable to many previous studies.\textsuperscript{15,17}

In present study we found significant improvement regarding maximum flow rate and PVR at 1, 3 months and at 6 months postoperatively with p-value <0.001. Preoperatively the median maximum flow rate (Q\textsubscript{max}) on uroflowmetry was 5.9 ml/sec ranges (4 to 15ml/sec) and median post void residual on ultrasonography was 70.65ml (40-190ml). Postoperative (Q\textsubscript{max}) improved to 18.2 at 1 month, 17.4 at 3 months and 16.8 ml/sec at 6 months. These results showed similarity to many of other studies in which patients showed significant improvement regarding maximum urinary flow rate with p-value <0.001.\textsuperscript{18,19} In our study we found, post-operative PVR values were 22 (10–60) ml, 30.4 (10–70) ml and 30.1 (10–70ml) at 1, 3 and at 6 months respectively. The median procedure time was 15.74 (10–25) minutes. These results were similar to several studies in which simple dilation procedure showed postoperatively significant difference regarding post void residual\textsuperscript{20,21}.

In our study we found fewer rate of post-operative complications, 1 patients showed bleeding and no patient with wound infection. The overall patients satisfaction rate was 90%. These results were comparable to some other studies.\textsuperscript{22,23}

**CONCLUSION**

Urethral stricture in men is the one of the malignant and painful disorder with high morbidity rate. Early and accurate diagnosis and better treatment modality helps to reduce the morbidity rate. We concluded that simple dilatation with addition of antibiotics is safe and effective treatment modality with fewer complications rate.

**Author’s Contribution:**

Concept & Design of Study: Mumtaz Ali Shah

Drafting: Irfan Ahmed, Nizamud Din

Data Analysis: Fazal Elahi, Fazal Akbar, Rashidullah

Revisiting Critically: Mumtaz Ali Shah, Irfan Ahmed

Final Approval of version: Mumtaz Ali Shah

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

**REFERENCES**

Comparison of the Treatment Outcomes of Different Surgical Procedures in Patients with Large Proximal Ureteral Stone

Asadullah, Muhammad Musa Kakar and Masha Khan

ABSTRACT

Objective: To compare the effectiveness in term of stone clearance between ureterolithotripsy, extracorporeal shock wave lithotripsy and Laparoscopic Ureterolithotomy.

Study Design: Comparative study

Place and Duration of Study: This study was conducted at the Urology Department Sandeman Civil Hospital Quetta, from April 2019 to June 2020.

Materials and Methods: In this study, 80 patients of both genders having large stones (>1cm) in proximal ureter were included. After taking informed consent, patient’s detailed history including age, sex and BMI were recorded. 24 patients received ureterolithotripsy, 27 patients received extracorporeal shock wave lithotripsy, and 29 patients received laparoscopicuretrolithotomy treatment. Effectiveness in term of stone clearance was recorded and compared between treatment procedures. Data was analyzed by SPSS 24.0.

Results: There were 46 (57.50%) males while 34 (42.50%) females patients with mean age 37.26±10.54 years. Mean BMI was 23.43±2.05 kg/m². Extracorporeal shock wave lithotripsy had significantly shorter operative time 40.85±4.62 minutes as compared to ureterolithotripsy and laparoscopic uretrolithotomy 68.72±5.22 minutes and 110.06±11.38 minutes (p-value <0.05). Patients received laparoscopic uretrolithotomy had significantly higher stone clearance rate 93.10% as compared to extracorporeal shock wave lithotripsy and ureterolithotripsy 55.56% and 58.33% (p-value <0.05).

Conclusion: Laparoscopic uretrolithotomy was more effective than extracorporeal shock wave lithotripsy and ureterolithotripsy in term of stone clearance.

Key Words: Ureteral, Calculi Stone, Ureterolithotripsy, Laproscopic, uretrolithotomy, Extracoporeal shock wave lithotripsy, Stone Clearance


INTRODUCTION

Ureteral stones are common in people worldwide, causing extreme pain and can lead to urinary tract infection and hydronephrosis. The primary cause of renal failure may also be ureteral stone. The ureteral stone (< 1 cm) of small dimension is normally transported into the bladder via a ureter, but the stones (> 1 cm) of large size can take more than two to three weeks to pass. For several years, the treatment of patients with ureteral stones was used for medical expulsions using Alpha blockers and calcium channel blockers, resulting in a high expultion rate of stones compared to placebo. The new multiple-center placebo-controlled exam has nevertheless resulted in a range of advantages over medical expulsive treatment. Surgical treatment is the better solution to remove large proximal ureteral stones. Furthermore, it is controversy about the correct technique or procedure to treat larger proximal stones. Several studies indicate that uretrosopic treatment is successfully exceeded. Uretroliothrapy and shock wave lithotripsy have been the first alternative treatment to the large proximal urinary tract stones. American urological association and European urology association have recommended the success rate by the URS in developing countries is high compared with shock wave lithotripsy.

Ureteroscopy is widely used in these conditions. Semi rigid and rigid URS for treatment of large proximal stones has been used. Multiple surgical complications may be caused by percutaneous nephrolithotomy. However, the technique of laproscopic lithotomy for treating large stones resulted in fewer complications and high effective ureteral clearance of stones. Several studies have been performed to evaluate the effectiveness of laproscopic lithotomy and...
ureterolithotripsy is the treatment and efficacy of large proximal ureteral stones. These studies have shown that laparoscopic lithotripsy is more successful than URSL \cite{7,8}.

We conducted this study to compare the effectiveness in term of stone clearance of ureterolithotripsy, extracorporeal wave lithotripsy and laparoscopic ureterolithotomy in patients presented with large ureteral stone.

**MATERIALS AND METHODS**

This comparative study was conducted at Department of Urology Sandeman Civil Hospital, Quetta from April 2019 to June 2020. Total 80 patients of both genders having large proximal stones >1cm in ureters were included. Patient’s age range was from 20 to 60 years. After taking informed consent, patient’s detailed history including age, sex and BMI were recorded. Pregnant women, history of open surgery, renal failure patients and those with no consent were excluded from this study.

Among all the patients, 24 patients received ureterolithotripsy, 27 patients received extracorporeal shock wave lithotripsy, and 29 patients received laparoscopic ureterolithotomy treatment. Effectiveness in term of stone clearance was recorded and compared between treatment procedures. Data was analyzed by SPSS 24.0. Chi-square test was done to compare the outcomes between surgical procedures with p-value <0.05 was taken as significant.

**RESULTS**

Out of 80 patients, 46 (57.50%) patients were males while 34 (42.50%) were females with mean age 37.26±10.54 years. Mean BMI was 23.43±2.05 kg/m². Mean stone size was 2.05±0.36 cm. (Table 1).

Table No 1: Demographics of all the patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency no.</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (Yrs)</td>
<td>37.26±10.54</td>
<td>-</td>
</tr>
<tr>
<td>Mean BMI (kg/m)</td>
<td>23.43±2.05</td>
<td>-</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46</td>
<td>57.5</td>
</tr>
<tr>
<td>Females</td>
<td>34</td>
<td>42.5</td>
</tr>
<tr>
<td>Mean Stone size (cm)</td>
<td>2.05±0.36</td>
<td>-</td>
</tr>
</tbody>
</table>

Extracorporeal shock wave lithotripsy had significantly shorter operative time 40.85±4.62 minutes as compared to ureterolithotripsy and laparoscopic ureterolithotomy 68.72±5.22 minutes and 110.06±11.38 minutes (p-value <0.05). Patients received laparoscopic ureterolithotomy had significantly higher stone clearance rate 93.10% as compared to extracorporeal shock wave lithotripsy and ureterolithotripsy 55.56% and 58.33% (p-value <0.05) (Table 2).

Table No 2: Comparison of outcomes between techniques

<table>
<thead>
<tr>
<th>Variables</th>
<th>Uretrolithotripsy (n=24)</th>
<th>Extracorporeal shock wave Lithotripsy (n=27)</th>
<th>Laparoscopic ureterolithotomy (n=29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative Time (min)</td>
<td>68.72±5.22</td>
<td>40.85±4.62</td>
<td>110.06±11.38</td>
<td>0.001</td>
</tr>
<tr>
<td>Stone clearance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14 (58.33)</td>
<td>15 (55.56)</td>
<td>27 (93.10)</td>
<td>0.001</td>
</tr>
<tr>
<td>No</td>
<td>10 (41.67)</td>
<td>12 (44.44)</td>
<td>2 (6.90)</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

Ureteral stone is one of the most common urological disorders. The technological advances of upper urinary tract stones have gradually changed the treatment. Surgical treatment is the better solution to remove large proximal ureteral stones. However, the best method for treating large proximal stones is controversial; research indicates that ureteroscopic treatment is far more effective than extracorporeal shock waves lithotripsy\cite{9}. The main downside of shockwave lithotripsy is long-term treatment time and the auxiliary procedures being needed.

Ureterolithotripsy is an efficient and safe form of treatment for large proximal ureteral stones as shown in various studies\cite{10} and that stone removal procedure has a high degree of root clearance compared to ESWL\cite{11}. The results are close to those observed in our study, which suggests a 58.3 and 55.6% stone removal ratio. Another research by Cout et al showed that ureterolithotripsy has better advantages than shock wave treatments without any significant complications differences\cite{12}. Several ureteral stones studies have shown that stones observed in the upper urinary tract may lead to serious complications\cite{13}. The most common and severe complications found in ureterolithotripsy treatment procedure is uretralevulsion and perforation and studies shows that the incidence rate 0 to 1\%\cite{14}. In our study, 46 (57.50%) patients were males while 34 (42.50%) were females with mean age 37.26±10.54 years. Mean stone size was 2.05±0.36 cm. A study conducted by Asif et al in which the male ratio was high as compared to females,\cite{15} previous studies demonstrated that average age of patients with large proximal stone was 35 years.\cite{16}

In present study we found that Extracorporeal shock wave lithotripsy had significantly shorter operative time 40.85±4.62 minutes as compared to ureterolithotripsy and laparoscopic ureterolithotomy 68.72±5.22 minutes and 110.06±11.38 minutes (p-value <0.05). These results showed similarity to many of previous studies in
which laparoscopic ureterolithotomy had significantly longer operative time as compared to extracorporeal shock wave lithotripsy and ureterolithotripsy 16-17. In our study we found that patients treated with ureterolithotripsy and laparoscopic ureterolithotomy had higher satisfaction rate as compared to extracorporeal shock wave lithotripsy. Some other studies showed similarity, in which laparoscopic ureterolithotomy had higher patients satisfaction rate as compared to extracorporeal shock wave lithotripsy 18-19.

CONCLUSION

We concluded Laparoscopic ureterolithotomy was more effective than extracorporeal shock wave lithotripsy and ureterolithotripsy in term of stone clearance. Laparoscopic ureterolithotomy has better treatment outcomes than other techniques, but has certain drawbacks that are longer operative time and being costlier than other procedures.

Author’s Contribution:
Concept & Design of Study: Asadullah
Drafting: Muhammad Musa Kakar
Data Analysis: Masha Khan
Revisiting Critically: Asadullah, Muhammad Musa Kakar
Final Approval of version: Asadullah

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

REFERENCES

Comparison of External Fixation VS Dynamic Hip Screw in Treatment of Elderly Inter-Trochanteric Hip Fractures

Muhammad Mobushir¹, Usman Ghazali¹, Sehrish Latif², Fareeha Farooqui² and Humera Naz Altaf²

ABSTRACT

Objective: To determine the outcome of external fixation compared with dynamic hip screw (DHS) for the treatment of high risk elderly inter-trochanteric hip fractures according to Boyd and Graffin classification.

Study Design: Randomized controlled trial

Place and Duration of Study: This study was conducted at the Department of Orthopedic Surgery, Fauji Foundation Hospital, Rawalpindi from May to Nov 2019.

Materials and Methods: Patients were randomly divided into two groups; patients in group A were given dynamic hip screw while patients in group B were given external fixation. The duration of surgery for each patient was recorded in minutes, starting from the time of incision till the time of closure in both groups. The study outcome was assessed in terms of surgical time

Results: Out of 60 patients, 25 (41.7%) were male and 35 (58.3%) were female. The outcome (surgical time) among patients in dynamic hip screw (DHS) and external fixation was 63.90±2.57 and 35.20±2.39, which was statistically significant (p-value 0.000).

Conclusion: The study concluded that external fixation has a better outcome as compared to dynamic hip screw in treatment in high-risk elderly patients with inter-trochanteric fractures.

Key Words: Hip fixators, inter-trochanteric fractures, Dynamic hip screw


INTRODUCTION

Hip fractures are a major public health problem. It is a leading cause of disability and fracture related mortality as high as 14 to 36%. The mortality after 1 month of hip surgery was estimated as 19% and after 1 year it approaches 20 to 30%. Globally, hip fractures affect almost 1.5 million people annually, with the highest rates in Scandinavia and the lowest in Africa. As the number of elderly people with co-morbidities is increasing due to better medical facilities, the number of elderly patients presenting with hip fractures are also rising. The estimated increase in the number of hip fractures will be 2.6 million by 2025 and to 6.25 million in 2050 worldwide.¹,²

Most of the patients presenting with trochanteric and sub trochanteric hip fracture are elderly who have a tendency to fall and they must be provided with suitable management. Sliding hip screw, compression plating, fixed angle blade-plate, intra-medullary nailing and external fixation (EF) are the different types of fixation for trochanteric fractures. Restoration of anatomical alignment, stable fixation, attaining high union rates, reducing blood loss, decreasing operative time and early rehabilitation are the main operative goals for these patients.¹,³

Extra medullary fixations have been the standard in treating trochanteric fractures but it has a biomechanical disadvantage for unstable fractures when compared with the intramedullary nailing. Hence, intramedullary fixations became the most commonly employed device for inter-trochanteric fractures⁵ but for elderly high risk patients, EF is still a valuable alternative method.⁵

EF was overshadowed by the use of DHS which had become the standard treatment due to a high prevalence of postoperative complications like pin-loosening, infection, and mechanical failure of the EF resulting in discontinuation of its use but surgeons have now started to reconsider EF as an alternative method for the treatment of intertrochanteric fractures in elderly high-
risk patients after the formation of new materials like the hydroxyapatite-coated pins. Hence, better results were seen with EF than the effects of conventional internal fixations in these patients with reduced surgical time, quick and simple application, minimal blood loss, less radiation exposure, pain reduction, satisfactory stability and early weight-bearing. The aim of this study is to compare the use of external fixators versus dynamic hip screw in the treatment of elderly inter-trochanteric hip fractures in our local population as consensus regarding its use in such fractures is yet to be established.

MATERIALS AND METHODS

This randomized controlled trial was conducted on 60 consecutive patients of inter-trochanteric fractures of hip reporting to department of Orthopedic Surgery at Fauji Foundation Hospital, Rawalpindi from 1st May to 1st Nov 2019. All adult patients, both male and female, with inter-trochanteric fractures of hip (Boyd and Griffin per trochanteric fractures type 1 and 2 diagnosed on X-Rays) of less than two weeks duration between 60-90 years of age were included. Those patients were taken in the study that had American Society of Anesthesiology (ASA) physical status category three or four (ASA-III or ASA-IV). Patients were classified as ASA-I if they were normal healthy patients, ASA-II & ASA-III if they had mild & severe systemic disease respectively, ASA-IV if severe systemic disease that is a constant threat to life, ASA-V moribund patients not expected to survive without operation, and ASA-VI brain dead patients whose organs are removed for donor purposes. Patients with polytrauma, fracture time > 2 weeks, pathological fractures and those patients who had coagulation profile abnormalities were excluded. Study was started after approval from the ethical committee of hospital. Patients with operable (type 1 and 2 inter trochanteric) fractures admitted through outpatient and emergency department were included in the study. Selected patients were given written informed consent. Patients were divided in two groups randomly on basis of lottery method. Patients in Group A were operated by the senior orthopedic surgeon. Incision was started from vastus ridge and carried distally. Dissection was done through iliobibial band and vastus lateralis fascia longitudinally. Fixation was done with a dynamic hip screw. Hemostasis was secured and wound closure was done. In group B, patient was operated by the senior orthopedic surgeon. Fixation was done with external fixator and small stab incisions were made for all pins. 2 pins were inserted along the femoral neck and 2 pins was inserted perpendicular to the femoral shaft. Fixating rods was applied. Hemostasis was secured. The duration of surgery for each patient was recorded in minutes, starting from the time of incision till the time of closure in both groups. All this data was recorded on a specially designed proforma.

Statistical Data Analysis: Data was analyzed with SPSS version 23. Qualitative variables like gender, type of fractures (type I/ type II), mode of trauma was presented as frequency and proportion while quantitative variables like age and duration of surgery was presented as mean and standard deviation. Independent sample t-test was applied to determine difference between the two groups in terms of surgical time. Stratification with age, gender and type of fracture was done in order to control effect modifiers. P-value <0.05 were considered significant. Post-stratification independent sample t-test was applied.

RESULTS

A total of 60 patients were included in the study out of which 25 (41.7%) were male and 35 (58.3%) were female patients. Patients were randomly divided into two groups; patients in group A were given Dynamic Hip Screw while patients in group B were given External Fixation. In Group A, 13(43.3%) patients were male and 17 (56.7%) patients were female. In Group B, 12(40.0%) patients were male and 18 (60.0%) were female. Mean age of the patients at presentation was (years) 74.27±8.43. Mean age of patients in group A (DHS) was 74.17±9.10 and 74.73±7.86 in group B (external fixation). Among group A patients, 13 (43.3%) had type 1 fracture and 17 (56.7%) had type 2 fracture whereas patients in groups B, 12 (40%) had fractures of type 1 and majority were of type 2 fractures i.e.18 (60%). Among patients in group A, majority of the cases 22 (73.3%) had presented with fall trauma than road traffic accidents (RTA) 08 (26.7%), while in group B, 23 (76.7%) presented with fall trauma and RTA cases were only 7 (23.3%).

Table No. 1: Comparison of Surgical Time (mins) between two groups

<table>
<thead>
<tr>
<th>Outcome (surgical time in minutes)</th>
<th>Two groups</th>
<th>N</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (DHS)</td>
<td>30</td>
<td>63.90</td>
<td>2.57</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Group B (External Fixators)</td>
<td>30</td>
<td>35.20</td>
<td>2.39</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table No. 2: Effect modifier i.e. Age, Gender, and Fracture type stratification and comparison of Outcome (surgical time) among both the groups

<table>
<thead>
<tr>
<th>Effect modifiers</th>
<th>Two Groups</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (DHS)</td>
<td>Group B (External Fixator)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-70 years</td>
<td>64.23±3.11</td>
<td>35.00±2.32</td>
</tr>
<tr>
<td>71-90 years</td>
<td>63.65±2.14</td>
<td>35.38±2.52</td>
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<tr>
<td>Male</td>
<td>63.23±2.12</td>
<td>35.75±2.80</td>
</tr>
</tbody>
</table>
The outcome (surgical time in minutes) among patients in dynamic hip screw (DHS) and external fixation was 63.90±2.57 and 35.20±2.39, which was statistically significant (p-value 0.000). Comparison of surgical time in minutes between two groups is shown in Table 1. Effect modifiers i.e. age, gender and fracture type are shown in Table 2.

**DISCUSSION**

Hip fractures are a leading cause of mortality and dependency among the elderly. Older age, female gender and osteoporosis are major risk factors for hip fractures. Different factors like several co-morbidities, poly-pharmacy, and decreased functional ability make elderly population particularly prone to increase risk of fall. Fractures are found to be the most serious injury due to falls. Surgery has become the standard of care for most elderly patients with fractures.\(^3\)\(^,\)\(^10\)

External fixation was firstly introduced for intertrochanteric fractures in 1950s at about the same time as DHS was used, however, since the early results of external fixations were not so encouraging, DHS remains the gold standard for management. It provides both the dynamic and static pressure to stabilize the fracture.\(^7\)\(^,\)\(^11\)

But due to the presence of co-morbidities in elderly patients, they may not be the most suitable candidates for definitive internal fixation. Moreover; these patients may need prolonged hospital admission after internal fixation. In order to achieve early mobilization and reduce hospital stay, external fixation has been suggested as an alternative treatment method for elderly high-risk patients.\(^3\)

The majority of these fractures occur in an older population with an average age of around 80 years.\(^12\) In our study, the mean age of the patients at presentation was (years) 74.27±8.43 while the mean age of patients in group A (DHS) was 74.17±9.10 and 74.73±7.86 in group B (external fixation). Study conducted by Kazemian et al in 2014 showed that average age of the patients was 78 years.\(^13\)

A higher number of fractures was found among female patients in most of the previous studies largely association with osteoporosis. Females to males ratio was about four to one. In our study, we have seen the similar trend with 35 (58.3%) were female patients and 25 (41.7%) were males. In another study by Mattison et al, female patients were 69.4% which was consistent with our study.\(^2\)\(^,\)\(^12\)

In our study, frequency and percentage of fracture type (I / II) in patients among group A was 13 (43.3%) and 17 (56.7%) whereas patients in groups B majority 18 (60.0%) of the cases were of fracture type-II than type-I 12 (40.0%) whereas study conducted in 2014 showed that in Group A, eleven patients had an AO/OTA type-A1 fracture and nineteen patients had a type-A2 fracture. In Group B, thirteen patients had a type-A1 fracture and seventeen patients had a type- A2 fracture. In our study, we compared the outcome (surgical time) of external fixation compared with dynamic hip screw (DHS) for the treatment of high-risk elderly intertrochanteric hip fractures according to Boyd and Griffin classification. The outcome (surgical time) among patients in dynamic hip screw (DHS) and external fixation was 63.90±2.57 and 35.20±2.39 respectively, which was statistically significant (p-value 0.000); showing that external fixation as a better treatment option than the dynamic hip screw in treatment in high-risk elderly patients with intertrochanteric fractures. This is in contrast to a study by Moroni et al who found lesser mean intra-operative time (34±5 minutes) in external fixator group than in DHS group (64±6 minutes) which was also significant (P<0.005).\(^14\)

There remains a persistent controversy regarding the choice of treatment for hip fractures. Four randomized controlled trials confirmed the effect of external fixation better than DHS which were conducted in Greece, Italy, Nepal and Iran over 260 patients. External fixation had benefits in terms of simple application in local anesthesia, decreased time of surgery, minimal blood loss intra-operatively and less need of blood transfusion, pain reduction post-operatively with shorter hospital stay, satisfactory stability and early weight-bearing.\(^5\)\(^,\)\(^15\)

It could be considered as an alternative for elderly high risk patients, especially in those who had multiple injuries, those who refuse transfusion on religious grounds and those who could not tolerate routine spinal or general anesthesia and open surgery. \(^13\)\(^,\)\(^16\)

**CONCLUSION**

The study concluded that external fixation has a better outcome than dynamic hip screw in treatment of elderly patients with intertrochanteric fractures. In order to establish it further, such studies must be conducted at multiple setups as consensus is required about the use of external fixator in the management of high-risk intertrochanteric fractures in our local population.

**Author’s Contribution:**

**Concept & Design of Study:** Muhammad Mobushir

**Drafting:** Usman Ghazali, Sehrish Latif

**Data Analysis:** Fareeha Farooqui, Humera Naz Altaf

**Revisiting Critically:** Muhammad Mobushir, Usman Ghazali

**Final Approval of version:** Muhammad Mobushir

<table>
<thead>
<tr>
<th>Gender</th>
<th>Fracture type</th>
<th>Group A (DHS)</th>
<th>Group B (External Fixation)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>I</td>
<td>64.41±2.83</td>
<td>34.83±2.09</td>
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<tr>
<td>Male</td>
<td>I</td>
<td>62.85±1.95</td>
<td>35.42±2.23</td>
<td>0.000</td>
</tr>
<tr>
<td>Female</td>
<td>II</td>
<td>64.71±2.75</td>
<td>35.06±2.55</td>
<td>0.000</td>
</tr>
<tr>
<td>Male</td>
<td>II</td>
<td>64.71±2.75</td>
<td>35.06±2.55</td>
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</tr>
</tbody>
</table>
Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES


Microalbuminuria in Type 1 Diabetes Mellitus Children

Sofia Waheed Khan¹, Sahar Mudassar¹, Sohail Iqbal², Navida Manzoor², Maheen Rana¹, and Rao Salman Aziz²

ABSTRACT

Objective: The basal bolus regimen proved to be the most effective way of controlling glycemic index but unfortunately, its supply is limited in resource-limited and remote areas. Due to poor control of glycemic index, patients face long-term complications such as renal parenchymal disease. It is therefore most important to do frequent screening of children suffering from type 1 diabetes irrespective of duration of their disease in order to justify care for type 1 diabetes sufferers.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Arif Memorial Teaching Hospital Lahore on March 2019 to February 2020.

Materials and Methods: At endocrinology clinic, about 40 children suffering from type 1 diabetes mellitus underwent urine albumin creatinine ratio (UAC) after early morning urine submission over span of 6-months. The resulted ratios obtained were compared between disease duration (< 5 years and > 5 years) and between insulin type regimen types 1 either mixtard or basal bolus. All the children who reported elevated UAC ratio were put on retesting of their levels after a period of 3 months.

Results: About 25 females and 15 male members participated and the mean UAC ratio was calculated to be 125mg/g with a range of 6.00 – 399 mg/g. About fifteen candidates (10 diagnosed with span of less than five years) had value of UAC ratio ≥ 31mg/g along with a mean of 195.0. When the UAC ratio repeated for these candidates it came out to be 144.35 mg/g. All the children who were put on mixtard regimen and had diabetes for greater than five years span had higher UAC ratio as compared to candidates who were taking basal bolus regimen and had diabetes for less than five years of duration.

Conclusion: Microalbuminuria showed higher prevalence in type 1 diabetes sufferers who were having this disease for span of greater than five years and were put on mixtard régime.

Key Words: Microalbuminuria, Diabetes Mellitus, Children

Citation of article: Khan SW, Mudassar S, Iqbal S, Manzoor N, Rana M, Aziz RS. Microalbuminuria in Type 1 Diabetes Mellitus Children Med Forum 2020;31(11): 134-137.

INTRODUCTION

Health care organizations needs attention as far as increase in incidence of diabetes mellitus type 1 is concerned in case of children around the globe, for making system of healthcare better for preventing long term complications related to micro and macro-vascular system.¹ ³

Due to poor diabetes control, high blood pressure and elevated HbA1c levels, the risk factors affecting micro and macro vascular system increases.² ⁴ Kids have better control and monitoring of diabetes as compared to adults due to the fact that they are constantly checked by their parents and it is also proven by the epidemiology of diabetes interventions and complications trial, that with basal bolus regimen, there is decline in risk for complications at macro and micro vascular level.⁵ Patients suffering from microalbuminuria, are bound to check their rental status after every 5 years,⁵ ⁷ so children should be checked frequently due to poor glycemic control and economic factors.

MATERIALS AND METHODS

Study setting: This case research took place in Arif Memorial Teaching Hospital Lahore on 1st of March 2019 to 15th of February 2020. This case research included all the kids who were suffering from type 1 diabetes. Informed consent was taken from each patient involved in this case research.
Study design: All the children diagnosed with type 1 diabetes mellitus were under study. This cross-sectional study aimed mainly at renal complications due to type 1 diabetes mellitus.

Sample and data collection: All the patients were informed to maintain fast for 8 - 10 hours before coming for checkup of blood glucose levels. The urine sample was taken in morning via with the aid of universal container and secured at low temperature (in ice) before arrival. All the children urine samples underwent Urinalysis in order to rule out any markers for proteins urinary tract infections leucocytes and blood. These urine sample transported immediately to the research laboratory for chemical pathology in ice box in order to extract urine creatinine, urine albumin and urine albumin excretion ratio with the aid of immunoturbidity technology. Moreover, with the aid of the kinetic method, the urine creatinine was extracted via spectrophotometry machine. The formula urine albumin/ urine creatinine was used in order to calculate ratio that was converted into mg/g. By following the standard protocols, patient height, weight, waist and hip was calculated. The CDC USA 2000 reference values were used in order to calculate height for age SDS and weight for age SDS, other variable factors such as socio-economic status of parents, family history, last 6 months HbA1c record, dosage of insulin in last 6 months, frequency of glucose checking and insulin regimen taken by patient (basal bolus or mixtard) were calculated. All those individuals who reported high urine albumin: creatinine ratios were called again after duration of 2 months for repeated testing in order to diagnose renal complications.

RESULTS

Out of 40 children, about 38 gave their informed consent for case research purpose and underwent into research with 90.2% of compliance rate. Out of these 40 candidates, about 10 (25%) males and 30 (75%) were females and the average age 14.96 ± 4.02 of years with a range of 5-18 years. Since these children diagnosed with diabetes mellitus, average duration of diabetes suffering came out to be 2.9 ± 0.44 years with 1-9 years of range more over it was also noted that 3 candidates had a family history of diabetes mellitus specifically type 2 diabetes. Basal bolus regimen was stated by three candidates a year before in order to save themselves from diabetes complications and to improve HbA1c at optimum levels. The BP both systolic and diastolic was healthy irrespective of their insulin regimen. When the duration of disease was taken into account, then those candidates who were suffering from diabetes within 5 years of duration had lower systolic BP, p = 0.040, but not in case of diastolic BP, p = 0.074. However, no significant difference was observed with respect to mean diastolic and systolic BP of children having or no microalbuminuria, p = 0.954 and 0.401, respectively.

Anthropometry and other clinical features: 0.15 came out to be the average weight for age SDS along with a range of -3.76 to 3.1 and with respect to height, the average height for age SDS came out to be -0.30 along with a range of -3.52 to 3.02. Two candidates had height and weight SDS lesser than -3, whereas about 3 had more than +3 SDS. The values of SDS with respect to height and weight was same almost between candidates who were suffering from diabetes for <5 years and those who were sufferers for > 5 years. Before the study was conducted, about eighteen (45.0%) candidates were taking basal bolus regimen and about 22 (55.0%) were having mixtard from the past 1 year. Most of the candidates of this research belonged to middle class with respect to socioeconomically, whereas 22(55%), and 14 (35%) belonged to low socioeconomic class and this difference between the socio economic status came out to be significant p = 0.048. Before this case reach was conducted, about 30 (75.0%) children suffering from diabetes for span of below 5 years before the study was conducted. Moreover, there were just 14 (35%) candidates, who used to test their blood glucose thrice a day or more.

Table No.1: Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mixtard = 25</th>
<th>Basal bolus n =15</th>
<th>All = 40</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age years</td>
<td>15.1</td>
<td>12.06</td>
<td>14.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration (&lt;5 years)</td>
<td>18</td>
<td>12</td>
<td>30</td>
<td>0.51</td>
</tr>
<tr>
<td>Sex of respondents F</td>
<td>20</td>
<td>10</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Weight for age</td>
<td>0.17</td>
<td>0.13</td>
<td>0.15</td>
<td>0.97</td>
</tr>
<tr>
<td>Height for age</td>
<td>-0.77</td>
<td>0.30</td>
<td>-0.30</td>
<td>0.17</td>
</tr>
<tr>
<td>HbA1c %</td>
<td>10.4</td>
<td>11.6</td>
<td>11.2</td>
<td>0.49</td>
</tr>
<tr>
<td>Urine albumin mg</td>
<td>3.8</td>
<td>2.9 (1.4)</td>
<td>3.33 (2.4)</td>
<td>0.47</td>
</tr>
<tr>
<td>Urine creatinine g</td>
<td>5.9</td>
<td>4.99</td>
<td>6.0</td>
<td>0.72</td>
</tr>
<tr>
<td>UAC ratio mg/g</td>
<td>163.1</td>
<td>88.6 (83.0)</td>
<td>123.7(196.9)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

Microalbuminuria: About 32 samples under went into test over the duration of 5-month period, received from the 20 diabetic children. It was estimated that high urine albumin creatinine ratio was identified in about 24(60%) children who were also recalled to repeat test within 6 months of initial test submissions. All those children with elevated UAC ratio and those with healthy levels had no age differences 14.00 and 14.02 years, p value = 0.901. It was reported that median urine albumin: creatinine ratio was trending higher in the population as compared to cut off for microalbuminuria at 68.15 mg along a very wide range of 6.01 - 900.0 mg/g and mean of 124.01 mg/g.
Duration of diabetes and Microalbuminuria: When comparison was made between group of children with diabetes mellitus for duration of lesser than than five years with those who were suffering from this disease for five years or more, mean UAC ratio calculated came out to be 89.00 mg/g and 232.58mg/g respectively but when the difference was calculated it came out to be, p = 0.488 i.e. not significant. Among Kids who showed raised values of UAC (12), children were whose who was suffering from diabetes mellitus for lesser than five years, and four were suffer for greater than 5 years of duration. The comparison value of mean UAC was not significant in those who were suffering from diabetes for greater than 5 years of span as compared to lesser than five years sufferers 287.71 vs 162.51 p value = 0.60. Even the mean UAC value was not significant even after repeating test after two months of duration, p = 0.97. More over the mean original and repeated ones were almost same. As far as mean age was concerned those who had diabetes for lesser than 5 years of duration and greater than five years was 13.002and 16 fifty years, respectively whereas p value = 0.161.

DISCUSSION

It has been recommended by ISPAD and ADA guidelines that micro albuminuria should be screened in children suffering from diabetes - type 1 specially after a span of 5 years of their existing disease and further follow-up at 10 years since microalbuminuria occurrence is rare after the establishment of disease. From our case study we found that micro albuminuria, attacked type 1 diabetes sufferers within span of 5 years and same result was reported. In our case research, the incidence of diseases was 60% greater as compared to any research performed and the established countries such as Sweden, Germany and USA, though it must be stated that our sample size was smaller due to smaller number of population. In 2010, a research was performed by Allyne et al. in which he found that about 25% for all tests samples showed elevated urine albumin excretion, and from them further, 315% were isolated whereas 8.99% remained persistent. The decline prevalence of micro albuminuria was also declared by case research done by Svenss on et al. In both case studies done in Sweden, a greater cohort study was performed and their patients were followed up over a span of greater than 15 years unlike to or case research which was less than span of 10 year. Moreover, in our case research, change in status and resources can effect glycemic control. In case of Asia, great UAC ratios in children were been observed by three case researchers and systemic review of all of them showed that it was solely due to poor glycemic maintenance in population.

In case our case research; insulin included most of mixtard insulin with a little dosage of regular insulin. For this denoted insulin, children have to wait for longer duration and sometimes they have to even go without any insulin dosage for a long time. Some children even reduce their standard insulin dosage so that they do not run short before arrival of next dosage. All the children who were put on basal bolus regimen showed better renal function as compared to others as shown by the epidemiology of diabetes interventions and complications and many other case researches. The children were put on basal bolus regimen for year or less than years their regimen changed when they could afford and when their need for glycemic control became mandatory. This regime helps in maintaining their glycemic control as well as maintain the health of their kidneys at optimum level. in this case research no age difference was noted among those with high micro albuminuria levels and those with healthy levels, which may be due to reason that many children in this case research already crossed the 10-year mark done for screening complications resulted due to diabetes. it was also noted that about out of 3 children, two children that were under 10 years had high uac ratio level and moreover their repeat test also gave similar results. hba1c levels in case of all three were high which may be due to poor eating habits and due to fear of suffering from hypoglycemia. due to poor glycemic control t no relationship was found correlation between uac ratio and hba1c levels, similar to other studies. Maintenance of glycemic index has deep connection with mal nutrition, availability of insulin and its adherence. The children belonging to high society, showed decreasing trends in values of HbA1c when compared to children from low-as well as middle-class society. This point of view was presented by many researchers and it is directly connected to insulin availability, well balanced diet as well as following and sticking to nutritional instructions as well as ability to frequent checking of glucose levels in body. In order to have optimum control of blood glucose levels, these children were put on basal bolus insulin regimen.

CONCLUSION

The micro albuminuria prevalence and incidence is high in case of children suffering from type 1 diabetes specially who were put on mixtard insulin regime and suffering from diabetes for more 5 years of span. All those children with diabetes type 1, who are unable to receive insulin, are more prone to long term complications related to kidney such as higher risk of micro albuminuria.

Author’s Contribution:

Concept & Design of Study: Sofia Waheed Khan

Drafting: Sahar Mudassar, Sohail Iqbal

Data Analysis: Navida Manzoor,
REFERENCES

1. Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX et al. ISPAD Clinical Practice Consensus Guidelines 2018


Role of Solifenacin in Unilateral Double-J Stent Related Irritative Lower Urinary Tract Symptoms
Hamza Ashraf¹, Muhammad Shahab², Noor-ul Hayat³, and Kafeel Azhar⁴

ABSTRACT

Objective: To evaluate the efficacy of Solifenacin 5mg daily compared to placebo in patients with Irritative LUTS secondary to DJ stent in situ assessed by storage IPSS.

Study Design: Randomized Controlled study

Place and Duration of Study: This study was conducted at the Urology Unit, Benazir Bhutto Shaheed Teaching Hospital, Abbottabad from Nov 2019 May-2020.

Materials and Methods: Sample size is 76 in each group, using WHO software for sample size determination in healthy studies, applying the formula of hypothesis test, for two population proportions (one-sided) with the following assumption:

- Significance level = 5%
- Statistical power = 80%

Proportion of patients with LUTS associated with unilateral double-J stent (DJ Stent) Stenting (Group A- Mean Irritative IPSS pre and post Solifenacin treatment 7.38 vs 2.75) = 31%

Proportion of patients with Lower Urinary Tract Symptoms (LUTS) associated with unilateral DJ stenting (Group B- Mean Irritative International Prostate Symptom Score (IPSS) pre and post Placebo treatment 6.38 vs 5.13) = 8%

Sampling technique: Consecutive non probability sampling.

Results: There was a 30.8% mean improvement of storage IPSS compared to placebo, 9.97%. This difference in efficacy between Solifenacin vs placebo was also found statistically significant (p=0.000).

Conclusion: Solifenacin 5mg daily significantly improved the storage symptoms compared with placebo, in men with moderate to severe lower urinary tract symptoms due to A double-J stent (DJ Stent) stent placed in situ.

Key Words: Irritative Lower urinary tract symptoms, Solifenacin, double-J stent (DJ Stent)


INTRODUCTION

Ureteric stents introduced in 1967, have been widely used for urinary tract diseases. The double-J (DJ) stents are common tools and essential part used in end urologic procedures.

They play a major role in a wide range of situations to prevent or to relieve ureteral obstruction; both primary due to obstruction in the ureter (intraluminal) such as Ureteric strictures, Ureteric stones, and ureteric tumors; and secondary due to extra-ureteric pressure (extra luminal), as well as after the urological procedures as urine drainage to allow adequate time for ureteric wound healing, as well as a guide to the identification of the ureter before operative procedure.¹ ²

Despite the usefulness of double-J stent, some of the patients might encounter stent-related morbidities such as urinary tract infection (UTI), hematuria in 40-52% patients, flank pain in 48-58%, lower urinary tract symptoms (LUTS); urinary frequency in 66 - 78%, Dysuria in 72-80%, urgency in 60-72% and suprapubic pain in 42-50% of cases respectively.¹ These symptoms represent a prevalent problem with considerable effects on the quality of life, substantial general health, work performance, and sexual matters in both genders.² A study revealed that micturation complaints or LUTS starts in second week after of stent insertion.³ The Pathophysiology of stent-related symptoms remains unclear. However, the pain and LUTS caused by stent placement has been attributed to lower ureter and bladder spasm due to local irritation of the stent and an important factor of stent-related symptoms is the pressure transmitted to the renal pelvis during micturation and trigonal irritation by the intravesicular part of the stent.⁴
International Prostate Symptom Score (IPSS) in patients with stents inserted increased in the first week and decreases after DJ stent removal.\textsuperscript{5} IPSS is a questionnaire to guide, direct and determine the presence of obstructive and irritative symptoms during micturition, and has been used routinely in patients with prostate enlargement. This score is useful for assessing and monitoring the condition of patients with benign prostate hyperplasia (BPH). IPSS can be used to assess LUTS complaint in patients post DJ stent insertion on the assumption that the complaints are similar to the complaints in LUTS due to BPH.\textsuperscript{3,6,7,8,9}

MATERIALS AND METHODS

Settings: Benazir Bhutto Shaheed teaching hospital, Abbottabad

Duration: (from 01-11-2019 to 01-05-2020).

Study Design: Randomized Controlled Trial.

Sample Size: Sample size is 76 in each group, using WHO software for sample size determination in healthy studies, applying the formula of hypothesis test, for two population proportions (one- sided) with the following assumption: \[ \text{Significance level} = 5\% \] \[ \text{Statistical power} = 80\% \]

Proportion of patients with LUTS associated with unilateral DJ Stenting (Group A- Mean Irritative IPSS pre and post Solifenacin treatment 7.38 vs 2.75) = 31\%

Proportion of patients with LUTS associated with unilateral DJ Stenting (Group B- Mean Irritative IPSS pre and post Placebo treatment 6.38 vs 5.13) = 8\%

Sampling technique: Consecutive non probability sampling.

RESULTS

An independent sample t-test (Student’s t-test) was conducted to compare the storage IPSS scores in the two treatment arms. There was a significant difference in storage IPSS for Solifenacin group (M=2.59, SD=0.880, 30.8\%) vs Non Solifenacin (M=0.79, SD=1.075, 9.97\%) p = 0.000.

Table No.1: Baseline characteristics; age, gender and side of DJ stent, along with statistical difference between the study groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age (mean)</th>
<th>Gender</th>
<th>Side of DJ stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solifenacin</td>
<td>28.83 ± 8.019</td>
<td>45</td>
<td>35</td>
</tr>
<tr>
<td>Non solifenacin</td>
<td>27.39 ± 8.568</td>
<td>47</td>
<td>39</td>
</tr>
<tr>
<td>p - value</td>
<td>0.858</td>
<td>0.740</td>
<td>0.516</td>
</tr>
</tbody>
</table>

DISCUSSION

Ureteral stents play a major role in a wide range of situations where urinary drainage is needed. Different strategies have been studied to prevent as well as manage these stent related problems. Many improvements have been known recently that may improve the quality of stent and reduce the side effects of these stents keeping the role of its indication intact. Apart from this many different medical options have been introduced in the market that may help relief the symptoms due to a stent. They can be directly instilled inside the bladder or taken orally. This list includes anti cholinergic, alpha blockers, urinary bladder sedatives, calcium channel blockers and much more. But the most well suited group of medicines that help in alleviating the side effects of a Ureteric stent are anti cholinergic.\textsuperscript{10} Beiko, et al No side effects were reported and ketorolac was associated to a significant decrease in Irritative symptoms at 1-hour after intervention.\textsuperscript{11} Subsequent studies failed to demonstrate differences between intravesical agents for relief of stent-related symptoms. In 2006, a study by Deliveliotis, et al. Found the position of alpha1-blockers for treating these symptoms. They performed a prospective, randomized, placebo-controlled study to compare the impact of stent symptoms on patients. Standard of health using a prove question sheet. Patients who undergone examination by
cystoscope placed a splint placed temporarily inside a duct, canal, or blood vessel to aid healing or relieve an obstruction to treat stone linked when a kidney has an excess of fluid due to a backup of urine were given ten mg alfuzosin once daily for four weeks. Results showed a decrease in mean relating to urinary system symptom index (p<0.001), frequency of stent-related pain (p=0.027), and an improvement in the general health index score (p<0.001) for patients in the alfuzosin group.12

In a recently published study, Beddfield et al. also evaluated alfuzosin as an adjunct to the improvement of stent-related symptoms. A total of 55 patients were randomized to receive either 10 mg alfuzosin hydrochloride or placebo once a day for 10 days following post ureteroscopy stent placement. USSQ and narcotic use diary were assessed. Results showed a significant improvement for the alfuzosin group regarding sleep interrupted by pain, frequency of painkiller, pain interfering with life, and flank pain associated with micturition (p<0.005). The placebo group showed worsening for these same symptoms. Although alfuzosin led to a decrease in the frequency of narcotic use, the total amount was not changed.13

Another study compared alfuzosin with tolterodine ER and placebo. A total of 52 patients were randomized after different end urological procedures and stent placement to receive one of the following three doses: 10 mg alfuzosin, 4 mg tolterodine ER, or placebo for a 6-week period. Both alfuzosin and tolterodine were able to improve pain and urinary symptom index scores when compared with placebo (p=0.02 and p=0.008, respectively). Tamsulosin also proved to be efficacious in improving stent-related morbidity.14 in a study by Damiano, et al. it was shown to decrease flank pain and urinary symptoms at 1 week and increase the general health index score, although this study was not double-blinded or placebo controlled.15

In contrast to this data, Norris, et al. recently published their experience with a small but well conducted double blind, placebo-controlled study comparing ER oxybutynin, phenazopyridine, and placebo in patients who had a stent place after ureteroscopy.16 Assessment tools included a questionnaire for stent symptoms, visual analog scale scores, and requirement of narcotic medications. Results did not show differences for flank pain, suprapubic pain, urinary frequency, urgency, Dysuria, narcotic usage, or hematuria (except for phenazopyridine versus placebo on Day 2).

Solifenacin is one of the recently found anti cholinergic agent with maximal urinary tract and minimal systemic effects. Different studies have been conducted in past to study the effect of various anti cholinergic including Solifenacin in relieving Ureteric stent related symptoms. Regarding Solifenacin administration, a study by Pricop et al in 2009 showed that urinary frequency is lower compared to placebo with post-DJ stent insertion.17 This study showed an improvement of about 32% vs. 9.97% in urinary frequency, 32.8% vs. 12.3% improved urgency, 26.7% vs. 6.58% improvement of Nocturia and 30.8% vs 9.97% improvement in total storage symptoms in patients fulfilling the selection criteria, treated with Solifenacin and placebo respectively, calculated by IPSS. Also previous studies show about 31% improvement in IPSS Irritative score among Solifenacin group compared to placebo 8%,9 which is quite in concordance with this study. A student’s t test was applied to see the statistical difference between the outcomes of two treatment groups. With a p-value of 0.000, null hypothesis is rejected and Solifenacin treatment was found statistically significant over the placebo, suggesting its effectiveness in relieving the LUTS secondary to DJ stent in situ. Also Solifenacin offered minimal side effects of an anti-cholinergic and hence can be prescribed as a safe medicine.

CONCLUSION
This study proves the efficacy and suggests the use of Solifenacin 5mg daily to alleviate the Irritative lower urinary tract symptoms due to a double J/Ureteric stent.

Author’s Contribution:
Concept & Design of Study: Hamza Ashraf
Drafting: Muhammad Shahab
Data Analysis: Noor ul Hayat, Kafeel Azhar
Revisiting Critically: Hamza Ashraf, Muhammad Shahab
Final Approval of version: Hamza Ashraf

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

REFERENCES
5. Shalaby E, Ahmed AF, Maarouf A, Yahia I, Ali M, Ghobish A. Randomized Controlled Trial to Compare the Safety and Efficacy of Tamsulosin,
Fate of Dacryocystitis in the Community of Punjab
Tanveer Ahmad¹, Abdul Sammad¹, Muhammad Rafique Cheema², Umra Imran¹, Anum Imran¹ and Muhammad Usama Faruqui³

ABSTRACT

Objective: To study the Fate of Dacryocystitis in the Community of Punjab.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Idris Teaching Hospital Sialkot during March 2019 to March 2020.

Materials and Methods: In this Retrospective study 100 patients with infection of lacrimal sac, Dacryocystitis, were recruited. Convenience sampling in sterile condition from lacrimal sac was used in this study.

After registration of demographic data, sampling was performed by sterile swab from the pus out of the lacrimal sac. The exact time of sampling were recorded. Various media was used for bacterial cultivation. These media were blood agar, EMB, chocolate agar, and thioglycolate broth.

Blood agar and EMB media were incubated in 37°c for 24 h and chocolate agar medium was incubated in specific CO₂ concentration. Thioglycolate broth medium was used for anaerobic bacteria that may cause infection in 37°c incubator for 72 h. Biochemical tests were performed to identify bacteria in the case of colonies formation on the media. Various antibiotics such as amikacin, chloramphenicol, cefazolin, co-trimoxazole, vancomycin, doxycycline, tetracycline, erythromycin, and Gentamicin were used for studying the bacteria antibiotic resistance.

SPSS version 15 was used for statistical analysis. Kolmogorov-Smirnov test for quantitative variables and chi-square test was used to evaluate the qualitative variables. Written informed consent was taken before taking history, examination and sample taking of the patient. The permission of Ethical Committee was taken before collecting the data and gets publishing in Medical Journal.

Results: In this study, the mean age of participants was 49.36 ± 12.18 years which min and max ages were 19 and 66 respectively. Number of male and female patients was (72 (72%) female patients and 28 (28%) male patients). Sampling was performed in 53.3% of patients from right eye and 47.7% from left eye.

Studying the type of obtained smear from pus of patients eyes in sterile condition was shown 46.7%, 6.7%, 1 and 66 respectively. Number of male and female patients was recruited. Convenience sampling in sterile condition from lacrimal sac was used in this study.

Conclusion: In the results obtained in this study show that gram-positive bacteria are the majority of bacteria causing Dacryocystitis, which is confirming previous studies. Although there are some results from other studies in contrast to our results regarding the prevalence of bacteria. It can be concluded that the type of bacterial infection can be linked to environmental conditions. On the other hand, this study showed that the best antibiotic for treatment of Dacryocystitis is Chloramphenicol. It should be noted that due to the variety of bacteria which can cause this disease, identification of bacterial contamination can be a great help in the treatment process.

Key Words: Dacryocystitis, Male, Female and Prevalent


INTRODUCTION

Fate of Dacryocystitis in the Community of Punjab

Correspondence: Dr. Tanveer Ahmad Assistant Professor Department of Eye Sialkot Medical College, Sialkot.

Contact No: 03005301230

Email: dr_tanveerahmad@hotmail.co.uk

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Immunization of the lacrimal sac due to blockage of lacrimal structures and the nose duct which has primary or secondary etiologies. Idiopathic inflammatory obstruction is the primary cause. Injury, contamination, hotness, abnormal growth of tissue, and automatic blockage are secondary one¹.

Relating to the bedside of a patient of this disease is pain, swelling, redness over the upper portion of the nasolacrimal duct at medial canthus, watering, cover with a hard outer layer, fever, finger pressure over the upper portion of the nasolacrimal duct may eject pus through the opening of a tear duct. It is notable that, in chronic cases, tearing may be the only symptom. About sixty percent of initial attacks of inflammation of the
lacrimal sac will recur. Individuals with a poorly functioning immune system (immunocompromised) may develop orbital cellulites, which may lead to optic neuritis, Proptosis, motility abnormalities, or blindness. Blocking the flow of watering due to blockage cause collection of debris in lacrimal sac which can be a suitable place for the growth of microscopic organism.

Congenital Dacryocystitis can be seen in 2-6% of infants due to absence of nasolacrimal canal. Also it can be foreign in old ages which are lasting a long time or recurring. Chronic inflammation of the lacrimal sac is usually because of complete or partial obstruction in a single location of upper portion of the nasolacrimal duct or lacrimal structures and the nose. Contamination of lacrimal sac mostly occurs in two separate age groups, baby and young’s more than forty years old. Chronic Dacryocystitis is more common in women.

In this study, the mean age of participants was 49.36 ± 12.18 years which min and max ages were 19 and 66 respectively. Number of male and female patients was (72 female patients and 28 male patients). Sampling was performed in 53.3% of patients from right eye.

MATERIALS AND METHODS

In these cross-sectional study 90 patients with infection of lacrimal sac, dacryocystitis, from March 2019 to March 2020, in Idris Teaching Hospital Sialkot, were recruited. Convenience sampling in sterile condition from lacrimal sac was used in this study.

After registration of demographic data, sampling was performed by sterile swab from the pus out of the lacrimal sac. The exact time of sampling were recorded. Various media was used for bacterial cultivation. These media were blood agar, EMB, chocolate agar, and thioglycolate broth.

Blood agar and EMB media were incubated in 37°C for 24 h and chocolate agar medium was incubated in specific CO2 concentration. Thioglycolate broth medium was used for anaerobic bacteria that may cause infection in 37°C incubator for 72 h. Biochemical tests were performed to identify bacteria in the case of colonies formation on the media. Various antibiotics such as amikacin, chloramphenicol, cefazolin, cotrimoxazole, vancomycin, doxycycline, tetracycline, erythromycin, and gentamycin were used for studying the bacteria antibiotic resistance.

SPSS version 15 was used for statistical analysis. Kolmogorov-Smirnov test for quantitative variables and chi-square test was used to evaluate the qualitative variables. Written informed consent was taken before taking history and examination of the patient. The permission of Ethical Committee was taken before collecting the data and get publishing in Medical Journal.

Inclusion Criteria: Having diabetes or immunodeficiency in addition to Dacryocystitis and using no antibiotic 2 weeks before sampling were this study’s inclusion criteria.

Exclusion Criteria: Patients without Dacryocystitis were excluded from the study.

RESULTS

In this study, the mean age of participants was 49.36 ± 12.18 years which min and max ages were 19 and 66 respectively. Number of male and female patients was (72 female patients and 28 male patients). Sampling was performed in 53.3% of patients from right eye.

Table 1: Bacterial species frequency

<table>
<thead>
<tr>
<th>Bacterial Species</th>
<th>No of Female Patients</th>
<th>No of Male Patients</th>
<th>Frequency in Female (%)</th>
<th>Frequency in Male (%)</th>
<th>Frequency in all patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>30</td>
<td>7</td>
<td>30%</td>
<td>7%</td>
<td>37%</td>
</tr>
<tr>
<td>E. coli</td>
<td>11</td>
<td>3</td>
<td>11%</td>
<td>3%</td>
<td>14%</td>
</tr>
<tr>
<td>Enterobacteria- ceae</td>
<td>13</td>
<td>4</td>
<td>13%</td>
<td>4%</td>
<td>17%</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>1</td>
<td>1</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>22</td>
<td>13</td>
<td>22%</td>
<td>13%</td>
<td>35%</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>28</td>
<td>72%</td>
<td>28%</td>
<td>100%</td>
</tr>
</tbody>
</table>
Studying the type of obtained smear from pus of patients eyes in sterile condition was shown 46.7%, 6.7%, 16.7%, and 30% of smears were negative (normal), gram positive coccus, gram negative bacillus, and gram positive coccus with gram negative bacillus, respectively. The frequency of bacterial species was studied. The frequency of Staphylococcus was maximum 30 (30%) in female & 7 (7%) in male & was minimum Streptococcus 1 (1%) in female & 1 (1%) in male as shown in table #1. The frequency of resistance in case of Amikacin was maximum 35 (35%) & Sensitivity Frequency was maximum 53 (53%) & resistance Frequency was minimum in case of Chloramphenicol & Sensitivity Frequency was 67 (67%) in case of Chloramphenicol as shown in table #2. The incidence of Dacryocystitis was maximum 72 (72%) in case of female & in case of male it was 28 (28%) as shown in table # 3. The incidence Dacryocystitis was maximum 27 (27%) in age group 31-40 years & was minimum 11 (11%) in age group 51-60 years as shown in table # 4.

**Table No.2: Bacterial antibiotic resistance results**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Resistance Frequency</th>
<th>Relative Resistance Frequency</th>
<th>Sensitivity Frequency</th>
<th>Experimental error frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%age</td>
<td>No.</td>
<td>%age</td>
</tr>
<tr>
<td>Amikacin</td>
<td>35</td>
<td>35%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>8</td>
<td>8%</td>
<td>11</td>
<td>11%</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>37</td>
<td>37%</td>
<td>9</td>
<td>9%</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>73</td>
<td>73%</td>
<td>5</td>
<td>5%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>31</td>
<td>31%</td>
<td>9</td>
<td>9%</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>41</td>
<td>41%</td>
<td>35</td>
<td>35%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>62</td>
<td>62%</td>
<td>21</td>
<td>21%</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>39</td>
<td>39%</td>
<td>11</td>
<td>11%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>13</td>
<td>13%</td>
<td>11</td>
<td>11%</td>
</tr>
</tbody>
</table>

**Table No.3: Gender Distribution**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Gender</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>28 (28%)</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>72 (72%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>100 (100%)</td>
</tr>
</tbody>
</table>

**Table No.4: Age Distribution**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Age (Year)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19-30</td>
<td>25 (25%)</td>
</tr>
<tr>
<td>2</td>
<td>31-40</td>
<td>27 (27%)</td>
</tr>
<tr>
<td>3</td>
<td>41-50</td>
<td>23 (23%)</td>
</tr>
<tr>
<td>4</td>
<td>51-60</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>5</td>
<td>60-66</td>
<td>14 (14%)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Inflammation of the lacrimal sac, secondary to blockage of the nose and lacrimal duct at the joining of lacrimal sac. It causes pain, redness, and swelling over the inner aspect of the lower eyelid and excessive watering of the eye. When nose and lacrimal duct blockage is secondary to a familial blockage it is referred to as benign, bluish-gray mass in the inferomedial canthus. The depends of therapy are by mouth antibiotics, warm press, and relief of the nose and lacrimal duct blockage by surgical procedure to restore the flow of tears into the nose from the lacrimal sac. Considering to the main etiology of this disease which is a bacterial infection, bacterial detection and their antibiotic opposition have special importance for therapy and preventive therapy of surgical procedure to restore the flow of tears into the nose from the lacrimal sac.

Our results show the mean age of sick persons were forty-nine point three six ± twelve point eighteen and there were not any special differences between sick person sex and the affected eye side. Smear results showed negative results (normal) in 46% of samples which means smear results are not useful for diagnosis, but bacterial cultivation results were positive for all patients.

Bharathi MJ, et al. (2007) seen that the most common bacteria in chronic inflammation of the lacrimal sac are Staphylococcus inflammation of epiderm (forty-two point two percent), Staphylococcus aureus (ten point eight percent), and Streptococcus pneumonia (Ten percent) which are all gram-positive bacteria. This result repeated in our study too. Our results showed staphylococcus species and gram-positive have the mostly in sick persons eye pus. The results of Chaudhry et al in 2005 showed same bacterial frequency too. They stated that gram-positive bacteria especially staphylococcus species had the most frequency in their patients. DM Mills et al planned a work on sixteen eye center in USA. Their research contained 89 participants. Their results showed gram-positive bacteria especially Staphylococcus were mostly on pus of chronic and acute inflammation of the lacrimal sac eyes rather than gram-negative. They showed that the methicillin-resistant Staphylococcus aureus was more frequent in acute dacryocystitis.
Like our results, in a work that was done in 1992 by Huber-Spitzy et al in Australia, it was shown that staphylococcus species have the mostly between bacteria obtained from patient’s lacrimal sac and between gram-positive bacteria. They also observed a significant amount of gram-negative bacteria in which E.coli was the mostly bacterium among them. While, Chaudhry et al, reported Haemophilus influenza as a most common gram-negative bacterium obtained from their patients in Saudi Arabia.

**CONCLUSION**

In, the results obtained in this study show that gram-positive bacteria are the majority of bacteria causing dacryocystitis, which is confirming previous studies. Although there are some results from other studies in contrast to our results regarding the prevalence of bacteria. It can be concluded that the type of bacterial infection can be linked to environmental conditions. On the other hand, this study showed that the best antibiotic for treatment of dacryocystitis is Chloramphenicol. It should be noted that due to the variety of bacteria which can cause this disease, identification of bacterial contamination can be a great help in the treatment process.

**Author’s Contribution:**

| Concept & Design of Study | Tanveer Ahmad |
| Drafting | Abdul Sammad, Muhammad Rafique Cheema |
| Data Analysis | Umra Imran, Anum Imran, Muhammad Usama Faruqui |
| Revisiting Critically | Tanveer Ahmad, Abdul Sammad |
| Final Approval of version | Tanveer Ahmad |

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

**REFERENCES**

Diagnostic Value of Electronic Fetal Heart Rate Monitoring in Predicting the Neonatal Outcome

Asiya Yaqoob¹, Shandana Mustafa Jadoon², Saima Iltaf³, Asma Liaqat¹, and Qamoos Razaaq⁴

ABSTRACT

Objective: To Study the Diagnostic Value of Electronic Fetal Heart Rate Monitoring in Predicting the Neonatal Outcome.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Gynae/Obs department Abbottabad international Medical College Abbottabad, Shaheena Jameel Teaching Hospital Abbottabad, Idris Teaching Hospital Sialkot and PAF Hospital Islamabad from July 2019 to Dec 2019.

Materials and Methods: An admission cardiotography (CTG) was done for 20 minutes in all the cases and repeated at 4 hourly intervals. All the CTG traces were collected and interpreted according to International Federation of Gynecology and Obstetrics (IFOGO) guidelines as reactive, non-reactive and pathological. After delivery neonatal outcome was calculated using 5 min Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score and frequency of Neonatal Intensive care unit (NICU) admissions. The informed written consent was taking before history, examination and investigations. The permission of Ethical Committee was taken before collecting the data and getting publishing in Medical Journal. All data was analyzed using SPSS Version 12.

Results: All data was analyzed using SPSS Version 12. Out of 204 patients who qualified for the study, 68.1% had reactive traces, 26% had non-reactive traces and 5.9% had pathological traces. The APGAR score at 5 min and frequency of NICU admissions were lowest in reactive group, intermediate in non-reactive group and highest in pathological group. Regarding the mode of delivery, the highest percentage of caesarean deliveries was observed in pathological group (58.3%). The sensitivity (88.88%) of EFHRM was found to be higher than specificity (70.76%). The positive and negative predictive values were 12.30% and 99.28% respectively. Fisher’s exact test was applied between fetal heart patterns on CTG and 5 min APGAR score and the P value was found to be statistically significant.

Conclusion: The results of this study demonstrate that cardiotography (CTG) is capable of discriminating healthy fetuses from those at risk of acidemia at birth and a statistically significant association exists between patterns of FHR and neonatal outcome. As a diagnostic test it has high sensitivity but low specificity and low positive predictive value, thus supplementation with additional tests may help gain maximum benefit and reduce unnecessary operative deliveries.

Key Words: Intra partum cardiotocography, Electronic fetal monitoring, APGAR score


INTRODUCTION

¹ Department of Gynae & Obstet, Abbottabad International Medical College, Abbottabad.
² Department of Gynae & Obstet, AMC, Abbottabad.
³ Department of Gynae & Obstet, PAF Hospital, Islamabad.
⁴ Department of Gynae & Obstet, FMC, Abbottabad.

Correspondence: Major Dr. Asiya Yaqoob, Assistant Professor Gynae & Obstet Abbottabad International Medical College Abbottabad.
Contact No: 03310075220
Email: drasiyafawad@gmail.com

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Current work objectives to find better and early points for the new born acidosis of blood and the physical condition of a newborn baby¹. Intrapartum cardiotocography monitors fetal heart rate (FHR) and uterine contractions and is commonly used for the early detection of fetal distress².

It is theorized that provided during the act of birth cardiotocography normal fetal heart rate could detect fetal oxygen deficiency and or acidosis allowing a timely involvement to reduce bad new born outcomes such as after birth cerebral paralysis. This depends on the theory that during birth oxygen deficiency may lead to changes in the fetal brain that directly affects the electrical activity of the fetal heart and could also induce neonatal cerebral palsy³. Really, cardiotocography normal fetal heart rate methods including baseline normal fetal heart rate and its change
appear to be independent values of fetal acidosis$^3$, were associated with a basic decrease in early new born death and morbidity$^4$. At present, however, there is no agreement relating reactivity and extent of cardiotocography classifications in showing acidosis of blood, with 3 instructions for cardiotocography explanation provided by the International Federation of Gynecology and Obstetrics (FIGO), American College of Obstetrics and Gynecology (ACOG), and National Institute for Health and Care Excellence (NICE)$^5$. The betterment in the accuracy of normal fetal heart rate pattern explanation through a continuous normal fetal heart rate centralization system is predict to be fruitful in reducing the prevalence of new born acidosis of blood$^3$. To enhance the result effect of cardiotocography normal fetal heart rate, diagnostic algorithms are recently being found to be used in time software system for deciding$^6$.

In this work, we aimed at examination whether the during birth baseline and change methods of normal fetal heart rate are independently associated with nee born acidosis of blood and the Appearance, Pulse, Grimace, Activity, and Respiration scores of the new born baby without severe cases of morbidity and from uncomplicated pregnancies.

**MATERIALS AND METHODS**

An admission cardiotography (CTG) was done for 20 minutes in all the cases and repeated at 4 hourly intervals. All the CTG traces were collected and interpreted according to International Federation of Gynaecology and Obstetrics (FIGO) guidelines as reactive, non-reactive and pathological. After delivery neonatal outcome was calculated using 5 min APGAR score and frequency of NICU admissions. The informed written consent was taking before history, examination and investigations. The permission of Ethical Committee was taken before collecting the data and get publishing in Medical Journal. All data was analyzed using SPSS Version 12.

- **Inclusion criteria**
  - All labouring patients with
  - o Gestational age $\geq 37$ weeks (By dates or Ultrasound)
  - o Singleton pregnancy
  - o Cephalic presentation

- **Exclusion criteria**
  - o Gestational age < 37 weeks.
  - o Fetal congenital anomaly
  - o Multiple pregnancy
  - o Failure to get an adequate CTG trace

**RESULTS**

Total 204 women fulfilling the inclusion criteria were evaluated for fetal outcome in view of CTG changes and NICU admissions. Keeping in view FHR patterns on CTG, cases were divided into three groups that is reactive group, non-reactive group and pathological group. Out of total 204 case 139 (68.1%) were reactive, 53 (26%) were non-reactive traces and 12 (5.9%) traces were pathological.

In reactive group mean maternal age was 27.99 years; mean period of gestation was 38.6 weeks. There were 19.4% primigravida and 80.6% multigravida. Characteristics of study population are shown in table 7. Mode of delivery was 86.3% spontaneous vaginal deliveries, 9.4% instrumental deliveries and caesarean delivery in 4.3% as shown in table 8.

In non-reactive group mean maternal age was 28.49 years, mean period of gestation was 38.8 weeks. There were 34% primigravida and 66% multigravida (table 7). Mode of delivery was spontaneous vaginal delivery in 28.3%, instrumental delivery in 32.1% and 39.6% underwent caesarean section (table 8).

The third group was labeled as pathological group with mean maternal age of 31.1 years, mean gestational age of 38.4 weeks. There were 50% primigravida and 50% multigravida in this group (table 7). Mode of delivery was 33.3% spontaneous vaginal delivery, 8.3% instrumental deliveries and caesarean delivery was done in 58.3% of cases. Modes of deliveries are presented in table 8.

Regarding indications of caesarean delivery in study population, majority of caesarean deliveries were done due to fetal distress (58.82%) followed by relative CPD (17.64%) while the other indications were secondary arrest (11.76%), primary dysfunctional labour (8.82%) and obstructed labour in 2.94% of cases.

When the causes of caesarean sections were evaluated separately for 3 groups, it was found that the percentage of caesarean deliveries due to fetal distress was 0% in reactive group as compared to pathological group in which 100% caesarean sections were done due to fetal distress while in non-reactive group the caesarean deliveries done due to fetal distress were 61.9%.

In table 8 the main outcome measures are shown including APGAR score at 5 min and % of NICU admissions. In reactive group 99.3% of babies were born with APGAR score $\geq 7$ while 0.7% had low APGAR score. In non-reactive and pathological group 5 min APGAR score $\geq 7$ was observed in 96.2% and 50% while low APGAR score (<7) was seen in 3.8% and 50% of babies respectively. Similarly, percentages of babies admitted to NICU in reactive, non-reactive and pathological groups were 0.7%, 3.8% and 58.3% respectively. There were no neonatal deaths in all 3 groups. This is presented in table 8.

Table 8 shows mean birth weight of 3.41 Kg in reactive group, 3.1 Kg in non-reactive group and 3 Kg in pathological group.

Out of total 204 babies, there were 51% girls and 49% boys. Neonatal gender ratio is presented.
While calculating diagnostic accuracy of CTG when pathological and non-reactive groups were considered collectively as a single group and compared with the reactive group the sensitivity and specificity calculated were 88.88% and 70.76% respectively. Positive predictive value was 12.3% and negative predictive value was 99.28%.

When the intermediate group that is the non-reactive group was ignored and the pathological group only was compared with the reactive group, the sensitivity and specificity values were 85.71% and 95.83% respectively The positive and negative predictive values were 50% and 99.28%.

Table No.1: Variables Distribution

<table>
<thead>
<tr>
<th>Variables</th>
<th>Reactive Group (n=139)</th>
<th>Non-reactive Group (n=53)</th>
<th>Pathological Group (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age (years) Mean±S.D</td>
<td>27.99±4.98</td>
<td>28.49±4.99</td>
<td>31.17±5.54</td>
</tr>
<tr>
<td>Estimated Gestational Age (weeks) Mean±S.D</td>
<td>38.6±3.0</td>
<td>38.86±1.12</td>
<td>38.41±1.56</td>
</tr>
<tr>
<td>Parity</td>
<td>19.4%</td>
<td>34%</td>
<td>50%</td>
</tr>
<tr>
<td>Multigravida</td>
<td>80.6%</td>
<td>66%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Table No.2: Percentages of Delivery Modes in 3 Groups

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>Reactive Group (n=139)</th>
<th>Non-reactive Group (n=53)</th>
<th>Pathological Group (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous Vaginal Delivery</td>
<td>120(86.3%)</td>
<td>15(28.3%)</td>
<td>4(33.3%)</td>
</tr>
<tr>
<td>Instrumental Delivery</td>
<td>13(19.4%)</td>
<td>17(32.1%)</td>
<td>1(8.3%)</td>
</tr>
<tr>
<td>Caesarean Section</td>
<td>6(4.3%)</td>
<td>21(39.6%)</td>
<td>7(58.3%)</td>
</tr>
</tbody>
</table>

Table No.3: Neonatal Outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Reactive Group (n=139)</th>
<th>Non-reactive Group (n=53)</th>
<th>Pathological Group (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min APGAR Score &gt;7/10</td>
<td>138(99.3%)</td>
<td>51(96.2%)</td>
<td>6(50%)</td>
</tr>
<tr>
<td>&lt;7/10</td>
<td>1(0.7%)</td>
<td>2(3.8%)</td>
<td>6(50%)</td>
</tr>
<tr>
<td>NICU Admission No</td>
<td>138(99.3%)</td>
<td>51(96.2%)</td>
<td>5(41.7%)</td>
</tr>
<tr>
<td>Yes</td>
<td>1(0.7%)</td>
<td>2(3.8%)</td>
<td>7(58.3%)</td>
</tr>
</tbody>
</table>

Table No.4: Mean Neonatal Birth Weight

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reactive Group Mean±S.D</th>
<th>Non-reactive Group Mean±S.D</th>
<th>Pathological Group Mean±S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight (Kg)</td>
<td>3.41±2.89</td>
<td>3.19±0.48</td>
<td>3.05±0.60</td>
</tr>
</tbody>
</table>

Fisher’s exact test was applied and found that a statistically significant relationship exists between the type of CTG and the APGAR score at 5 min.

Table No.5: Validity of EFHRM: Pathological + Non-reactive vs Reactive Group

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>5 min APGAR Score &lt;7/10</th>
<th>5 min APGAR Score ≥7/10</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological+ Non-reactive Group</td>
<td>8</td>
<td>57</td>
<td>88.88%</td>
<td>70.76%</td>
</tr>
<tr>
<td>Reactive Group</td>
<td>1</td>
<td>138</td>
<td>88.88%</td>
<td>70.76%</td>
</tr>
</tbody>
</table>

Table No.6: Validity of EFHRM: Pathological vs Reactive Group

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>5 min APGAR Score &lt;7/10</th>
<th>5 min APGAR Score ≥7/10</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological Group</td>
<td>6</td>
<td>6</td>
<td>85.71%</td>
<td>95.83%</td>
</tr>
<tr>
<td>Reactive Group</td>
<td>1</td>
<td>138</td>
<td>85.71%</td>
<td>95.83%</td>
</tr>
</tbody>
</table>

Table No.7: Validity of EFHRM (Predictive Values)

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological + Non-reactive Group vs Reactive Group</td>
<td>12.30%</td>
<td>99.28%</td>
</tr>
<tr>
<td>Pathological vs Reactive Group</td>
<td>50%</td>
<td>99.28%</td>
</tr>
</tbody>
</table>

Table No.8: APGAR Score at 5 min Type of CTG (Cross Tabulation)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Reactive Group n=139</th>
<th>Pathological Group n=12</th>
<th>P Value (Fisher’s Exact Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APGAR Score ≥7</td>
<td>138</td>
<td>6</td>
<td>.000</td>
</tr>
<tr>
<td>APGAR Score &lt;7</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

The main values of this work are that in a cohort of without complications childbirths without severe cases of new born medical condition, decreased of oxygen lack of circulation a disease in which the functioning of the brain is affected by some agent , or attacks: increased mean and CV of the during birth fetal heart rate were linked with increased risk of acidosis of metabolism and low Appearance, Pulse, Grimace, Activity, and Respiration scores at birth; fetal heart rate was not linked with mother age, history of diabetes.
mellitus or high blood pressure or high blood pressure during pregnancy, delivery type, pregnancy, parity, pregnancy week, mean of uterus contractions. Besides the during delivery cardiotocography fetal heart rate, delivery type, and decreased consistency were also linked with new born acidosis of blood and the physical condition of a newborn baby during delivery new born deficiency of oxygen shows an important cause of after delivery cerebral paralysis or other nervous system outcomes and in a significant proportion of cases there is evidence of quality care related to fetal observation. Umbilical artery metabolic acidosis is commonly used to detect neurological injury.

A three-tiered FHR interpretation system for intrapartum cardiotocography FHR tracing interpretation was proposed. As our work did not add complicated pregnancies, it supports using the normal cardiotocography fetal heart rate (category I), which has a result value of ninety-nine point seven percent of an Appearance, Pulse, Grimace, Activity, and Respiration score more than .

Using multivariate models to control confounds, cardiotocography fetal heart rate was recently found to be an independent values of fetal acidosis, respiratory morbidity in term new born, and results for preterm cesarean delivery for increased risk of neonatal and childhood morbidity. In our multivariate model analysis, acidosis of metabolism at birth had an independent link with the cardiotocography fetal heart rate mean and variable and also with the type of delivery (delivery through surgery over vaginal) and parity. Our results are in agreement with the study of Heinonen et al. who also found that pregnancy, but not mother age, was an independent danger factor for new born acidosis. Corroborating our results with another study of women with a singleton term pregnancy that found previous cesarean delivery and null parity as risk factors for neonatal metabolic acidosis may indicate that not only previous but also the current cesarean delivery may represent an actual challenge to the fetus. In two studies of poor new born adjustment at birth with severe new born acidosis (umbilical artery pH less than seven point ten) independent danger factors added abnormal cardiotocography fetal heart rate, maternal age thirty five years or older, parity, prior neonatal death or cesarean delivery. Our data shows a costly role for cardiotocography fetal heart rate in showing new born acidosis in deliveries with Appearance, Pulse, Grimace, Activity, and Respiration five ranging from fairly low to normal without nervous system dangers.

Heart rate variability (HRV) analysis with search for new algorithms is commonly employed to measure alterations in autonomic tone with predictive value in diseases. We have identified the CV of the heart rate as a sensitive measure of autonomic dysfunction and independently associated with vascular atherosclerosis. In this work, we found that CV of during delivery cardiotocography fetal heart rate is an independent values of new born acidosis of blood and CONCLUSION

EFHRM can distinguish healthy fetuses from compromised fetuses with a high sensitivity but due to its low specificity and positive predictive value, the incidence of operative deliveries has increased. The neonatal outcome in terms of APGAR score has a statistically significant association with intrapartum FHR patterns.

Recommendations: Adequate knowledge to interpret CTG traces is essential. The limitations of CTG should be known. The clinical picture of the labouring patients should also be considered. Additional tests like FBS should be used when in doubt especially in non-reactive patterns. Further research is required to predict fetal hypoxia in order to minimize perinatal morbidity and mortality.

Author’s Contribution:
Concept & Design of Study: Major Asiya Yaqoob
Drafting: Shandana Mustafa, Jadoon, Saima Ilfat
Data Analysis: Asma Liaqat, Qamoos Razaq
Revisiting Critically: Major Asiya Yaqoob, Shandana Mustafa, Jadoon
Final Approval of version: Major Asiya Yaqoob

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

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4. Devane D, Lalor JG, Daly S, Mcguire W, Smith V. Cardiotocography versus intermittent auscultation of fetal heart on admission to labour ward for


Kala Pather Poisoning and Liver Function Tests in Children
Mohammad Sarwar¹, Nighat Sultana¹, Umar Waqar¹, Fareeha Kausar¹, Anila Jamil¹ and Mohammad Asif²

ABSTRACT

Objective: To Study the Kala Pather Poisoning and Liver Function Tests in Children.
Study Design: Experimental study
Place and Duration of Study: This study was conducted in ICU of Children Hospital Lahore during Jan 2014 to Jan 2019.
Materials and Methods: This study was performed in ICU of Children Hospital Lahore. Fifty-two patients with Paraphenylenediamine (PPD) poisoning who came to emergency from 2014 to 2019 were included in it. History was recorded and physical examination was done. All cases were of accidental poisoning. Both males and females were included. Their age was less than 9 years. LFTs were measured. Intubation, tracheostomy and ventilators were needed for proper management.
Results: Maximum level of serum bilirubin, AST and ALT was 3 mg/dl, 760 mg/dl and 784 mg/dl respectively. All the patients showed abnormal LFTs. 77% were intubated, 42% needed tracheostomy and 65% needed ventilator. Only one child died so survival of cases was 96%. Manner of poisoning was accidental in all cases.
Conclusion: Paraphenylenediamine poisoning is fatal one. But if properly managed with tracheostomy or ventilators the mortality can be very much reduced.
Key Words: Paraphenylenediamine, poisoning, cervicofacial edema, human, hair-dye, accidental

INTRODUCTION

Paraphenylene diamine is a chemical used to give color to the grey hairs, fascinating designs on palms and soles and also used to form different forms of tattoos¹. PPD is supplied in the market both in grounded and ungrounded form. The products made to color the grey hairs contain PPD. In Pakistan, India and some countries in Africa its mixture with henna is also used. As henna is found in abundance naturally so it’s allergic reactions are very rare. On the other hand, PPD, when oxidized produces very lethal product which causes fatal allergic reactions². In Pakistan, India and African countries poisoning cases of PPD, are seen in emergencies of hospitals³⁴. When taken by mouth, PPD produces very lethal chemicals which harm the body. This action is proportional to amount taken. 7 Gms are enough to cause life threatening damage to the body⁵.

Toxic hepatitis, myocarditis and convulsions are other manifestations⁶. Pure PPD is in the form of white crystals, which turns brown on exposure to air. It is produced in Germany, Japan, and the United Kingdom.⁸⁹ Oral ingestion of PPD can lead to the development of angioneurotic edema, or cardiotoxicity leading to fatal arrhythmias and death within the first six to 24 hours.¹⁰¹¹ PPD can also cause skin irritation and allergies. Furthermore, its role as a carcinogen in animals has also been described¹²¹³. Paraphenylene diamine (PPD) ingestion is manifesting as one of the more common ways of committing suicide in Southern Punjab, Pakistan, especially Bahawalpur. PPD is an ingredient of a compound commonly known “Kala Pathar” which means “Black Stone” in Urdu. Very little is known about the impact of PPD intoxication on liver tissue.⁶ In a study LFTS very much deranged from normal⁷.

MATERIALS AND METHODS

This was a retrospective study of 52 (32 males and 20 females) patients with history of hair dye (Kala pather) poisoning, admitted in ICU of the children hospital Lahore. This study included patients came to emergency with ingestion of hair dye, from 2014 to 2019. Both genders were included in the study regardless of the age. But children came with poisoning were less than 9 years (although age above 9 was not an exclusion criteria). All the patient was physically and mentally normal before ingestion of poison, according
to history. All these patients gave a history of accidental intake of hair dye containing Kala pather. Data regarding age, sex, time of onset of symptoms, appearance of swelling on face and neck was collected. Blood was taken to measure the serum levels of Bilirubin, ALT and AST. SPSS 25 version was used to do statistical analysis. How many patients needed Intubation, tracheostomy and ventilators was also studied.

**Statistical Analysis:** SPSS version 25 was used to get graphs, descriptive data and to calculate value of person correlation coefficient between age and serum bilirubin, AST and ALT.

**RESULTS**

Descriptive data indicated that study included 52 patients (32 males and 20 females). 62 % were males and 38 % females. Other data is given in table no 1.

**Table No.1: Descriptive Data**

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2.00</td>
<td>8.00</td>
<td>4.7196</td>
<td>1.59007</td>
</tr>
<tr>
<td>S_Bilirubin</td>
<td>1.10</td>
<td>3.00</td>
<td>1.8538</td>
<td>0.52401</td>
</tr>
<tr>
<td>ALT</td>
<td>73.00</td>
<td>784.00</td>
<td>264.230</td>
<td>169.4481</td>
</tr>
<tr>
<td>AST</td>
<td>147.00</td>
<td>760.00</td>
<td>431.653</td>
<td>157.0653</td>
</tr>
<tr>
<td>Start_of_Symptoms</td>
<td>.30</td>
<td>1.45</td>
<td>.8558</td>
<td>.37211</td>
</tr>
</tbody>
</table>

Following figures indicate frequency, mean and std Dev of calculated Serum Bilirubin, ALT and AST respectively in fig no 1, 2 and 3.

**Figure No.1: Frequency distribution of S Bilirubin**

**Figure No.2: Frequency distribution of ALT**

**Figure No.3: Frequency distribution of AST**

**Table No.2: Average number of patients who needed intubation, tracheostomy and ventilator along with facial and neck swellings**

<table>
<thead>
<tr>
<th></th>
<th>Intubation</th>
<th>Tracheostomy</th>
<th>Ventilator</th>
<th>Facial swelling</th>
<th>Neck swelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no of patients</td>
<td>52</td>
<td>52</td>
<td>52</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>No of patients who needed/developed</td>
<td>40</td>
<td>22</td>
<td>34</td>
<td>52</td>
<td>51</td>
</tr>
<tr>
<td>Average no of patients who needed/developed</td>
<td>77%</td>
<td>42%</td>
<td>65%</td>
<td>100%</td>
<td>96%</td>
</tr>
</tbody>
</table>

**Table No.3: Average number of patients who needed intubation, tracheostomy and ventilator (males) along with facial and neck swellings**

<table>
<thead>
<tr>
<th></th>
<th>Intubation</th>
<th>Tracheostomy</th>
<th>Ventilator</th>
<th>Facial swelling</th>
<th>Neck swelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no of patients</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>No of patients who needed/developed</td>
<td>26</td>
<td>22</td>
<td>26</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Average no of patients who needed/developed</td>
<td>82%</td>
<td>69%</td>
<td>81%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table No.4: Average number of patients who needed intubation, tracheostomy and ventilator (females) along with facial and neck swellings**

<table>
<thead>
<tr>
<th></th>
<th>Intubation</th>
<th>Tracheostomy</th>
<th>Ventilator</th>
<th>Facial swelling</th>
<th>Neck swelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no of patients</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>No of patients who needed/developed</td>
<td>14</td>
<td>0</td>
<td>8</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Average no of patients who needed/developed</td>
<td>70%</td>
<td>0%</td>
<td>40%</td>
<td>100%</td>
<td>96%</td>
</tr>
</tbody>
</table>
All cases were of accidental poisoning. All were discharged other than one who died.

DISCUSSION

This study indicates that in children it is accidental poisoning. Most of previous studies were carried out on adult patients. Time of appearance of symptoms was from half an hour to 105 minutes. Time of onset of symptoms had no correlation with values of LFTs. Age showed a weak positive statistically significant correlation with serum bilirubin value but there was no significant correlation found with AST and ALT values. Mean value of AST and ALT was 438.1 and 264.2 respectively, which is much less than a study carried out in PMC Nawabshah. In that study it was 1365 and 851 respectively. Some other studies showed elevated values of AST and ALT. But that study was on adults. Facial swelling was found in all cases. Neck swelling was found in all male cases and 96% female cases. In a previous study carried out in Bahawalpur it was concluded that all cases of PPD poisoning had caused elevated serum levels of ALT and AST. It also caused both facial and neck swelling. In Abbotabad a study was done in which it was found that 49.2% of PPD poisoning cases needed tracheostomy and 32.3% needed ventilator. While in this study it was found that 42% needed tracheostomy and 65% needed ventilator. In that study mortality was up. Only 20% were discharged but in this study, survival was 96%. Only one death took place. PPD is not only poisonous in human beings but also in other mammals. Mostly it is used for suicidal purposes but in this study all cases were of accidental poisoning.

Only serum bilirubin and age showed statistically significant and positive correlation i.e., 0.419 with p value less than 0.05. AST and ALT did not have statistically significant correlation with age with p value far greater than 0.05.

CONCLUSION

Poisoning with kala pather is very fatal until managed properly. It causes drastic effects upon liver functions. It causes swelling on face and neck. If tracheostomy is not done and ventilators are not provided mortality is very high. But in this study only one child died of poisoning and survival was upto 96%.

Author's Contribution:
Concept & Design of Study: Mohammad Sarwar, Nighat Sultana

Table No 5: Pearson correlation coefficient was also calculated as depicted

<table>
<thead>
<tr>
<th></th>
<th>AGE</th>
<th>AGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value of r</td>
<td></td>
<td>Value of p</td>
</tr>
<tr>
<td>S Bilirubin</td>
<td>0.419</td>
<td>0.002</td>
</tr>
<tr>
<td>AST</td>
<td>0.05</td>
<td>0.706</td>
</tr>
<tr>
<td>ALT</td>
<td>0.156</td>
<td>0.269</td>
</tr>
</tbody>
</table>

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

REFERENCES

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INTRODUCTION

The Prevalence of meconium-stained amniotic fluid (MSAF) has been associated with the increased risk of poor foetal outcomes and life-threatening complications like the meconium aspiration syndrome and perinatal asphyxia in perinatal and neonatal stages. Meconium is a dark, black-green and odourless paste-like material formed in the intestines of a foetus. It first appears around 12 weeks of gestation in the intestine of the fetus and remains in the fetus colon throughout the gestation period. Exact etiology of the MSAF is still unclear. From the literature, it has been proven that the MSAF incidence increases with the gestation age. Research by Rao S, showed that mothers with acute chorioamnionitis/funisitis have higher risk (p<0.05) of MSAF incidence. He also studied that in newborn ICU, the prevalence of respiratory distress, meconium aspiration syndrome, and presumed sepsis is relatively higher in MSAF group (p<0.05). In another research by Mathews and Warshaw it was shown that the admission of neonates to ICU is confirmed in 98.4% cases of meconium stained AF. Matured neonates were given 37 weeks after gestational age when the autonomic nervous system was autonomous. Placental insufficiencies, maternal hypertension, pre eclampsia, olygohydramnios and maternal medication (toback or cocaine) are the risk factors that make meconium development in the uterus. Meconium aspiration can contribute to meconium aspiration syndrome (MAS),
the principal cause of foetal death, during intrauterine life.

Pakistan has one of the highest rates of maternal and neonatal morbidity due to low standards of the healthcare system and inaccessibility of healthcare in many areas. Due to scarcity of data from Pakistan, the current study was undertaken. The objective of the present study was to evaluate the frequency of MSAF in women who delivered at term at a tertiary care hospital, Khairpur Mirs, Pakistan and the associated factors.

MATERIALS AND METHODS

The case-control study was conducted at Obstetrics and Gynecology, Department unit 2, Kausar hospital Mother & Child Health Care Center, Khairpur, and Khairpur Medical College, Khairpur Mirs between January to August, 2020. An ethical approval was obtained from the institutional review board. A non-probability convenience sampling technique was used to enroll participants in the study. During the study period, a total of 73 cases with meconium stained amniotic fluid were recruited and 73 healthy subjects with clear amniotic fluid acted as control.

All socio demographic data of mothers was entered into an electronic predefined questionnaire via face to face interview. Those who were not able to understand Urdu language, were interviewed by a translator. Information like maternal age, parity, gravidity, body mass index, gestational age, mode of delivery, and other related data were recruited. Women with breech presentation, congenital abnormality, twin births, stillbirth cases were excluded from the study.

Women in the case group were divided into 3 grades, i) Grade I, thin yellow colour meconium, ii) Grade II, light green coloured meconium, and iii) Grade III, thick pasty meconium. Women in the control group had thin clear amniotic fluid. Fetal and maternal heart rate were regularly monitored for both groups.

Data was analyzed using SPSS version 26. The continuous data was presented as mean and standard deviation, while the non-numerical data was presented as frequency or percentages. The two groups were compared for maternal characteristics and associated factors of MSAF. Chi square tests were applied and a p-value of < 0.05 was set as statistical significance.

RESULTS

There were seventy-three cases of MSAF during the study period. The mean age and standard deviation of women in the case (MSAF) group was 36.06 years with the range 26 - 42 years. The mean maternal age was significantly lower in the control group (p-value < 0.00001). (Table 1).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>36.08±8.12</td>
<td>27.41±7.21</td>
<td>0.00001</td>
</tr>
<tr>
<td>&lt;30</td>
<td>29(39.73%)</td>
<td>55(75.4%)</td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>44(60.27%)</td>
<td>18(24.66%)</td>
<td></td>
</tr>
</tbody>
</table>

There were 16 women with Grade I MSAF, 40 women with Grade II, and 17 women with Grade III MSAF. Prolonged labour of greater than 12 hours was more frequently observed in the MSAF group compared to the control healthy subjects with clear amniotic fluid. (Table 2).

<table>
<thead>
<tr>
<th>Grade of MSAF</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>16(21.92%)</td>
</tr>
<tr>
<td>Grade II</td>
<td>40(54.79%)</td>
</tr>
<tr>
<td>Grade III</td>
<td>17(23.29%)</td>
</tr>
</tbody>
</table>

Out of the 73 women with MSAF, about 59 participants delivered via caesarean section while the rest 11 had spontaneous vaginal delivery. In contrast, a relatively lower number of women in the control group delivered via C-section.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal</td>
<td>11(15.07%)</td>
<td>49(67.12%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Caesarean</td>
<td>59(80.82%)</td>
<td>13(17.81%)</td>
<td></td>
</tr>
<tr>
<td>Instrumental</td>
<td>3(4.11%)</td>
<td>11(15.07%)</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

A widely observed phenomenon is meconium stained amniotic fluid (MSAF). Increased incidence of perinatal disease and mortality is correlated with the presence of thick meconium. The current study revealed certain maternal and obstetric traits which had major effects of MSAF in our people. The increasing gestational age, the maternal age at the time of conception, the duration of labour, were some of the factors attributed to the development of MSAF. These findings are in accordance with the existing international and local literature.

Addisu et al., recently reported that maternal age, spontaneous onset of labor, incidence of preeclampsia, prolonged or delayed labor, were significantly associated with the occurrence of MSAF. The authors found that MSAF was 5.6 times more likely to occur in mothers with age of greater than thirty [adjusted odds ratio = 5.6. 95% CI = 3.35 - 9.44]. Furthermore, in women with prolonged duration of labor of more than twenty-four hours, MSAF was 7 times more likely to develop [adjusted odds ratio =7.1. 95% CI =1.67 - 29.68]. Another study from Nigeria revealed similar findings. They reported an incidence rate of MSAF 20.4%. The MSAF incidence increased with the rising gestational age. Other factors significantly associated with MSAF were primigravida (p = 0.005), prolonged rupture of fetal membranes (p = 0.0013), and obstructed or delayed labour (p = 0.000002).
CONCLUSION

Increased gestational age, delayed or obstructed labor, induced-labor, and cesarean section may be associated with increased risk of development of meconium-stained amniotic fluid. MSAF should be carefully investigated and a mother with MSAF and the fetus during delivery should be regularly and vigilantly monitored. Thick green meconium-stained amniotic fluid is associated with increased neonatal morbidity and mortality. Further large-scale, multi-centre studies should be conducted to evaluate the risk factors and sociodemographic profile of cases with in-utero excretion of meconium.

Author’s Contribution:
Concept & Design of Study: Bushra Begum Ramejo
Drafting: Syed Sohail Abbas, Tehmina Mahar
Data Analysis: Sanober Soomro
Revisiting Critically: Bushra Begum Ramejo, Syed Sohail Abbas
Final Approval of version: Bushra Begum Ramejo

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

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**Assessment of Length, External Outer Diameter and Positional Variations in Normal and Inflamed Appendix**

Fauzia Siraj\(^1\), Bilal Hassan\(^1\), Zafar Iqbal\(^2\), Rifat Shamim\(^2\), Faryal Azhar\(^3\) and Muhammad Usama Faruqui\(^4\)

**ABSTRACT**

**Objective:** To assess the length, external outer diameter and positional variations in normal and inflamed appendix among the adult population of Rawalpindi operated for acute appendicitis.

**Study Design:** Cross sectional

**Place and Duration of Study:** This study was conducted at the Department of Surgery and histopathology of Benazir Bhutto Hospital. Two years (Jan 2018 to Feb 2020).

**Materials and Methods:** Two hundred patients operated for acute appendicitis were included in the study. Out of these, patients confirmed on gross examination and histopathology were classed as true cases. Length and external outer diameter were calculated for both inflamed and non-inflamed appendices. Mean length and external outer diameter was compared in both the groups. Positional variations were also noted for all the appendices removed may they be inflamed or not inflamed.

**Results:** Out of 200 patients operated with clinical suspicion of acute appendicitis, 179 (89.5%) showed the presence of inflammation on gross and histopathology while 21 (10.5%) had non-inflamed appendix. Mean age of the study participants was 30.6±2.17 years. Mean length of the appendix in cases with confirmed inflammation was 4.22±2.1mm while without inflammation was 3.37±1.4 mm. Mean external outer diameter of the appendix in cases with confirmed inflammation was 0.837±0.3 cm while without inflammation was 0.672±0.3 cm (p-value<0.01). Mean external outer diameter of the appendix was 4.22±2.1 mm while without inflammation was 3.37±1.4 mm (p-value<0.01). Most common type of location in both the groups was retrocecal.

**Conclusion:** Inflammation may pose a direct effect on length and diameter of the appendix as there was a significant increased length and diameter recorded in patients with confirmed inflammation as compared to those without any inflammation. Position of appendix was almost same in both the groups.

**Key Words:** Appendicitis; Anatomical Parameters; Relationship


**INTRODUCTION**

Statistics from studies performed around the globe conclude that acute appendicitis has been a common clinical condition.\(^1\) Appendectomy has been one of the most commonly performed surgical procedures around the world.\(^2\) Diagnosis is usually clinical, supported by relevant investigations.

\(^1\) Department of Anatomy, Al Nafees Medical College, Isra University Islamabad.

\(^2\) Department of Anatomy, Rai Medical College, Sargodha.

\(^3\) Department of Medicine, SMC, Sialkot.

\(^4\) Department of Physiology, LMDC, Lahore.

Correspondence: Dr. Fauzia Siraj, Senior Lecturer, Department of Anatomy, Al Nafees Medical College, Isra University Islamabad.

Contact No: 03332923355

Email: drsirajahmad.786@gmail.com

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Most of the patients undergo surgical management for this inflammatory condition.\(^1\) Inflammation may bring about certain anatomical changes in the organ or there may be certain anatomical predispositions which could increase the chance of getting inflamed.

Appendix has a unique anatomical profile. It is basically a true diverticulum at the base of the cecum. It is worm-like, long organ with tubular architecture. In comparison to take an abnormal sac or pouch formed at a weak point in the wall of the alimentary tract, it is a true an abnormal sac or pouch formed at a weak point in the wall of the alimentary tract of the colon and contains all of the layers of colon: mucosa, submucosa, longitudinal and circular muscles, and tissue of a serous membrane. It has multiple variations in its position which include retrocecal, subcecal, pre-ileal and post-ileal, and pelvic. Usually when this organ gets inflamed there is disruption in routine anatomical profile and length or diameter of this organ may vary depending upon the duration and extent of inflammation.\(^3,4,5\)

Various anatomical parameters related to appendix and variation in them due to inflammation have been discussed in various papers published in the past.
Willekens et al. in 2014 did a backdated evaluation of one hundred eighty-six sick persons undergoing CT of abdomen without feeling of acute appendicitis. In a given sample of representation and measurements (including maximum outer diameter, thickness of wall, length, content, location of base and tip) of normal tube-shaped sac attached to and opening into the lower end of the large intestine were noted. They came up with the findings that the mean maximal diameter of the appendix was 8.19 mm±1.6 (SD) (range, 4.2-12.8 mm). The mean length of the tube-shaped sac attached to and opening into the lower end of the large intestine was eighty-one point eleven mm± twenty-eight point forty-four (SD) (range, seven point two-one hundred fifty-eight point eight mm). The mean thickness of wall the tube-shaped sac attached to and opening into the lower end of the large intestine was two point twenty-two mm± zero point fifty-six (SD) (range, one point fifteen-three point eighty-five mm). The most common site of the tube-shaped sac attached to and opening into the lower end tip of the large intestine was pelvic in sixty-six percent appendices. The most common location of the tube-shaped sac attached to and opening into the lower end of the large intestine base was inferior, medial, and posterior in thirty-seven percent. The normal appendix contained high-density material in 2.2%. There was a significant correlation between gender and appendiceal length, with men having longer appendices than women.6 Park et al. studied this phenomenon long ago in 2007 and concluded that a maximum outer diameter (MOD) >6 mm has been regarded as the most reliable feature in diagnosing acute appendicitis. In a recent report, a MOD > 5.7 mm was suggested as the optimal criterion to diagnose acute appendicitis in children.7 Mwachaka et al. in 2014 performed a similar study on the normal population and revealed that commonest appendicular types in males were retrocecal 10 (27%) while in females was subileal 4 (36.4%). The average length of the appendix was seventy-six point five ± twenty-three point six mm. The base of the appendix was located along, below, and above the spinoumbilical line in 25 (52.1%), 9 (18.8%), and 14(29.2%) cases, respectively.8 Abegaz et al published a similar study in 2016 with a conclusion that retrocecal appendix was found to be the most common (72.73%), followed by pelvic (11.69%), preileal (10.39%), and subcecal (5.19%). Postileal position was not observed in this study. The association between age of the patients and the occurrence of appendicitis was statistically significant (P < 0.05) while the association between sex and position of appendix was not significant. 

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of Surgery and histopathology of Benazir Bhutto Hospital. Two years (Jan 2018 to Feb 2020). WHO sample size calculator was used to calculate the sample size for this study with population prevalence proportion of 12.5%. Nonprobability consecutive sampling was done to recruit the patients for this study. All the patients between the age of 18 and 60 years presenting with symptoms of acute appendicitis and diagnosed and operated at the surgical unit by the consultant surgeon. Exclusion criteria were the patients more than 60 years of age or those who did not consent to or those with a past or current history of any abdominal surgery. Patients with any autoimmune disorder or hematological or lymphoid malignancy were also excluded from the study.

Ethical approval (IREB letter number: F,2/IUC-ANMC/EC-127/2016) was granted by the ethical committee and formal consent from the patients and controls after providing them all the information regarding the study and mentioning them their right to withdraw at any time from the study if they don’t feel comfortable being the part of study. The abdomen was opened by a xifopubic midline incision. The vermiform appendix was located by simple exposure of the lower ileocecal recess or, in difficult cases, we followed the teniae to their junction at the apex of the cecum and base of the appendix.12 The appendix positions were defined as follows: Retrocecal/retrocolic: the appendix courses upwardly behind the cecum, and may reach the initial portion of the ascending colon; pelvic: the appendix is directed downward, over the psoas major, with its tip surpassing the upper edge of the lower pelvis. Post-ileal: the distal portion of the appendix is in a position posterior-superior to the terminal ileum and directed to the spleen; Subcecal: the appendix is located under the cecum, resting on the right iliac fossa and separated from the iliac muscle by a local peritoneal lining; Pre-ileal: the distal portion of the appendix is located in a position anterior-superior to the terminal ileum and directed to the spleen; Paracecal position: the appendix is situated laterally to the cecum and ascending colon; Other (ectopic) positions: the appendix does not fit in any of the positions above described.13,14 Length and external diameter was measured in each case according to the standard method.15 Descriptive statistics were used in the study to describe the variables of the study. Qualitative variables like patients with and without obvious inflammation and variations in anatomical position of appendix were mentioned in frequency and percentage. Mean and standard deviation was calculated for age, length of appendix and external diameter in patients with and without obvious inflammation. Student t-test was applied to look for the difference of mean values of length and external diameter in patients with and without confirmed inflammation. SPSS-23.0 was the software used to process all the data and perform the analysis. Differences between groups were considered significant if p-values were less than or equal to 0.05.
RESULTS

Out of 200 patients operated with clinical suspicion of acute appendicitis, 179 (89.5%) showed the presence of inflammation on gross and histopathology while 21 (10.5%) had non-inflamed appendix. Mean age of the study participants was 30.6±2.17 years. Table I shows the general characteristics of the study participant. Table II shows that mean length of the appendix in cases with confirmed inflammation was 08.37 ± 3.4 cm while without inflammation was 6.72 ± 3.1 cm (p-value<0.01 on student t-test). Table II also reveals that mean external outer diameter of the appendix in cases with confirmed inflammation was 4.22 ± 2.1 mm while without inflammation was 3.37 ± 1.4 mm (p-value<0.01 on student t-test). Most common type of location in both the groups was retrocecal followed by pelvic.

Table No.1: Characteristics of study participants

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean ± SD</th>
<th>Range (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>30.6±2.17</td>
<td>12 years - 59 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>150 (75%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>50 (25%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gross and histopathology</th>
<th>Inflamed</th>
<th>Not inflamed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflamed</td>
<td>179 (89.5%)</td>
<td>21 (10.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Position of Appendix in Inflamed</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrocecal</td>
<td>54 (30.1%)</td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>50 (27.9%)</td>
<td></td>
</tr>
<tr>
<td>Sub cecal</td>
<td>7 (3.9%)</td>
<td></td>
</tr>
<tr>
<td>Para cecal</td>
<td>3 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>Post ileal</td>
<td>31 (17.3%)</td>
<td></td>
</tr>
<tr>
<td>Pre ileal</td>
<td>30 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Sub hepatic</td>
<td>3 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>1 (0.5%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Position of Appendix in Non-Inflamed</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrocecal</td>
<td>6 (28.5%)</td>
<td></td>
</tr>
<tr>
<td>Pelvic</td>
<td>4 (19.1%)</td>
<td></td>
</tr>
<tr>
<td>Sub cecal</td>
<td>1 (4.7%)</td>
<td></td>
</tr>
<tr>
<td>Para cecal</td>
<td>1 (4.7%)</td>
<td></td>
</tr>
<tr>
<td>Post ileal</td>
<td>3 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>Pre ileal</td>
<td>3 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>Sub hepatic</td>
<td>2 (9.5%)</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>1 (4.7%)</td>
<td></td>
</tr>
</tbody>
</table>

Table No.2: Comparison of Study Parameters in both the groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Inflamed</th>
<th>Not inflamed</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>179</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Appendix Length (cm)</td>
<td>08.37 ± 3.4</td>
<td>6.72 ± 3.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EOD (mm)</td>
<td>4.22 ± 2.1</td>
<td>3.37 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

This study is instrumental in understanding the changes that occur in the normal anatomical parameters of this organ known as appendix. Acute appendicitis has not been uncommon condition all over the world. Situation is not different in our part of the world and all age groups get affected by this condition but young population is usually more at risk. It would be of utmost importance if clinicians and researchers first note the normal anatomical parameters associated with this organ and then look for the changes that take place once inflammation has set in in Clinicians of Europe, expert of diet and expert of research have been studying on this event for years but limited study has been done in Pakistan. We therefore planned this study with the objective to assess the length, external outer diameter and positional variations in normal and inflamed appendix among the adult population of Rawalpindi operated for acute appendicitis. Iqbal et al. published a study on Pakistani population in 2012 with the conclusion that retrocaecal position of appendix was most commonly seen (57%) followed by pelvic (28.6%), post-ileal (9.4%) and pre-ileal (4%). The paracaecal and ectopic varieties were 5%. Results of our study were in accordance with their results and most common type of location in both the groups of our study was retrocecal followed by pelvic. Rettenbacher et al. in 2001 conducted a study with the objective to evaluate the usefulness and limitations of the outer diameter of the vermiform appendix at cross-sectional ultrasonography to confirm or rule out acute appendicitis. They came up with the results that outer appendiceal diameters in the control subjects ranged between 2 and 13 mm, and in 55 (23%) of 240 control subjects, diameters were 6 mm or more. Parameters in the symptomatic sick persons without acute inflammation of appendix ranged between two and eleven mm, and fifty-seven (thirty-two percent) of one hundred eighty sick persons had parameters of six mm or more. Parameters of acute inflammation appendix ranged between six and thirty mm. A diameter of six mm or more confirmed acute inflammation of appendix with a sensitivity of hundred percent; a specificity of sixty-eight percent; positive and negative given values of sixty-three percent and one hundred percent, respectively; and an accuracy of 79%. Our results also supported their findings as mean diameter in inflamed case was significantly higher than the diameter in non-inflamed cases. Yaqoob et al. published an interesting study with the objective to assess the frequency of visualization, position and diameter of normal appendix on 128-slice multi detector computed tomography (MDCT) in adult population. Their statistics showed that appendix was noted as definitely visualized in ninety-nine percent of sick persons and mean outside diameter of the appendix was five point six ± one point three mm (range three-eleven mm). Though our study design was very different and we confirmed inflammation after the surgery and then measured the length and diameter and...
they both turned out to be increased significantly among the inflamed cases.

Mwachaka et al. in 2014 performed a study on the normal population and revealed that commonest appendicular types in males were retrocecal 10 (27%) while in females was subileal 4 (36.4%). The average length of the appendix was 76.5 ± 23.6 mm.8 Results of our study strengthened their results both in terms of length and positional variations of the appendix. There was no record of appendicular parameters before the diagnosis of acute appendicitis therefore it cannot be concluded that current length and diameter of appendix determined during the study has been merely due to the current inflammation. Multiple studies with involvement of cases and healthy controls may help us in determining the exact figures regarding the anatomical parameters of inflammed and non-inflamed appendix.

CONCLUSION

Inflammation may pose a direct effect on length and diameter of the appendix as there was a significant increased length and diameter recorded in patients with confirmed inflammation as compared to those without any inflammation. Position of appendix was almost same in both the groups.

Author’s Contribution:

Concept & Design of Study: Fauzia Siraj
Drafting: Bilal Hassan, Zafar Iqbal
Data Analysis: Rifat Shamim, Faryal Azhar, Muhammad Usama Faruqui
Revisiting Critically: Fauzia Siraj, Bilal Hassan
Final Approval of version: Fauzia Siraj

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

REFERENCES


Determine the Diagnostic Accuracy of MRI for Diagnosis of Rotator Cuff Tear in Patients Presented with Shoulder Pain

Muhammad Rizwan Asghar¹, Aisha Asghar¹, Adeel Qamar² and Hafiza Sobia Ramzan²

ABSTRACT

Objective: The main objective of the study is to determine the diagnostic accuracy of MRI for diagnosis of rotator cuff tear in patients presented with shoulder pain.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the conducted in the department of radiology, Mayo Hospital Lahore for 6 months i.e. Feb 2019 to Feb 2020.

Materials and Methods: At that point patients were go through MRI. Multi-planar MR imaging of the shoulder was performed utilizing coronal slanted proton thickness, coronal sideways T1 weighted, coronal diagonal T2 weighted with fat immersion, sagittal angled T2-weighted with fat immersion, and hub T2 weighted arrangements.

Results: The mean age of the patients was 50.01±11.28. There were 62(41.3%) males and 88 (58.7%) females in our study. The mean tear size was 3.15±1.42 cm. Sensitivity and specificity of MRI for the diagnosis of 3 rotator cuff injuries was 90.67% and 96.00%. However, PPV and NPV values for MRI was 95.77% and 91.14% respectively. Overall diagnostic accuracy of MRI for the diagnosis of rotator cuff tear in patients presenting with shoulder pain.

Conclusion: Results of this study showed that diagnostic ability of MRI is excellent in diagnosing rotator cuff tear in patients presented with shoulder pain.

Key Words: Diagnostic Accuracy, MRI, Shoulder Pain

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INTRODUCTION

Shoulder torment is a typical protest by patients during doctor visits, and it very well may be because of an assortment of causes. The significant reason for shoulder torment in patients more seasoned than 40 years is rotator sleeve impingement and tears.¹,² Rotator sleeve pathology is a typical wellspring of shoulder pain.³ Reported pervasiveness of rotator sleeve tear shift from 6% to 34%, and increment with age.⁴ Ultrasound (US) and attractive reverberation imaging (MRI) are two of the most broadly utilized imaging instruments to explore such side effects. Notwithstanding equivalent indicative precision, restrictions of every methodology exist.³

¹ Department of Diagnostic Radiology, Mayo hospital, Lahore.
² Institute of Molecular Biology and Biotechnology, University of Lahore.

Correspondence: Dr. Muhammad Rizwan Asghar, Department of diagnostic Radiology, Mayo hospital Lahore.
Contact No: 0331-4172313
Email: rizwanasghar190@gmail.com

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With the advancement of new arthroscopic methods for treating rotator sleeve problems, MRI has assumed an inexorably significant part as a noninvasive test for figuring out which patients may profit by surgery.⁴⁷ An investigation revealed the affectability and particularity of MRI were 91.7% and 84.2% separately. The determined PPV, NPV were 91.7% and 84.2% separately. The general demonstrative exactness of MRI was 89.1% accepting careful discoveries as gold standard.⁵ Reasoning of this examination is to decide the symptomatic precision of attractive reverberation imaging for analysis of rotator sleeve tear in patients gave shoulder torment accepting careful discoveries as gold standard.⁹ Literature has revealed that MRI has positive function in location of rotator sleeve tear and can be utilized for definite conclusion. In schedule, radiologists don't utilize MRI for identification of rotator sleeve tear, rather patients go for a medical procedure, think that MRI may have some side effects.¹⁰¹²

Medical procedure itself has a few dangers. Neighborhood extents likewise need. So to keep patients from unnecessary medical procedures, we need to lead this examination to build up a system to analyze patients on MRI rather than medical procedure and nearby sizes will likewise be achieved. So that negative patients can be kept from a medical procedure and
positive patients can be overseen in like manner. This will reduce burden of hospital and patients.\textsuperscript{13}

**MATERIALS AND METHODS**

This cross sectional study was conducted in the department of radiology, Mayo Hospital Lahore for 6 months i.e. 12 Feb 2019 to 11 Feb 2020. The data was collected through non-probability consecutive sampling technique. Sample size of 150 cases is calculated with 95% Confidence level, 7% margin of error for sensitivity and 7% margin of error for specificity of MRI.

**Inclusion criteria**
- Age 30-70 years of both genders with shoulder pain of moderate to severe intensity (VAS scale \(>5\)) indicative of rotator cuff tear.

**Exclusion criteria**
- Patients having contraindications for surgery e.g.: hemodynamically unstable, cardiac failure or INR>2.
- Having co-morbid conditions as DM (BSR>186mg/dl), cerebrovascular accident (clinical examination), deranged LFT (AST>40IU, ALT>40IU), deranged RFT (serum creatinine>1.5mg/dl).
- Patients with h/o shoulder accident or previous surgery, or osteoarthritis

**Data Collection:** 150 patients fulfilling the selection criteria were recruited for the study from Department of Radiology, Mayo Hospital Lahore. After taking informed consent, demographic information like name, age, sex and contact was obtained. At that point patients were go through MRI. Multi-planar MR imaging of the shoulder was performed utilizing coronal slanted proton thickness, coronal sideways T1 weighted, coronal diagonal T2 weighted with fat immersion, sagittal angled T2-weighted with fat immersion, and hub T2 weighted arrangements. All MRIs was performed by scientist himself under management of an expert Radiologist. Patients were named as certain or negative based on MRI discoveries. At that point patient's gone through a medical procedure under broad sedation and medical procedure results was utilized to affirm the discoveries of MRI. All the data was noted on an organized proforma.

**Data Analysis:** The data was entered and analyzed in SPSS version 17.0. Quantitative variables like age was measured in the form of mean ± SD. Qualitative variables like gender, full or partial thickness on MRI and surgery was measured in the form of frequency and percentages.

**RESULTS**

The mean age of the patients was 50.01±11.28 years. Minimum age was 30 years and maximum age was 70 years. There were 62(41.3%) males and 88 (58.7%) females. There were 81 (54%) patients in which right shoulder was involved and in 69(46%) left shoulder was involved. According to MRI findings in 71% patients there was full thickness and in 79 (52.7%) patients there was partial or no thickness. According to surgical findings there were 75 (50%) patients with full thickness and 75 (50%) with partial or no thickness. The mean tear size was 3.15±1.42 cm. The minimum tear size was 1 cm and maximum was 5 cm.

**Table No.1:** Descriptive Statistics for Tear Size

<table>
<thead>
<tr>
<th>n</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>3.15</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>1.425</td>
</tr>
<tr>
<td>Minimum</td>
<td>1</td>
</tr>
<tr>
<td>Maximum</td>
<td>5</td>
</tr>
</tbody>
</table>

MRI correctly picked 68 cases with full thickness and correctly identified 72 patients with partial/no thickness. So the sensitivity and specificity of MRI was 90.67% and 96.00%. PPV and NPV were 95.77% and 91.14% respectively.

**Table No.2:** Diagnostic Accuracy of Rotator Cuff Tears Taking Surgical Findings as Gold Standard

<table>
<thead>
<tr>
<th>MRI</th>
<th>Surgery</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full thickness</td>
<td>68(90.67%)</td>
<td>3(4%)</td>
<td>71</td>
</tr>
<tr>
<td>Partial/No thickness</td>
<td>7(9.33%)</td>
<td>72(96%)</td>
<td>79</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>75</td>
<td>150</td>
</tr>
</tbody>
</table>

Sensitivity= 90.67% Specificity= 96.00%
PPV= 95.77% NPV= 91.14%
Diagnostic Accuracy= 93.33%

**Table No.3:** Diagnostic accuracy of rotator cuff tears taking surgical findings as gold standard stratified for age

<table>
<thead>
<tr>
<th>Age</th>
<th>MRI</th>
<th>Surgery</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤50 yrs</td>
<td>Full thickness</td>
<td>27</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Partial/No thickness</td>
<td>2</td>
<td>46</td>
<td>48</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>29</td>
<td>47</td>
<td>76</td>
</tr>
</tbody>
</table>

| >50 yrs | Full thickness | 41      | 2     | 43      | 0.000   |
|         | Partial/No thickness | 5       | 26    | 31      |
| Total   |                 | 46      | 28    | 74      |

Data was stratified for age of patients. In patients of age≤50 years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 93.1%, 97.9%, 96.4%, 95.8% and 96.1%. In patients of age>50 years, the
sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 89.1%, 92.9%, 95.3%, 83.9% and 90.5%. Data was stratified for gender of patients. In males, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 85.7%, 97.1%, 96.0%, 89.2% and 91.9%. In females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 93.6%, 95.1%, 95.7%, 92.9% and 94.3%. Data was stratified for anatomical side of shoulder. In left side, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 85.4%, 97.5%, 97.2%, 86.7% and 91.4%. Data was stratified for duration of symptoms. In duration<6months, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 84.2%, 94.7%, 94.1%, 85.7% and 89.5%. In patients of duration≥6months, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 93.6%, 95.0%, 96.0%, 92.9% and 94.3%. Data was stratified for anatomical side of shoulder. In left side, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI were 97.3%, 97.3%, 97.3%, 97.3% and 97.3%.

Table No.4: Diagnostic accuracy of rotator cuff tears taking surgical findings as gold standard stratified for duration of symptoms

<table>
<thead>
<tr>
<th>Duration</th>
<th>MRI</th>
<th>Surgery</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full thickness</td>
<td>Partial / No thickness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 months</td>
<td>32</td>
<td>2</td>
<td>34</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>36</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>38</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>≥6 months</td>
<td>36</td>
<td>1</td>
<td>37</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>36</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>37</td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Shoulder pathology is normal and related with significant utilitarian impediments that expansion with age.16 Disorders of the rotator sleeve (RC) ligaments establish the most well-known gathering of pathologies of the shoulder. RC messes are of multifactorial source and may bring about a reformist degeneration of the RC tendons.17 Knowledge of the honesty of the RC ligaments in a scene of subacromial torment is a significant factor to consider in treatment dynamic (careful versus moderate administration), and clinicians utilize an assortment of analytic tests to identify RC messes and to characterize the degree of damage.18

Following clinical assessment, a wide range of radiological investigations have been prescribed to aid diagnosis.19 These have filled in prominence in the course of recent years, especially given the trouble in recognizing the specific reason for shoulder torment, halfway as a result of the cover of indications from various etiologies. Radiological investigations have included plain X-beam, regular X-beam arthrography, ultrasound and attractive reverberation imaging (MRI).20 The last has picked up favor, being referred to as a valuable radiological appraisal with its high delicate tissue picture goal and having the option to separate among tendinopathy and halfway and full thickness rotator sleeve tears.21 Using this data, the best administration methodology can be detailed to advance the early return of shoulder work for this patient gathering.22

In this MRI findings showed that 71(47%) patients had full thickness and 79(53%) patients were diagnosed with partial/no thickness. However surgical findings of patients showed that there were 75(50%) patients who had full thickness and 75(50%) had partial/no thickness. When diagnostic results of surgical findings and MRI findings were compared it was observed that MRI misdiagnosed 7(9.33%) patients with as partial/no thickness however on surgical findings those patients had full thickness and similarly.23 On the other hand, MRI misdiagnosed 3(4%) patients as full thickness however these patients surgical findings showed that these patients had partial/no thickness. Sensitivity and specificity of MRI for the diagnosis of rotator cuff injuries was 90.67% and 96.00%.24 However PPV and NPV values for MRI was 95.77% and 91.14% respectively. Overall diagnostic accuracy of MRI for the diagnosis of rotator cuff tear in patients presenting with shoulder pain.

CONCLUSION

It is concluded that diagnostic ability of MRI is excellent in diagnosing rotator cuff tear in patients presented with shoulder pain. Since full thickness tear establishes a vital thought for surgical repair, this is a significant trademark while choosing an imaging methodology for RC issue.

Author’s Contribution:
Concept & Design of Study: Muhammad Rizwan Asghar
Drafting: Aisha Asghar, Adeel Qamar
Data Analysis: Hafiza Sobia Ramzan
Revisiting Critically: Muhammad Rizwan Asghar, Aisha Asghar
Final Approval of version: Muhammad Rizwan Asghar

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

REFERENCES
Total Versus Subtotal Thyroidectomy for the Management of Benign Multinodular Goiter at DHQ Teaching Hospital Gujranwala

Mudassir Rasool, Liaqat Ali Zia, Muhammad Khalid, Imran Amin, Muhammad Ansar Aslam and Hafiz Muhammad Khizar Nawaz Cheema

ABSTRACT

Objective: Goiter is an indicator of constant iodine inadequacy which is a significant general health issue for populace living with iodine insufficient climate. The aim of this analysis is to assess and validates the feasibility and safety of total thyroidectomy (TT) when compared to subtotal thyroidectomy for benign multinodular goiter.

Study Design: Retrospective Study

Place and Duration of Study: This study was conducted at department of General Surgery DHQ-Teaching Hospital Gujranwala (Pakistan) from January 2013 and July 2018.

Materials and Methods: A total of 409 patients who underwent thyroidectomy for benign multinodular goiter. The study protocol was endorsed by the morals advisory group before the beginning of the investigation.

Results: There were 409 thyroidectomy cases of which 258 (63%) and 151 (37%) underwent total thyroidectomy and subtotal thyroidectomy, respectively. The signs for medical procedures were kind multinodular goiter. The mean age was 41.5 ± 12.7 years for all patients, 42.2± 12.4 years in complete thyroidectomy gathering and 40.3± 12.4 years in subtotal thyroidectomy gathering. The most youthful patient was 17, and the most seasoned was 80 years.

Conclusion: Our study showed that there is no significant difference with respect to early stage postoperative complications between TT and STT. However, TT has the benefit of staying away from the danger of decline repeat, reoperation and dispenses with any ensuing danger of dangerous in thyroid organs.

Key Words: Subtotal, Thyroidectomy, Multinodular Goiter

INTRODUCTION

Goiter is an indicator of constant iodine inadequacy which is a significant general health issue for populace living with iodine insufficient climate. The pervasiveness of goiter was accounted for by (WHO) world health association it assessed 20-60% of total populace. Pakistan is the one of most seriously iodine lacking nations on the planet. Multinodular goiter is far and wide one instance of iodine lack.

In any case, treatment of multinodular goiter is as yet being discussed. Already subtotal thyroidectomy is a treatment of decision of amiable multinodular goiter¹.

Yet, as of late, thyroid medical procedure for considerate ailment and the effect of careful convention on the patient and specialist, explicit danger factors for explicit difficulty rates. Thyroid organ resection mean to eliminate all nodular tissue while leaves a little leftover in situ to save thyroid capacity². There by forestalling long lasting thyroid hormone supplementation treatment. Anyway there is hazard that the illness will persevere or reoccur in the leftover tissue. 40% of patient with multinodular goiter have knobs confined in the dorsal aspect of the organ, which are typically left during ordinary subtotal resection most focuses have received all out a close to add up to thyroidectomy and revealed low horribleness rates like the subtotal procedure albeit absolute thyroidectomy procedure of decision for the executives of thyroid malignant growth in view of increment endurance pace of patients. The ideal careful methodology for kind multinodular goiter has stay dubious³. The name purpose behind playing out a subtotal thyroidectomy is apparently low occurrence of post usable difficulty including intermittent laryngeal nerve loss of motion and hyperparathyroidism. Post – employable euthyroid state keep up by leaving a little leftover of thyroid tissue in site to keep up sufficient hormone creation⁴.

Department of General Surgery, DHQ-Teaching Hospital Gujranwala.

Correspondence: Prof Dr. Liaqat Ali Zia, Professor of General Surgery DHQ Teaching Hospital Gujranwala.

Contact No: 0301-8742901

Email: liaqataliz@yahoo.com

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Printed: November, 2020
There is, anyway a danger that the illness continues or reoccur in the remainder. Latest examinations supported all out thyroidectomy as favored procedure in careful administration of generous multinodular goiter in light of the fact that the lingering after subtotal thyroidectomy was bad recently accepted and intricacy hang tight for not diverse among aggregate and subtotal thyroidectomy procedure. The aim of this meta-analysis study is to assess the feasibility and safety of total thyroidectomy (TT) when compared to subtotal thyroidectomy for benign multinodular goiter.

**MATERIALS AND METHODS**

A total of 409 patients who underwent thyroidectomy for benign multinodular goiter between January 2013 and July 2018 at the department of General Surgery DHQ-Teaching Hospital Gujranwala (Pakistan) were reviewed retrospectively. The segment properties of patients, the signs for medical procedure, post operatively beginning phase deararness (transient and perpetual intermittent laryngeal nerve paralysis, transient relentless hypocalcaemia, post usable draining and wound site contamination) and length of remain in clinic were assessed. Thyroid test and other pathology tests were taken in the lab. The patients found to have hyperthyroidism before activity were treated with antithyroid medications (propylthiouracil and methimazole) until they became euthyroid and were then worked on. Patients who went through one-sided lobectomy, finish thyroidectomy, thyroidectomy because of Baredow Grave's malady, thyroiditis and thyroid malignancy were excluded from the examination. The chose patients were isolated into two gatherings in particular the all-out thyroidectomy and subtotal thyroidectomy gatherings. All patients in the two gatherings were worked on by some accomplished specialist. Exertion was made to see the parathyroid organ during all tasks. For the cases where the parathyroid organs were not noticeable, the organs are looked for at conceivable ectopic locales. Those parathyroid organs whose blood perfusion was wrecked were cut into 1 mm 3 pieces and afterward relocated into the ipsilateral sternocleidomastoid muscle. In all out thyroidectomy bunch the repetitive laryngeal nerve was seen during medical procedure and was saved. During the subsequent period, those whose vocal line developments discovered to be ordinary were viewed as having transient RNL paralysis, when vocal string paralysis over a half year, it was viewed as steady RNL paralysis.

**Serum Calcium levels:** Serum Ca level were resolved preoperatively in all patients and on the principal postoperative day. Ca++ levels were re-decided on the ensuing postoperative days as vital. Patients with hypocalcemia indications were treated with Vit D and calcium substitution. Patients with hypercalcemia indications enduring over a half year were acknowledged as having tenacious hypoparathyroidism.

The data was analyzed by using SPSS version 19. A value of P < 0.05 was accepted as statistically significant.

### RESULTS

There were 409 thyroidectomy cases of which 258 (63%) and 151 (37%) underwent total thyroidectomy and subtotal thyroidectomy, respectively. The signs for medical procedures were kind multinodular goiter. The mean age was 41.5 ± 12.7 years for all patients, 42.2± 12.4 years in complete thyroidectomy gathering and 40.3± 12.4 years in subtotal thyroidectomy gathering. The most youthful patient was 17, and the most seasoned was 80 years. There were 324 (79.2%) females and 85 (20.8%) guys. Among benevolent multi nodular goiter 258 (63.0%) were in the complete thyroidectomy (TT) and 151(37.1%) were in subtotal thyroidectomy (STT). Of the 258 patients in TT gathering, 195 (75.6%) were given euthyroidism while 43(28.5%) were given hyperthyroidism. The mean length of remain in medical clinic was 3.4±2.15 days in TT gathering and 3.6± 2.12 days in the STT gathering. There was no huge contrast between the two groups regarding age, sex, hormonal status, term of remain in medical clinic and sign of medical procedure (table 1).

<table>
<thead>
<tr>
<th>Patient properties</th>
<th>Groups</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (n=258)</td>
<td>STT (n=151)</td>
<td></td>
</tr>
<tr>
<td>Males (%)</td>
<td>53(20.5%)</td>
<td>32(21.2%)</td>
</tr>
<tr>
<td>Females (%)</td>
<td>205(79.5%)</td>
<td>119(78.8%)</td>
</tr>
<tr>
<td>Benign multinodular goiter</td>
<td>258(63.0%)</td>
<td>151(37.1%)</td>
</tr>
<tr>
<td>Length of stay in hospital (days)</td>
<td>3.4±2.15</td>
<td>3.6± 2.12</td>
</tr>
<tr>
<td>Hormonal status</td>
<td>3(1.1%)</td>
<td>4(2.6%)</td>
</tr>
</tbody>
</table>

Hematoma created in three (1.9%) cases while wound site disease created in one (.6%) tolerant in STT gathering. In TT gathering, hematoma created in three (1.1%) cases while wound site disease created in three (1.1%) patients. No measurably contrasts were found between the two gatherings as for the improvement pace of hematoma and wound site contamination (P >0.05) ensuing to the thyroidectomies in the general injury site issues (disease and hematoma) created in 10 (2.4%) cases. RNL paralysis happened in (2.3%) cases in the TT gathering and in 3 (1.9%) cases in the STT gathering. All RNL paralysis cases were one-sided. Perpetual paralysis was not reported in either gathering and there was no measurable contrast between the gatherings as for RNL paralysis (p > 0.05). In the postoperative period, hypocalcaemia created in 40
(15.5%) cases in the TT gathering and in 27 (17.8%) patients in the STT gathering. Though no tireless hypocalcaemia was seen in the STT gathering, it was seen in 1 (.4%) cases in the TT bunch as for hypocalcaemia happened in 67 (16%) patients. No different difficulties were noted in either gathering. The cost usable difficulties pace of the gatherings are appeared in table 2.

**Table No.2: Post-operative complications rates of the patients**

<table>
<thead>
<tr>
<th>Complications</th>
<th>TT n (%)</th>
<th>STT n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematoma</td>
<td>3 (1.1%)</td>
<td>3 (1.9%)</td>
<td>0.514</td>
</tr>
<tr>
<td>Wound site infection</td>
<td>3 (1.1%)</td>
<td>1 (0.6%)</td>
<td>0.611</td>
</tr>
<tr>
<td>Hypocalcaemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient</td>
<td>40 (15.5%)</td>
<td>27 (17.8%)</td>
<td>0.571</td>
</tr>
<tr>
<td>Permanent</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>RLN palsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient</td>
<td>6 (2.3%)</td>
<td>3 (1.9%)</td>
<td>0.805</td>
</tr>
<tr>
<td>Permanent</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

As a result of its high complexities rates, this procedure was once in a while utilized in non-malignant cases. High repeat rates, in spite of hormonal concealment treatment after subtotal thyroidectomy for amiable thyroid infection, expanded the enthusiasm for all out resection. As of late TT has gotten more worthy in the treatment of generous multi nodular goiter. 40% of the knobs are situated close to the back case of the thyroid organ in kind multi nodular goiter, so a few knobs remain unresected in STT. The best impediment of STT in favorable multi nodular goiter is the high repeat rate. 14.5% repeat rate in patients who got clinical treatment after STT and 43% in patients to do. 42% repeat rate in a long term follow up of STT patients. Repeat in thyroid ailment by the by acts troubles for reoperation like stringy tissues lead to lose of ordinary anatomic structure, which thusly, prompts extremely high entanglement rates. Reoperations because of repeat have a 10 crease expanded in RLN and parathyroid organ wounds. Wound disease and draining rates Recurrent laryngeal nerve palsy (RLNP) rate was 1.9% and there were no permanent paralysis cases after subtotal thyroidectomy was performed. We discovered no factually critical distinction regarding the paces of transient and permanent RLN Palsy between Total Thyroidectomy (TT) and Subtotal Thyroidectomy (STT).

The reason for transient hypocalcemia may incorporate parathyroid organ ischemia, postoperative hemodilution and thyroid organ control prompting expanded calcitonin secretions. Persistant hypocalcemia result from an inadvertent expulsion of the parathyroid organs alongside the thyroid organ or from the disturbance of blood perfusion of the parathyroid organ.

We discovered the paces of transient hypocalcemia to be 1.5% and that of persevering hypocalcemia to be 0.4% after TT. Also, the transient hypocalcemia rates was17.5% and that of constant hypocalcemia rate was 0% after STT. No significant measurably contrasts were seen regarding transient and steady hypocalcemia between the TT and STT gatherings. As indicated by the new literature, the recurrence of postoperative drain and wound disease runs somewhere in the range of 0% and 2%. Some examinations say, the discharge rate was 0.4% after TT and 0% after STT. Wound disease rate are likewise higher in portrayals.

Another significant factor prompting abstinence from the subtotal mediation of favorable multinodular goiter (MNG) is the threat possible the thyroid knobs. The mysterious disease rate is by and large somewhere in the range of 7% and 10%. The 5% of all thyroid knobs have harmful characteristics. Moreover, the most well-known purpose behind complexity in thyroid medical procedure is the coincidental finding of danger in obsessive assessments. Hoarsness because of RLN paralysis, hypocalcemia because of parathyroid organ injury and beginning phase discharge because of inadequate draining control are the most noteworthy intricacies occurring after thyroidectomy activities.

A few investigations have detailed that TT is related with higher danger of complications. However, a few examinations found the entanglement chances related with TT to be lower. However, in numerous different investigations, no noteworthy contrasts were found regarding the paces of confusion between TT and STT. Moreover, our study didn't locate any huge complexities among TT and STT.

The current writing shows the permanent RLN paralysis rate after TT goes from 0%-0.7% and STT from 0%-1.3% performed by experienced surgeons. In a similar report, the paces of transient and permanent RLN paralysis were accounted for as 4% and 1% individually after STT. In our investigation the transient RLN paralysis rate was accounted for as 1.9% and there were no permanent RLN paralysis cases after TT was performed. Moreover, the transient was 0% after TT and 0.6% after STT.

In our arrangement of cases, no extreme discharge or wound site contamination requiring reoperation was accounted for. The hematoma and wound site contamination rates were both 1.1% after TT. In STT hematoma and wound site contamination occurred at the pace of 1.9% and 0.6% separately. Cut site problems (wound site disease and hematomata) occurred altogether of 10 (2.4%) patients. Patients with wound site contaminations were treated with fitting anti-infection treatment and wound dressing. Those with hematomas were depleted. We found no factually
critical contrasts concerning wound site disease and hematomas between the gatherings.
In the same way as other different investigations, our examination results represented that utilizing TT for
kind MNG should be possible with little horribleness. The most significant factor in diminishing dreariness in
thyroid medical procedure is the careful method utilized. We accept that during the assembly and
dismemberment of the thyroid flaps, uncovering RLN, utilizing successful hemostasis during activity to
guarantee clean activity, seeing the four parathyroid organs, and ensuring their perfusion vessels may assist
with lessening intricacies.

CONCLUSION

It is concluded that there is no significant difference with respect to early stage postoperative complications
between TT and STT. However, TT has the benefit of staying away from the danger of decline repeat,
reoperation and dispenses with any ensuing danger of dangerous in thyroid organs. TT ought to in this way be
considered for treating kindhearted multi nodular goiter.

Author's Contribution:
Concept & Design of Study: Mudassir Rasool
Drafting: Liaqat Ali Zia
Data Analysis: Muhammad Khalid,
Ansar Aslam, Hafiz
Muhammad Khizar
Revisiting Critically: Nawaz Cheema
Final Approval of version: Liaqat Ali Zia

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

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18. Rojdomark J, Jarhult J. High long-term recurrence rate after subtotal thyroidectomy for nodular
Amelioration of Aminoglycoside Induced Nephrotoxicity by α Tocopherol and Selenium; A Morphological Study
Muhammad Zahid¹, Asma Inam¹, Khadija Mastoor², Anila Errum³, Muhammad Usman Tahir¹ and Faiza Khan⁴

ABSTRACT

Objective: The objectives of the study were to evaluate the morphological changes observed in aminoglycoside (Amikacin) induced nephrotoxicity in rabbits and their attenuation by concomitant administration of Alpha tocopherol and selenium in animal model.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Department of Pharmacology, Azra Naveed Medical College, Lahore for the duration of six months.

Materials and Methods: Twenty-four rabbits were divided equally into four groups. Group 1 being control group was given 2ml of isotonic solution while group 2 was induced nephrotoxicity by giving Amikacin 150 mg/kg body weight daily for 20 days intramuscularly twice a day. Group 3 Amikacin was given along with alpha tocopherol (1g/kg body weight) and selenium (2mg/kg body weight) Intramuscularly for the same study period. Group 4 was given only alpha tocopherol and selenium in above doses. At the end of study, histopathology of kidney tissues was evaluated and morphological changes were noted.

Results: Histological evaluation showed that Amikacin produced degenerative changes in proximal tubules causing interstitial infiltration and vascular congestion which were later on histologically seen to be minimized by giving treatment with alpha tocopherol and selenium.

Conclusion: It was concluded that morphological changes induced by Amikacin were attenuated when alpha tocopherol & selenium were co-administered in specific doses.

Key Words: Alpha tocopherol, Selenium, Nephroprotection, Oxidative stress, Tubular necrosis, nephrotoxicity, Aminoglycosides, Reactive oxygen species, Glutathione peroxidase


INTRODUCTION

Aminoglycosides have still maintained a central role in antimicrobial therapy for more than 70 years. Their story of success and continuing use can be claimed to their various properties which are unique to Aminoglycosides but such an extensive use is limited due to their adverse effects. Renal toxicity is one of the most frequent kidney troubles which might also be enhanced when aminoglycoside antibiotics, non-steroidal anti-inflammatory agents and chemotherapeutic agents are administered. Various chemical reagents including ethylene glycol, CCI4 and heavy metals such as lead, cadmium, mercury and arsenic can also possess definite nephrotoxic potential which also present as an increased serum creatinine and urea levels along with severe proximal renal tubular necrosis; though it is reversible renal damage because of high regenerative capacity of tubular cells. They can produce devastating effect on the kidneys resulting in acute renal failure, chronic interstitial nephritis and nephritic syndrome.

In the pathogenesis of renal injuries, inflammation and oxidative stress due to reactive oxygen species (ROS) are also documented as causative factors. Medic B et al (2019) even described that sometimes a single dose of aminoglycosides may lead to renal damage. As a consequence, drugs with prominent anti-inflammatory, anti-oxidative and nephroprotective properties were
tested in various research projects to be used as nephroprotectants. Since nephrotoxicity by aminoglycosides affects 15-20% of patients during treatment, preservation of normal renal function during life-saving treatments is a problem that needs to be resolved. So keeping in mind the nephrotoxic potential of so many substances, scientists are trying to find out nephroprotectants since decades to prevent nephrotoxicity.

Being the role of antioxidants and anti-inflammatory substances to shield nephrotoxicity, Alpha tocopherol is a lipophilic natural antioxidant while Selenium possesses essential elements & Co factor glutathione peroxidase protects DNA and other cellular organelles from oxidative stress. It has also some effects in preventing malignant transformation of cells. Literature also reveals a protective effect of selenium and alpha-tocopherol against prostate cancer in humans.

In our previous study, we observed biochemical changes in blood and urine in aminoglycoside treated animals and their attenuation by alpha tocopherol and selenium. Presently we investigated the morphological changes caused by aminoglycosides in renal tissue and possible nephroprotective effect of alpha tocopherol and selenium in animal model.

MATERIALS AND METHODS

The study was conducted on twenty-four males, local breed rabbits, weighing 1 to 1.5 Kg and age ranging from 7 to 8 months. They were fed on local diet with water ad libitum. Animals were divided in four groups at random with 6 animals in each group.

Group 1 (C) served as control group and was given isotonic solution 2ml twice a day, intramuscularly for 20 days. Group 2 (A) served as diseased group and was given Amikacin 150 mg/kg body weight daily for the same study period of time, intramuscularly in two equally divided doses to produce experimental nephrotoxicity while group 3 (ATS) served as treatment group and was administered amikacin in the same dose group alongwith alpha tocopherol (1g/kg dissolved in olive oil) and selenium (2mg/kg in form of sodium selenite) simultaneously. Group 4 (TS) was only administered with alpha tocopherol and selenium in above mentioned doses intramuscularly in two equally divided doses.

All animals were sacrificed after 24 hours of the last dose of the drugs. Renal tissues were fixed in 10% formalin. Four sections were taken from each kidney including cortex medulla and pelvis. Renal tissues after processing were embedded in Paraffin blocks and were cut by microtome in 4-5um thickness. Slides were studied in Histopathology section of the department by ordinary light microscope after staining with eosin and hematoxylin. Findings in all four groups of experimental animals were compared with control group for morphological changes.

RESULTS

Group 1 (Control) group showed normal morphology of kidney tissue (Fig. 1) while Group 2 revealed renal injury after administration of amikacin as indicator of nephrotoxicity. The morphological changes were mainly involving the renal tubules which showed patchy necrosis along with hyaline and granular casts in their lumina. Tubular cells were also seen shed in the lumina of renal tubules. There were hydropic changes in epithelial lining with cytoplasmic vacuoles at some areas. Glomeruli also showed congestion and loss of basement membrane. There was also lymphocytic infiltration in renal interstitium Fig. 2.

Figure No.1: Group (C) Control group showing normal morphology of renal sections (400 X)

Figure No.2: (Amikacin treated) showing vascular congestion, tubular necrosis and interstitial inflammation, congestion and hypercellularity (400X) (100X)
Figure No.3: (ATS; Amikacin, alpha tocopherol and selenium) revealing almost complete prevention of amikacin induced alteration in renal morphology by alpha tocopherol and selenium (100 X)

Figure No.4: (TS) Treated with alpha tocopherol and selenium only, showing no change in morphology as compared to control group

Group 3 treated with Amikacin along with alpha tocopherol and selenium showed preservation of tubular epithelial cells with mild changes in glomeruli (Fig. 3). Vascular congestion and interstitial inflammation were also reduced in group 3. Group 4 which was treated with alpha tocopherol and selenium showed normal renal morphology (Fig. 4).

DISCUSSION

Aminoglycoside antibiotics are continuously being used in clinical practice because of their bactericidal efficacy alone or in combination with other antibiotics. They are still indispensable in the treatment of so many life threatening infections because of their highly desirable properties.

Like all other Aminoglycosides, Amikacin induced nephrotoxicity is not only due to accumulation of drug in proximal and distal convoluted tubules but may also result in generation of reactive oxygen species which increase lipid peroxidation and lower the activity of antioxidant enzymes, so it can be blunted out by natural antioxidants like Vitamin E, Vitamin C, Selenium and Zinc. Various studies have been conducted in the past to test this hypothesis and they are found promising in this context. There is always a need to come up with natural nephroprotectants to counteract adverse effects of aminoglycosides.

In our study, Group 2 (Amikacin treated) showed patchy tubular necrosis, hyaline and granular casts in tubular lumen, and hydropic changes in epithelial cells and dropped out tubular epithelial cells in the lumina of tubules. At some sites, the tubular epithelial cells also showed hydropic changes with cytoplasmic vacuolization. So our findings are in accordance with many other previous studies including Zahid et al., 2007 and Elgami et al., 2016, in which Alpha tocopherol and selenium confirmed protective effect in lead induced hepatic and renal injury in fish. It is also in accordance with another study conducted by Bulan et al., in 2008 in which antioxidants like Vitamin E and C displayed some nephroprotection on biochemical markers and histopathological findings after cadmium induced renal toxicity in rats.

CONCLUSION

It is concluded the present in vitro study demonstrates that coadministration of amikacin with alpha tocopherol & Selenium can give impressive degree of amelioration against AG induced renal damage as assessed by histological criteria. Thus it is recommended to focus on supplementation of these agents to alleviate possible adverse effects of aminoglycosides. However, further studies are required to calculate safe dosage and elucidate exact mechanism of action of these two nephroprotectants.

Author’s Contribution:
Concept & Design of Study: Muhammad Zahid
Drafting: Asma Inam, Khadija Mastoor
Data Analysis: Anila Errum, Muhammad Usman Tahir, Faiza Khan
Revisiting Critically: Muhammad Zahid, Asma Inam
Final Approval of version: Muhammad Zahid

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

REFERENCES

Template of Medico-Legal Deaths in Tertiary Care Hospital of Karachi - Two Years Autopsy Based Study

Roohi Ehsan¹, Wasiq Ahmed¹, M. Faiz-ud-din² and Iqbal Ahmed³

ABSTRACT

Objective: To determine the frequency, gender and causes of medico-legal deaths autopsied at Abbasi Shaheed Hospital in Karachi.

Study Design: Retrospective study.

Place and Duration of Study: This study was conducted at the Abbasi Shaheed Hospital from January 2018 till December 2019.

Materials and Methods: This is a case study, involving the medico-legal deaths autopsied at Abbasi Shaheed Hospital. A detailed and complete autopsy was conducted in each case including both an external and an internal examination. The results were collected from the concerned authority on a structured Performa and analyzed statistically using SPSS version 15.

Results: A total 956 autopsies were conducted during the two years period at Abbasi Shaheed Hospital. Among all the causes, road traffic accidents were the most common cause of death followed by firearms, hanging, fall, electric current, other asphyxia causes and assault. Majority of the victims were male with male to female ratio of 8:1.

Conclusion: Road traffic accidents were the most common cause of death accounting for 42.25% of the total, followed by firearms which accounted for 24.5%, hanging accounted for 3.5% while fall accounted for 3.03%), electric current accounted for 2.71%, asphyxia was responsible for 2.19% of the total and assault accounted for 2.09%. The male to female ratio was 8:1 with 88.9% of victims being males. Victims belonged to the age group 21-30 years displaying the highest number (29.39%) of affection.

Key Words: Autopsy, Road traffic accident, Medico-legal deaths, Abbasi Shaheed Hospital, Karachi


INTRODUCTION

A medico-legal autopsy or forensic autopsy is a scientific examination of a dead body carried out under the laws of state to protect their citizens and to assist in the identification and prosecution of the guilty in cases of un-natural deaths.¹ It is an examination conducted post-mortem to address medico-legal objectives. Medico-legal autopsy acts as one of the investigative tool that helps the investigators in many ways.² Identification, determination of cause of death, time since death, manner of death, time between injury and death and to discover and recover any clue from the body, can possibly are few of the beneficial outcomes of a medico-legal autopsy as they can connect evidence to the criminal.³

Autopsy has to be conducted by a well trained and experienced doctor in the field of Forensic Medicine/ Forensic Pathology. The investigators require some vital queries to be answered by a medical personnel like cause, manner, fatal period and time since death. The answer to these questions will be possible with a detailed and meticulous autopsy.⁴ As per the legal procedure of our country, all medico-legal deaths require an investigation by the police or magistrate and then the final resolution by the courts.⁵ It is a procedure whereby a variety of observations can be made of internal organs and systems and the material is then submitted for myriad of modern laboratory investigations and tests.⁶ Autopsy findings can be used as strong basis for clinical audit.⁷ There are certain conditions where no findings are found at autopsy. In our study we have mentioned ‘reserved’ as a cause of death in about 7.9% cases. If no cause of death is detected during an autopsy and gross and if microscopic examination, toxicological analysis and laboratory investigations all fail to reveal a cause of death, the autopsy is considered to be negative which is happens about 2-10% of the times worldwide.⁸ A poorly performed autopsy may be considerably worse than no

¹ Department of Forensic Medicine / Pathology,² Karachi Medical & Dental College, Karachi.
³ Senior Lecturer, Fazaia Ruth Pfau Medical College.

Correspondence: Roohi Ehsan, Associate Professor Head of Forensic Medicine, Karachi Medical & Dental College, Karachi.
Contact No: 0333-2528545
Email: roohimurtaza@yahoo.com

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Printed: November, 2020
autopsy at all. It is certainly worse than an autopsy delayed for a short while to await the arrival of a specialist. Previous studies in Pakistan showed that firearms have become the weapon of choice. A study from Dera Ismail Khan reported 341 medico-legal autopsies conducted over a two years period where firearms caused 59% of deaths. Ehsan et al proclaimed 58.83% firearms medico-legal deaths in 6 years study. One year case study involving the medico-legal deaths autopsied at three major mortuaries in Karachi city also revealed firearms as the most common cause of death accounting for 44.6% of the total.

In the present two years study period, however, road traffic accidents (42.25%) are seen to outnumber firearms (24.5%) and other causes of medico-legal deaths autopsied. The main purpose of this study is to determine the frequency and causes of medico-legal deaths autopsied in both male and female at one of the tertiary care hospital of Karachi.

MATERIALS AND METHODS

The study includes all the cases of medico-legal deaths autopsied at Abbasi Shaheed Hospital from January 2018 to December 2019. Medico-legal injury cases and medico-legal deaths which were not reported and not autopsied were excluded.

Bodies were examined both externally and internally. Meticulous autopsy was conducted in every case in order to determine the cause of death. When ‘Reserved’ is the cause of death through conclusion on gross examination, specimens are sent for histopathological examination and chemical analysis wherever and whenever required, for the ascertainment of cause of death. The results were collected from the concerned department and were analyzed statistically using SPSS version 15. The frequency and percentages were calculated for all categorical variables including frequency, gender and causes of medico-legal deaths autopsied.

RESULTS

A total of 956 medico-legal deaths were autopsied during the period of January 2018 to December 2019, at Abbasi Shaheed Hospital, Karachi. Frequency of medico-legal deaths in relation to months during the study period showed that June accounts for the leading month followed by July, August, October, May, March, September, April, December, February, January and November respectively. (Table 1, Graph 1)

Males formed a significant portion of victims (88.91%) while females accounted for 11.08%. (Table 2, Graph 2) Frequency in relation to cause of death revealed that road traffic accidents (42.25%) were the leading cause of death followed by firearms (24.5%), hanging (3.5%), fall (3.03%), electric current (2.71%), asphyxia (2.19%), assault (2.09%), cut throat (1.35%), drowning (1.35%), poisoning (1.35%) and stab wound (1.35%) respectively. (Table 3)

<table>
<thead>
<tr>
<th>Table No.1: Frequency of Medico-Legal Deaths in relation to Months</th>
</tr>
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<tbody>
<tr>
<td>Month</td>
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<tr>
<td>-------</td>
</tr>
<tr>
<td>January</td>
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<tr>
<td>February</td>
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<tr>
<td>March</td>
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<tr>
<td>April</td>
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<tr>
<td>May</td>
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<td>June</td>
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<td>July</td>
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<td>August</td>
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<td>September</td>
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<tr>
<td>October</td>
</tr>
<tr>
<td>November</td>
</tr>
<tr>
<td>December</td>
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<tr>
<td>TOTAL</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No.2: Frequency of Medico-Legal Deaths in relation to Gender</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>
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</tbody>
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<table>
<thead>
<tr>
<th>Table No.3: Frequency of Medico-legal deaths autopsied in relation to cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cause of death</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Road traffic accident</td>
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<td>Firearm</td>
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<tr>
<td>Reserved</td>
</tr>
<tr>
<td>Hanging</td>
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<tr>
<td>Fall</td>
</tr>
<tr>
<td>Electric current</td>
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<tr>
<td>Asphyxia</td>
</tr>
<tr>
<td>Assault</td>
</tr>
<tr>
<td>Brought dead</td>
</tr>
<tr>
<td>Cut throat</td>
</tr>
<tr>
<td>Drowning</td>
</tr>
<tr>
<td>Poisoning</td>
</tr>
<tr>
<td>Stab wound</td>
</tr>
<tr>
<td>Head injury</td>
</tr>
<tr>
<td>Burns</td>
</tr>
<tr>
<td>Murder</td>
</tr>
<tr>
<td>Decomposed body</td>
</tr>
<tr>
<td>Machine injury</td>
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<tr>
<td>Custodial death</td>
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<tr>
<td>Kite thread cut</td>
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<td>Sexual assault</td>
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<td>Blast injury</td>
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<td>Marble stone injury</td>
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<td>Sharp edged injury</td>
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<td>Skeletal remains</td>
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<tr>
<td>Still birth</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
Frequency of medico-legal deaths in relation to age group showed that age group who was mainly affected was 21-30 years (29.39%) of age, followed by individuals from 31-40 years (20.29%) of age and then people from 41-50 years (17.05%) of age respectively. (Table 4).

**Table No.4: Frequency in relation to Age Group**

<table>
<thead>
<tr>
<th>Age group</th>
<th>2018</th>
<th>2019</th>
<th>2018 &amp; 2019 (n &amp; %)</th>
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<tbody>
<tr>
<td>1-10</td>
<td>28</td>
<td>19</td>
<td>47(4.91%)</td>
</tr>
<tr>
<td>11-20</td>
<td>69</td>
<td>58</td>
<td>127(13.28%)</td>
</tr>
<tr>
<td>21-30</td>
<td>146</td>
<td>135</td>
<td>281(29.39%)</td>
</tr>
<tr>
<td>31-40</td>
<td>82</td>
<td>112</td>
<td>194(20.29%)</td>
</tr>
<tr>
<td>41-50</td>
<td>73</td>
<td>90</td>
<td>163(17.05%)</td>
</tr>
<tr>
<td>51-60</td>
<td>32</td>
<td>34</td>
<td>66(6.90%)</td>
</tr>
<tr>
<td>61-70</td>
<td>15</td>
<td>29</td>
<td>44(4.60%)</td>
</tr>
<tr>
<td>71-80</td>
<td>4</td>
<td>2</td>
<td>6(0.62%)</td>
</tr>
<tr>
<td>81-90</td>
<td>1</td>
<td>0</td>
<td>1(0.10%)</td>
</tr>
<tr>
<td>91-100</td>
<td>0</td>
<td>1</td>
<td>1(0.10%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>11</td>
<td>15</td>
<td>26(2.71%)</td>
</tr>
<tr>
<td>Total</td>
<td>461</td>
<td>495</td>
<td>956(100%)</td>
</tr>
</tbody>
</table>

Previous similar studies conducted within Pakistan showed a major fraction of deaths due to firearms. A two years study from Bhawalpur showed that firearms accounted for 44.1%, of the total cause of death.17 A Study from Larkana reported firearms to account for 46% of the total causes during 1998.18 In Nigeria at Kano Teaching Hospital, 12.5% fatality was reported as a result of firearm injuries.19 Contradictory to previous studies in Pakistan, in our study road traffic accidents outnumber all other causes of medico-legal deaths autopsied. This finding favours the improvement in the law and order of the Karachi city. Nearly 1.2 million road traffic accidents death occur globally each year as reported by WHO.20 In Assam, India from January 1999 to December 2003, 23.84% medico-legal autopsies were of road traffic accident victims.21 Causes of increasing road traffic accidents are multiple which include cell phone use while driving, driving under influence of drug of addiction, over speeding, rough uneven roads and not obeying the traffic rules. Majority of the medico-legal deaths in this study belonged to a young age group that falls between 21-30 years (29.39%) followed by 31-40 years (20.29%) of age. Mirza et al in a study of medico-legal deaths declared 47.3% of the deaths from the age group of 19 to 32 years. Mostly 88.8% bodies were of male with male to female ratio was 9:1.13 However, in our study 88.9% bodies autopsied were of male with male to female ratio of 8:1.

**CONCLUSION**

A Road traffic accident surpasses/outnumber the other causes of medico-legal deaths autopsied. Measures should be taken to improve the infrastructure of the city and conditions of the roads. There was a male dominancy pattern seen in the study. Majority of the victims belonged to a young age group. Due to the improvement in the law and order of the city, we have seen that firearm deaths have declined and the overall frequency of medico-legal deaths autopsied has decreased.
Author’s Contribution:
Concept & Design of Study: Roohi Ehsan
Drafting: Wasiq Ahmed, M. Faiz
Data Analysis: Wasiq Ahmed, Iqbal Ahmed
Revisiting Critically: Roohi Ehsan, M. Faiz
Final Approval of version: Roohi Ehsan

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

REFERENCES

Analysis of the E-Learning Educational Atmosphere During Covid 19 Pandemic: Empirical Evidence from Medical Universities of Urban Pakistan

Sahar Mubeen¹, Asma Aijaz¹, Hina Mubeen², Hira Ahmed¹, Shazia Fahmi¹ and Talat Samreen¹

ABSTRACT

Objective: To analyze the level of satisfaction of medical students towards the existing e-learning educational environment and to determine its effectiveness enhancing learning outcomes.

Study Design: Descriptive Cross-sectional study

Place and Duration of Study: This study was conducted at the Online survey was conducted using google forms to collect data from MBBS and BDS students enrolled in various public medical universities of Karachi and who have attended online classes during COVID-19 pandemic from April to September 2020.

Materials and Methods: Structured questionnaire using a 5-point Likert scale was adopted for the study with reliable Cronbach’s alpha coefficient (0.85). Non-probability purposive sampling technique was used for selecting the participants. The study was approved by the Institutional Review Board of Dow University of Health Sciences.

Results: Significant p-value concluded that medical students are generally satisfied with e-learning educational atmosphere during COVID-19 pandemic in Pakistan. According to the survey, students of First and Second Professional year were highly satisfied (83%) with the e-learning atmosphere, whereas students of Third and Fourth year had mixed opinion. However, 60% of final year students were dissatisfied with the existing e-learning educational atmosphere.

Conclusion: The survey revealed positive attitude of medical students towards e-learning. However, clinical exposure of students is compromised which is a major challenge. Depending on the requirement of specific courses, adopting a hybrid approach involving some combination of e-learning and practical exposure seems more effective.

Key Words: Medical education, e-learning, COVID-19, distance learning, universities, higher education

INTRODUCTION

The rapidly spreading COVID-19 pandemic has attributed several changes not only on the lives of a common man but it has impacted the whole world. The novel Corona virus (COVID-19) emerged as a fatal lower respiratory tract infection in China in December 2019 and in no time i.e. March 2020, it was declared a pandemic by World Health Organization. Pakistan, as one of the developing countries, was also seriously impacted by the fatal infection¹-⁴.

Imports, exports, businesses, hospitals, schools, universities, all just came to a halt. The education sector of Pakistan is also seriously affected by the pandemic; worth to mention that public sector medical universities have severely suffered as not only they lack the required resources but the nature of the study mandates practical exposure. This emerged as a humongous challenge for medical institutions of Pakistan. The situation was not only novel but it was accompanied by lot of uncertainties. Online sessions were somehow conducted without any prior experience or training but the practical exposure of medical students was completely halted. The universities weren’t prepared to handle this challenge and there was significant reluctance among students and faculty to adopt e-learning strategy. Though e-learning is already in practice in developed countries where studies have been done on its readiness and effectiveness. They are of the view that e-learning is a useful supplement to conventional lecture-based teaching even for the medical curriculum⁵-⁹. Most medical schools around the globe have rapidly transformed their curricula from traditional face to face learning to online system of...
teaching recently\textsuperscript{10–11}. But this educational transition is a challenge for developing countries like Pakistan. E-learning is gaining a lot of attention in Pakistan with respect to its integration into educational system along with significant increase in the usage of cell phone and tablets in Pakistan\textsuperscript{12}. The major factors which hinder the adoption of e-learning include non-availability of proper technological infrastructure, restricted financial resources, limited assessment approaches and lack of required pedagogical skills required for teachers to deliver the content electronically\textsuperscript{13}. The advantages of e-learning include low delivery cost (including web server cost and technical support) than those for classroom equipment with additional plus point of saving teacher’s and student’s travel time. Other advantages include ease of access and flexibility, portability, improved student teacher contact and increased discussion with peers. The disadvantages include feeling of isolation, being unable to clarify doubts with a tutor and lack of in depth group discussions\textsuperscript{14}. Keeping in view the numerous advantages of e-learning, all possible efforts should be directed toward making e-learning meaningful and effective, both at institutional and governmental level which would surely enhance students’ learning and skills.

One of the most important determinants of successful and effective e-learning educational atmosphere is to analyze the level of student satisfaction with the system\textsuperscript{15}. The pandemic has forced a shift from face to face classroom lectures, practical and tutorials to challenging digital mode of learning\textsuperscript{16}. Medical students are getting no exposure to clinical side and hence, nil bedside experience causing inimical effects on their exam performance. It is a serious legitimate concern of medical education providers and students who are in the process of correlating subjective knowledge with clinical skills.

COVID 19 has made e-learning a new normal for the academia, it is crucial to take necessary steps to ensure uninterrupted and optimal learning of medical students in a congenial learning environment. Medical students are objectively trained to be educated physicians having broad knowledge of science and are equipped with the proper understanding of laboratory methods and practical knowledge of bedside medicine. But, unfortunately, the global COVID emergency has brutally disrupted the objectives of the professional medical education putting medical students at stake. Therefore, the current bewildered situation demands prompt attention and effective steps to be taken by the authorities to design the principles of digital learning keeping in view students’ attention and motivation. It is the dire need of time to implement e-learning for all the medical universities and colleges, but it’s equally important to continuously assess and evaluate this new online teaching system to timely diagnose the loop holes of the system making it efficient. It is the high time to assess their satisfaction towards this virtual system of medical education in order to improve their learning to keep pace with the advancing field of medicine. The main aim of the survey is to critically assess the level of satisfaction of medical students while going through e-learning educational atmosphere during COVID 19 pandemic and to determine its effectiveness so that timely measures could be taken to improve student’s knowledge, learning and to keep them motivated in these unprecedented times. The survey could also identify deficiencies in the system timely and help us to keep pace with global changes in knowledge acquisition and management. It will also provide the investors and policy makers with useful information in creation of some lasting education policy to vanquish the challenges faced by the students during the times of such inevitable situation or even when they are at home for their normal semester break or during a pandemic.

MATERIALS AND METHODS

This descriptive survey included students of MBBS and BDS (n=400) studying in various public sector medical universities and colleges of Karachi registered with Pakistan Medical Commission (PMC) who are taking online classes of different medical subjects on Zoom, Google classrooms or any other e-learning platforms during the COVID-19 pandemic.

The sample size was determined using estimation technique. The sample size is 384 at 95% confidence interval and ± 5% margin of error\textsuperscript{16–17}. Sekaran (2005) and Zikmund (2013) also suggest a sample size of 384 when the unit of analysis is an individual. Hence, the sample size for the questionnaire survey was 400 [18].

An online questionnaire survey was conducted using google forms to collect the data from the respondents since the outbreak and lockdown in the city did not allow physical contact. Particularly, online survey was conducted for data collection to comply with the social distancing policy outlined by World Health Organization (WHO) and the government of Pakistan for limiting the spread of corona virus. The scale was adopted from a previous study conducted on the participants of master programs of ‘E-Learning Planning’, ‘Medical Education’, ‘Educational Technology’, and ‘Family Medicine Management’\textsuperscript{19}. Considering the contextual requirements, it was further validated by the field experts. The questionnaire was administered by sharing link of google form via email, WhatsApp, Facebook and other social media platforms to get the responses from the target group. The purpose of the study was clearly explained to the participants and confidentiality of the data was assured. A five point Likert scale ranging from “Strongly disagree” (SD), “Disagree” (D), “Neutral” (N), “Agree” (A) to “Strongly agree” (SA) was used to measure the level of agreement or disagreement of respondents to a given...
statement. It is one of the most widely used techniques for descriptive studies to collect data from large sample, less time consuming, easy to compute and analyze findings and easily understandable for the respondents. Reliability statistics was assessed using Cronbach alpha (0.852). A coefficient value of 0.7 and above is considered good. Further, all items in the scale also had reliability above 0.8 indicating a good reliable scale as shown in Table 1. T-test was performed for hypothesis testing. Correlations and cross tabulation were also performed to see the difference.

RESULTS

Four hundred (n=400) students of MBBS (88%) and BDS (12%) studying in registered public sector medical universities and colleges of Karachi registered with Pakistan Medical Commission (PMC) responded to online survey. All students (72% females and 28% males) were taking online classes during COVID pandemic. The data shows that not only vast majority of females are studying in public sector medical colleges and universities of Karachi but are also actively participating in e-learning as well.

The analysis of the survey revealed that Zoom is the most popular tool used for e-learning in comparison to google classroom (27%) and other tools (2%). Furthermore, it was found that 67% students were enrolled in First Professional year, 21.8% in Second Professional, 4.5% in Third Professional, 1.8% in Fourth Professional and, 5% were enrolled in Final professional year.

Table No.1: Statistical Item Analysis of the Questionnaire Survey On Satisfaction Level of Medical Students with E-Learning Educational Atmosphere During Covid-19

<table>
<thead>
<tr>
<th>Item</th>
<th>Scale Mean if Item Deleted</th>
<th>Scale Variance if Item Deleted</th>
<th>Corrected Item-Total Correlation</th>
<th>Squared Multiple Correlation</th>
<th>Cronbach's Alpha if Item Deleted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>33.00</td>
<td>50.877</td>
<td>0.676</td>
<td>0.548</td>
<td>0.830</td>
</tr>
<tr>
<td>Q2</td>
<td>33.09</td>
<td>52.521</td>
<td>0.576</td>
<td>0.361</td>
<td>0.837</td>
</tr>
<tr>
<td>Q3</td>
<td>33.14</td>
<td>53.786</td>
<td>0.550</td>
<td>0.370</td>
<td>0.839</td>
</tr>
<tr>
<td>Q4</td>
<td>33.67</td>
<td>53.009</td>
<td>0.574</td>
<td>0.443</td>
<td>0.838</td>
</tr>
<tr>
<td>Q5</td>
<td>32.99</td>
<td>54.033</td>
<td>0.463</td>
<td>0.294</td>
<td>0.844</td>
</tr>
<tr>
<td>Q6</td>
<td>33.20</td>
<td>50.685</td>
<td>0.645</td>
<td>0.543</td>
<td>0.832</td>
</tr>
<tr>
<td>Q7</td>
<td>34.13</td>
<td>59.338</td>
<td>0.096</td>
<td>0.148</td>
<td>0.867</td>
</tr>
<tr>
<td>Q8</td>
<td>33.07</td>
<td>51.815</td>
<td>0.588</td>
<td>0.753</td>
<td>0.836</td>
</tr>
<tr>
<td>Q9</td>
<td>33.07</td>
<td>51.010</td>
<td>0.641</td>
<td>0.779</td>
<td>0.832</td>
</tr>
<tr>
<td>Q10</td>
<td>32.88</td>
<td>54.181</td>
<td>0.473</td>
<td>0.375</td>
<td>0.844</td>
</tr>
<tr>
<td>Q11</td>
<td>32.70</td>
<td>53.645</td>
<td>0.575</td>
<td>0.444</td>
<td>0.838</td>
</tr>
<tr>
<td>Q12</td>
<td>33.99</td>
<td>55.719</td>
<td>0.335</td>
<td>0.260</td>
<td>0.853</td>
</tr>
<tr>
<td>Q13</td>
<td>33.13</td>
<td>53.415</td>
<td>0.468</td>
<td>0.262</td>
<td>0.844</td>
</tr>
</tbody>
</table>

Table 2: One Sample T-Test

<table>
<thead>
<tr>
<th>Test Value</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
<th>Mean Difference</th>
<th>95% Confidence Interval of the Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-learning Atmosphere</td>
<td>25.428</td>
<td>399</td>
<td>.000</td>
<td>.76942</td>
<td>.7099</td>
</tr>
</tbody>
</table>
t(399) = 25.428, p-value .000

As per results indicated in Graph 1, students of First and Second Professional year seem highly satisfied with the e-learning atmosphere whereas students of Third and Fourth Professional year seems to have mixed opinion as shown in Graph 1. As for students of Final professional year, 60% of the students were dissatisfied with the existing e-learning atmosphere according to the findings of this study. This indicates that early year medical students are satisfied and motivated by this E-learning environment but dissatisfaction of the students after that period is possibly due to obstruction of clinical training and bedside exposure that is usually practiced from third professional year onwards.

![Figure No.1: Crosstab Analyzing Satisfaction Level in Medical Professional Years During Covid-19](image)
It is also observed that majority of the medical students (n=349) attended online classes from urban areas while a smaller number of students participated from urban areas (n=25) and outside Pakistan (n=26). According to the results of t-test indicated in Table 2, significant p-value concludes that medical students are satisfied with e-learning implemented because of the pandemic.

DISCUSSION

The COVID-19 pandemic has pushed academic institutions around the globe to create a digital learning environment yet poised a big and unique global challenge for academia peculiarly medical colleges and universities. The study findings would help stakeholders to accordingly take timely measures creating a conducive e-learning atmosphere for the medical students. Overall, majority of the students showed a positive attitude towards the e-learning and were satisfied with online teaching strategy currently adopted. The findings are similar to a previous study conducted on medical students of Iran who strongly agreed the effective role of e-learning in medical education. They agreed with the view e-learning enhances their learning. The most cited advantage of e-learning is the learning delivery as updating electronic content is easier and faster than updating textbooks. Though an acceptable level of satisfaction was found among medical students but their motivation for distance e-learning is at a bit lower scale which can be correlated to their internet self-efficacy.

According to survey, the first and second professional year students are highly satisfied while final year students are dissatisfied with e-learning atmosphere. The reason being their clinical training and patient exposure is adversely affected by this pandemic. These trainings range from clinical practice and ward rounds to on-the-job training in diagnostic skills and inter professional communication.

The limitation of the study was access to medical students due to pandemic. Since study was conducted on medical students of public sector universities of Karachi, results cannot be generalized to the students of private medical institutions or public medical universities in other cities of Pakistan. Since COVID19 pandemic has created a unique digital learning environment, there is scarcity of published empirical studies regarding satisfaction of medical students towards e-learning atmosphere in higher educational institutions and its effectiveness specially in a developing country like Pakistan. Hence, the current study is unique in this aspect. There is a dire need to conduct further research in this area to enhance the understanding of dynamics of e-learning atmosphere for medical institutions in Pakistan.

CONCLUSION

The survey concluded satisfaction of medical students towards e-learning environment. It suggested that depending on the requirement of specific courses and professional year of education, adopting a hybrid approach involving some combination of e-learning as well as practical exposure seems more feasible for effectively imparting medical education.

Author’s Contribution:
Concept & Design of Study: Sahar Mubeen, Asma Aijaz
Drafting: Asma Aijaz, Shazia Fahmi, Hira Ahmed
Data Analysis: Hina Mubeen, Talat Samreen
Revisiting Critically: Sahar Mubeen, Asma Aijaz
Final Approval of version: Sahar Mubeen

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

REFERENCES

Efficacy of Febuxostat Compared to Allopurinol in reducing Hyperuricemia

Akram Munir and Muhammad Akbar

ABSTRACT

Objective: Evaluating the efficacy of Febuxostat in reducing hyperuricemia compared to Allopurinol in adult male.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine, Isra University Hospital Hyderabad January 2019 – February 2020.

Materials and Methods: A sample of 200 adult healthy male diagnosed cases of systemic hypertension was selected according to the inclusion and exclusion criteria. Subjects were examined physically. Volunteers were asked for blood sampling. Serum Uric acid was estimated at baseline and after 12 weeks of febuxostat and allopurinol therapy. Data was analyzed in SPSS v 21.0 (IBM, Incor, USA) at 95% confidence interval (P ≤ 0.05).

Results: Serum uric acid at baseline was 8.14±1.4 mg/dl. After 12 weeks of Febuxostat and Allopurinol therapy, it was reduced to 2.91±0.75 and 4.2±0.55 mg/dl respectively (F=745.1, P=0.0001). Febuxostat reduced serum uric acid by 64% compared to 48.4% by the Allopurinol

Conclusion: Serum uric acid was reduced by both febuxostat and allopurinol, however, the former was more effective in alleviating hyperuricemia.

Key Words: Uric acid, Febuxostat, Allopurinol, Adult Male


INTRODUCTION

Hyperuricemia is a common problem of current era characterized by raised blood uric acid (UA) levels. Hyperuricemia is a disorder of purine metabolism. UA induces joint inflammation causing gout and has been associated with kidney disease, systemic hypertension, metabolic syndrome, etc. Kidneys are commonly affected by raised uric acid levels. Urate renal stones and interstitial nephritis are caused by uric acid. Hyperuricemia is observed commonly in the middle age adults and elderly persons. United States reported incidence of hyperuricemia approximates 18%.2 Hyperuricemia may be primary – caused by genetic enzyme defects and secondary – caused by dietary factors however, exact etiology and pathogenesis is not clear. Blood leukemias and lymphomas often induced hyperuricemia. Chronic diseases such as diabetes mellitus (DM), chronic kidney diseases (CKD) and atherosclerosis is often accompanied by hyperuricemia.3 During early stages, hyperuricemia shows no obvious symptoms, however, it may develop extremely fast. It may induce threat to patient health in comorbid conditions for example CKD.4 It is concluded that hyperuricemia once complicated, then chances of mortality show linear increase.5 Previously, most commonly used drug was the allopurinol and still used in clinical practice.6 Allopurinol is xanthine inhibitor of purine analogue, traditionally used for hyperuricemia with established clinical efficacy.7,8 Major drawback of allopurinol is inhibition of purine metabolism resulting in serious side effects as other active enzymes involved in purine metabolism are negatively affected.7,8 In cases of kidney disease, its toxic side effects have been perplexed.9 Another drug of new class is the febuxostat that is now widely used in clinical practice and has replaced the allopurinol. Febuxostat is a non-purine xanthine oxidase inhibitors hence adverse drug reactions are less compared to allopurinol. It is strong inhibitor of uric acid synthesis with little side effects.10 Febuxostat shows excellent therapeutic effect on hyperuricemia.11 Exact mechanisms of Febuxostat is not well elucidated and there is little research compared to allopurinol. The present study was conducted to analyze serum uric acid in hyperuricemia patients before and after febuxostat and allopurinol therapy and results were compared among healthy adult male population.

MATERIALS AND METHODS

The present observational cross sectional study was conducted at the Department of Medicine, Isra University Hospital Hyderabad January 2019 –
February 2020. A sample of 200 adult males diagnosed cases of systemic hypertension was selected. Sample size was estimated by Rao-software. Both in – and out of patient department subjects were included in the study. Study protocol observed strict inclusion and exclusion criteria. Inclusion criteria were; adult male of age 40-60 years. Subjects suffering from secondary systemic hypertension, CKD, CLD, DM, Ischemic coronary artery disease (CAD) and alcoholics were excluded from study protocol. Subjects taking ACE-Inhibitors, thiazide and loop diuretics were also excluded. Study was approved by ERC. Volunteer adult male of fulfilling inclusion criteria were asked for physical examination. Age, body weight, blood pressure was noted in a pre – structured proforma. Systemic hypertension was as per criteria of JNC-VIII. BP was measured by a mercury sphygmomanometer. Volunteers were requested for blood sampling that was taken from ante cubital fossa after area was cleaned with spirit swab. A tourniquet was tightened above ante cubital fossa. Blood was drawn from prominent vein in a 5 ml Disposable syringe. Blood was centrifuged for 15 minutes (x3000 rpm) for separating sera that were taken into sterilized Eppendorf tubes. Samples were stored at –20°C for analysis. Written participant consent was taken. Proforma were kept in lockers to maintain confidentiality of personal data. Serum uric acid and creatinine were estimated by colometric technique. All values were saved in proforma and typed in Microsoft Excel sheet. Data was analyzed on statistical software – SPSS v 21.0 (IBM, Incor, USA). Paired sample t – test analyzed the numerical data. Data was presented as mean +/- standard deviation (SD). Graphs were designed on Microsoft Excel sheet. % decrease in serum uric acid was calculated manually and graphed in Microsoft Excel sheet. Significance level of SPSS analysis was 95% CI (P ≤ 0.05).

RESULTS

General information of study subjects is shown in table 1. Serum uric acid at baseline was 8.14±1.4 mg/dl. After 12 weeks febuxostat and allopurinol therapy, it was decreased to 2.91±0.75 and 4.2±0.55 mg/dl respectively (F=745.1, P=0.0001). Table 2 and graph 1 show the serum uric acid levels at baseline and after febuxostat and allopurinol therapy. Febuxostat decreased serum uric acid by 64% compared to 48.4% by the Allopurinol as in line graph 2.

The present is the first study reporting on the efficacy of febuxostat and allopurinol in reducing serum uric acid level in adult male of systemic hypertension. Present study found 64% reduction of uric acid in febuxostat group compared to 48.4% in allopurinol group. Serum uric acid at baseline was 8.14±1.4 mg/dl. After 12 weeks febuxostat and allopurinol therapy, it was decreased to 2.91±0.75 and 4.2±0.55 mg/dl respectively. The findings are supported by previous studies. Febuxostat is a new class of non – purine drug that selectively inhibits xanthine oxidase (XO). Febuxostat was found superior in alleviating hyperuricemia in the present study. Now the Febuxostat is widely used drug in the country but the comparative studies with allopurinol are limited. The present study is worth in terms of inclusion and exclusion criteria for selecting the study protocol to be included. Results of present cross sectional study show Febuxostat had superior clinical efficacy compared to allopurinol (table – 1). Allopurinol was also effective in reducing uric acid level compared to baseline but less effective than Febuxostat. The finding is of utmost clinical importance in practice. Febuxostat had more effective clinical efficacy compared to allopurinol. The finding is consistent to a previous study that showed similar results. Febuxostat was quite safe as regards adverse drug reactions that are similar to previous studies. Renal function testing shows no significant difference in serum creatinine in two groups that is consistent with
Uric acid was improved and serum creatinine was found within normal limits in both drug groups. Febuxostat is suggested to reduce the reactive oxygen species (ROS) and inhibits XO, both mechanisms help in alleviating the hyperuricemia. ROS scavenging activity provides vascular protection. It has been speculated that the allopurinol may be toxic to the liver and kidney. Allergic reactions are frequent with allopurinol and were not observed with Febuxostat. XO is inhibited by the Febuxostat effectively compared to Allopurinol. Febuxostat is safe as it has no inhibitory effect on other enzyme systems of purine metabolism hence least side effects are complained it. Febuxostat is excreted through both renal and hepatic routes hence renal toxicity is minimized. Febuxostat has safe renal therapeutic effect for uric acid compared to Allopurinol because of its urate transport acceleration in the proximal renal tubule (PRT). Hence large volumes of uric acids are excreted in urine and are prevented from being deposited in the renal interstitium, this improves the clinical efficacy. A previous study reported Febuxostat does not affect the renal drug kinetic parameters. Febuxostat has an excellent bioavailability of 80% and has no significant limit on the drug dosage. Febuxostat has low use restriction and utilization rate is high compared to Allopurinol. In the present study, clinical value of Febuxostat was demonstrated in comparison to Allopurinol that is a known uric acid lowering agent of purine analogue. Allopurinol use is clinically unfavorable due to its adverse drug reactions. Evidence based findings of present study supported by published literature shows Febuxostat is an excellent, clinically effective drug for alleviating hyperuricemia in systemic hypertension patients without renal toxicity. However, further clinical studies are recommended as the sample size of present study was small enough and findings are not generalizable to other settings.

CONCLUSION

In present study, the Febuxostat reduced serum uric acid by 64% compared to 48.4% by the Allopurinol. Serum uric acid was reduced by both febuxostat and allopurinol however the former was more effective in alleviating hyperuricemia.

**Author’s Contribution:**

<table>
<thead>
<tr>
<th>Role</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concept &amp; Design of Study</td>
<td>Akram Munir</td>
</tr>
<tr>
<td>Drafting</td>
<td>Muhammad Akbar</td>
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<td>Data Analysis</td>
<td>Muhammad Akbar</td>
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<td>Revisiting Critically</td>
<td>Akram Munir,</td>
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<td>Muhammad Akbar</td>
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<tr>
<td>Final Approval of version</td>
<td>Akram Munir</td>
</tr>
</tbody>
</table>

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

**REFERENCES**


Frequency of Chronic Kidney Disease in Patients with Metabolic Syndrome

Syed Saif-ur-Rehman¹, Hidayat-Ul-Haq², Adnan Ghafoor³, Jahanzeb Maqsood¹, Abida Mateen Ansari¹ and Muhammad Wajad Munir¹

ABSTRACT

Objective: To determine the frequency of chronic kidney disease in patients with metabolic syndrome.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of General Medicine, Fauji Foundation Hospital, Rawalpindi for six months from May, 2017 to November, 2017.

Materials and Methods: A total of one hundred and thirty-four (n=134) clinically diagnosed cases of metabolic syndrome of either gender between age 18 to 70 years were enrolled in the study. Glomerular filtration rate was estimated in each patient and frequency of Chronic kidney disease was determined.

Results: Out of one hundred and thirty-four (n=134), 18.7% (n=25) patients were diagnosed with chronic kidney disease, which was significantly higher in patients with longer duration of Metabolic Syndrome (P<0.05). No significant difference was observed when results were stratified with respect to age and gender (P>0.5).

Conclusion: Significant percentage (18.7%) of patients with metabolic syndrome had chronic kidney disease which was significantly higher in patients with longer duration of disease.

Key Words: Chronic kidney disease, Metabolic syndrome, Glomerular filtration rate, Duration, Frequency

INTRODUCTION

Metabolic syndrome (MetS), previously called “syndrome X” is defined as a cluster of components associated with excessive adiposity due to over nutrition and sedentary life style.¹ These components are abdominal obesity, insulin resistance, dyslipidemia and increased blood pressure. CVD risk is increased by 2 times, whereas type 2 diabetes mellitus (DM) is increased by 5 times in MetS.² The prevalence of metabolic syndrome in Pakistani general population is well studied. According to different definitions it is reported to be from 18% to 46%.¹ Chronic kidney disease (CKD) is increasing being recognized as a major public health issue worldwide.³,⁶ Recent researches noted that the population prevalence of CKD has exceeded 10%, more than 50% of whom were in high-risk sub-populations.¹ Furthermore, mortality from kidney disease has increased by 83% since 1990. The adverse consequences associated with CKD including kidney failure, accelerated cardiovascular disease (CVD), and premature mortality have shown to have greater socioeconomic impact in low- and middle-income countries like Pakistan.⁷,⁸ The overall prevalence of chronic kidney disease in Pakistan ranges from 8% to 25%.⁸ Studies show that patients with MetS have a 2.5-fold higher risk of developing CKD.² A meta-analysis of eleven studies with 30146 subjects reported that MetS was associated with development of CKD (defined as eGFR < 60 mL/min per 1.73 m²), with odds ratio (OR) 1.55 (95%CI: 1.34-1.80). In a recent study authors investigated the association between metabolic syndrome and CKD in a 10-year population-based longitudinal study. They reported 14.7% of patients with metabolic syndrome developed CKD during the follow up period.³ The gathered data will help in better understanding of presence of CKD in metabolic syndrome and will help in identifying patients with metabolic syndrome who are at higher risk of developing CKD. This will eventually enable the physicians to implement more stringent monitoring to prevent the CKD in these patients.

MATERIALS AND METHODS

This Cross-sectional study was conducted at Department of General Medicine, Fauji Foundation Hospital, Rawalpindi for six months from 10th May, 2017 to 10th November, 2017 after approval from
hospital ethical committee. The sample size was calculated (n=134) with anticipated population proportion of 14.7%, significance Level of 5% and with precision of 6%. Non probability purposive sampling technique was employed. Clinically diagnosed cases of metabolic syndrome, with age 18 to 70 years of both genders are included in the study. Patients with history of hyperlipidemia secondary to nephrotic syndrome, hypothyroidism, and Cushing syndrome, on steroid therapy, Dialysis dependent diabetic CKD patients and patients who were not willing to participate in the study were excluded.

Patients from outpatient department of FFH Rawalpindi who fulfilled criteria was included in the study. Detailed history regarding the illness was obtained from each patient. Complete clinical examination was performed by the trainee researcher including measurement of blood pressure and abdominal obesity. Specific laboratory tests were performed including fasting blood glucose levels, lipid profile and renal function tests from the hospital laboratory. Estimated GFR was calculated as per operational definition in all these patients. All this information recorded on a preset Performa.

Data was entered on computer software SPSS version 20. Quantitative variables like age, duration of MS and GFR were expressed as mean ± SD. Frequencies and percentages were calculated for qualitative variables like gender, residence and presence of CKD. Effect modifiers like age, gender and duration of MS was controlled by stratification. Post stratification chi-square test was applied and P-value ≤ 0.05 was considered as significant.

RESULTS

A total of one hundred and thirty-four (n=134) clinically diagnosed cases of metabolic syndrome of either gender between age 18 to 70 years were enrolled in the study. GFR was estimated in each patient and frequency of CKD was determined. Distribution of gender, urban or rural distribution (years) and duration of MS (years) in the study population was presented in table 1.

Mean GFR (ml/min) in the study population was tabulated as shown in table 1. Out of one hundred and thirty-four (n=134), 18.7% (n=25) patients were diagnosed with chronic kidney disease. Results are shown in table 1.

No significant difference was observed when results were stratified with respect to age and gender (P>0.05 in both cases). Frequency of CKD was significantly higher in patients who had duration of Ms more than 5 years when compared to ones having less than 5 years duration (P=0.01). Results were tabulated in table 2.

| Table No.1: Demographic and clinical profile of the study Population (n=134) |
|--------------------------|--------------------------|--------------------------|
| Variables               | Frequency               | Percentage               |
| Gender                  |                          |                          |
| Males                   | 82                       | 61.2%                    |
| Females                 | 52                       | 38.8%                    |
| Residence               |                          |                          |
| Urban                   | 62                       | 46.3%                    |
| Rural                   | 72                       | 53.7%                    |
| Mean GFR                |                          |                          |
| Male                    | 89.2                     | 21.4%                    |
| Female                  | 85.8                     | 20.9%                    |
| Total                   | 87.9                     | 21.2%                    |
| Chronic kidney disease  |                          |                          |
| Present                 | 25                       | 18.67%                   |
| Absent                  | 109                      | 81.3%                    |
| Total                   | 139                      | 100.0%                   |
| Duration of metabolic syndrome (years) |            |                          |
| Gender                  | Age (years)             | Duration of ms (years)  |
| Male                    | 52.5 ± 15.8              | 2.9 ± 2.2                |
| Female                  | 48.1 ± 14.4              | 2.6 ± 2.5                |
| Total                   |                          |                          |
| Male                    | 52.5 ± 15.8              | 2.9 ± 2.2                |
| Female                  | 48.1 ± 14.4              | 2.6 ± 2.5                |
| Total                   |                          |                          |

| Table No.2: Age, gender and duration of metabolic syndrome based stratification of study population (n=134) |
|---------------------------------------------------------------------------------------------|--------------------------|
| Age category | Ckd | Present | Absent | Total | P-value chi-square |
| 18-40 years | 25.0% | 9      | 27     | 36     | 0.253              |
| 41-70 years | 16.3% | 16     | 82     | 98     |                    |
| Total       | 25.0% | 25     | 109    | 134    |                    |
| Total       | 18.7% | 81.3%  | 100.0% |        |                    |
| Males       | 14.1% | 14     | 68     | 82     | 0.555              |
| Females     | 11.7% | 11     | 41     | 52     |                    |
| Total       | 21.2% | 21.2%  | 78.8%  | 100.0% |                    |
| Total       | 18.7% | 81.3%  | 100.0% |        |                    |
| Metabolic syndrome < 5 years | 8.5% | 9      | 97     | 106    | 0.001              |
| Metabolic syndrome > 5 years | 57.1% | 57.1%  | 42.9%  | 100.0% |                    |
| Total       | 18.7% | 81.3%  | 100.0% |        |                    |
DISCUSSION

Several studies reported that metabolic syndrome was associated with development of chronic kidney disease. Present study was designed to study this association in local population. Our results showed that Out of one hundred and thirty-four (n=134), 18.7% (n=25) patients were diagnosed with chronic kidney disease as per our operational definition, which was significantly higher in patients with longer duration of MS (P<0.05). No significant difference was observed when results were stratified with respect to age and gender (P>0.5). These results are similar to data in Korean Genome Epidemiology Study. Huh JH et al analyzed 10,030 subjects who had 10-year of follow-up period. CKD developed in 893 subjects (14.7%). Compared to subjects without MS, the odds ratio (OR; 95% confidence interval, CI) of incident CKD in those with MS was 1.38 (1.16-1.64) after controlling for confounding factors.

Thomas G et al aimed to systematically review the association between MetS, its components, and development of microalbuminuria or proteinuria and CKD. Pooled results showed that MetS was significantly associated with the development of eGFR <60 ml/min per 1.73 m² (odds ratio, 1.55; 95% CI, 1.34, 1.80). The strength of this association seemed to increase as the number of components of MetS increased (trend P value = 0.02).

There are several other studies reported risk estimates for the development of eGFR <60 ml/min per 1.73 m² in patients with MetS. They further examined the associations of individual components of MetS and the risk for eGFR <60 ml/min per 1.73 m². All individual components of MetS showed a positive association with the development of eGFR <60 ml/min per 1.73 m². The strength of association between MetS and the development of eGFR <60 ml/min per 1.73 m² seems to increase as the number of components increased from 1 to 5 (trend P-value 0.02). Although patients with one component had no significant increase in the odds for development of eGFR <60 ml/min per 1.73 m², patients with all five components of MetS had an OR of 1.96 (95% CI 1.71, 2.24) for development of eGFR <60 ml/min per 1.73 m².

Singh AK, et al in their systematic review discusses the epidemiology, pathology and potential mechanisms for the relationship of MetS with CKD. They found that studies showed patients with MetS have a 2.5-fold higher risk of developing CKD. Renal dysfunction becomes apparent long before the appearance of hypertension or diabetes in MetS. More studies are needed to precisely elucidate the mechanisms that might lead upstream factors such as insulin resistance, hypertension, dyslipidemia and inflammation to cause renal fibrosis.

CONCLUSION

Significant percentage (18.7%) of patients with metabolic syndrome had chronic kidney disease which was significantly higher in patients with longer duration of disease.

Author’s Contribution:
Concept & Design of Study: Syed Saif-ur-Rehman Hidayat-ul-Haq, Adnan Ghafoor
Data Analysis: Jahanzeb Maqsood, Abida Mateen Ansari and Muhammad Wajad Munir
Revisiting Critically: Syed Saif-ur-Rehman, Hidayat-ul-Haq
Final Approval of version: Syed Saif-ur-Rehman

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REFERENCES
INTRODUCTION

Nephrolithiasis\(^1\) also called kidney stone disease is a worldwide medical issue. It is renamed as ureterolithiasis when the stone stuck in the distal ureter due to gradually increased size. Consequently, there is acute pain beside urine obstruction. Unmanaged recurrent multiple stones can lead to fatal\(^2\) consequences. Unfortunately, the disease is prevalent in Pakistan on account of un healthy life style and genetic tendency.\(^3\)

Hormonal or metabolic abnormalities make the males more prone to the LUS (lower ureteral stone) than females.\(^2,5\) Similarly, risk of the disease is high in early 30’s. The pain develops when unblocked \(\alpha_1\) adrenergic receptors of the ureter attempt to push forward the stuck stone from the inflamed region by peristalsis.\(^2\) Finding vitals satisfactory, medical expulsive therapy (MET)\(^5\) is advised for 5-9mm sized LUS. The noninvasive MET deserves prompt action as any delay increases the size of the stone beyond 9mm where costly surgical intervention becomes inevitable.\(^5,6\) Tamsulosin is the choice of urologists\(^7\) as it not only antagonists the \(\alpha_1\) adrenergic receptors to reverse the mechanism of forced peristalsis but also manages the spasm for early stone expulsion. Whereas, inflammation and pain can be addressed using Danzen DS- a serratiopeptidase\(^8\) with tamsulosin in combination therapy. Similarly, it saves from additional analgesic while discourages adverse effects like tadalafl.\(^1,5\) Like, in combination antibiotics,\(^9\) there is no possibility of drug resistance in the combination MET.

The online published literature is devoid of any evidence on use of Danzen DS-added tamsulosin for expulsion of the LUS. Perceiving its potential, present work was planned to know the efficacy of the combination therapy for the expulsion of the symptomatic LUS. The findings will support the researchers to test it before recommending for
clinicians in countries like Pakistan where MET is the only readily accessible decision for both, professionals and patients.

MATERIALS AND METHODS

The present descriptive cross-sectional study was conducted between June 2016 and February 2017 at outpatient Deptt. of Urology, Sheikh Zayed Hospital, Rahim Yar Khan, Pakistan subsequent to approval from the hospital ethics committee. Sample size was seen as 84 using \( P = 0.32 \) (derived from a pilot study on Danzen DS-added tamsulosin for expulsion of 5-9mm sized LUS) in a formula \( Z^2 = (1-P)/d^2 \). All male/female patients (aged = 19-40 years) with a 5-9mm sized LUS (affirmed by ultrasonography i.e. USG abdomen) and reporting colic pain for less than one month were registered using consecutive sampling technique. However, patients with hydrenephrosis (Grade 3 or 4), urinary tract infection, hematuria, previous experience of surgical/ nonsurgical removal of kidney stone(s), single kidney, or elevated serum creatinine (>2.0 mg/dl) were excluded. Finally, those patients were recruited who gave written participation consent.

Sociodemographic information (like age and sex), and clinical manifestations like duration since first episode of pain were documented. Similarly, severity level of the pain on presentation in the study setting was gauged using visual analogue scale ranging no pain (1) to extremely intense pain (10 score). The subjects were asked to take tab 10mg Danzen DS thrice a day and cap 0.4mg tamsulosin (once a day after mealtime) for two weeks while take plentiful fluids. Similarly, they were advised to use purpose-built mesh to detect any expelled whole/pieces of stone on urination and visit hospital on 5th, 10th and 15th day for USG to determine LUS’s positioning. They were additionally encouraged to report any adverse effects or pain episode(s).

Data were calculated in terms of mean or frequency. Chi-square test was applied to see any association and patients related symptoms including pain or burning during urination, smelly urine, and nausea/vomiting for an average about past seven days. The USG abdomen diagnostic technique revealed substantially large-sized stone (\( M = 7.92 \)mm in larger dimension) in lower ureter (right/left). The patients rated radiating colic pain in the range of 5 (moderate) to 9 (extremely severe) while assessment by duty doctor on 1-10 scored VAS.

Table No.1: Baseline information of the subjects with a LUS

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (rate in %age)/ Mean ± SD (min.- max.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>52 (61.9)</td>
</tr>
<tr>
<td>Female</td>
<td>32 (38.1)</td>
</tr>
<tr>
<td>Biological age; years</td>
<td>28.8 ± 4.8 (20-40)</td>
</tr>
<tr>
<td>Duration of stone-related symptoms; days</td>
<td>6.6 ± 0.6 (1-12)</td>
</tr>
<tr>
<td>Stone size; mm in larger length*</td>
<td>7.9 ± 1.3 (5-9)</td>
</tr>
<tr>
<td>Colic pain; severity level**</td>
<td>7.2 ± 1.1 (5-9)</td>
</tr>
</tbody>
</table>

*using USG technique, **self-reporting of patient on VAS

Combination therapy i.e. tamsulosin plus Danzen DS showed its efficacy in expulsion of lower ureteral stones against 61 (72.62% of total 84) non-hospitalized patients within a short time span i.e. \( M = 11.5, SD = 2.7 \) (range: 1-15) days under the supervision of research team. However, time was independent of stone size. Comparatively higher stone removal rate was recorded in males than females (75 vs. 68.76, \( p = 0.78 \)) as displayed in Table 2. Similarly, insignificant association was seen between the rate of the stone expulsion and age groups of the participants (\( p = 0.55 \)). Surprisingly, the rate was higher i.e. 77.08% (\( n = 37 \)) in the patients who reported stone-related symptoms for the less than last seven days than one or more than one weeks (66.67%, \( n = 24 \)). The 75% (\( n = 34 \)) medium sized (5-7mm) while 61.36% (\( n = 27 \)) large sized stones (8-9mm) were expelled on use of the medicines. Whereas, the two rates showed statistically significant difference when 2x2 cross tabulation was used in chi-squared test (\( p = 0.01 \)). Not a single significant adverse effect was reported/ examined in the study population. The episodes of colic pain decreased gradually and ultimately ended except in two patients (less severe than without medicines) where MET failed for LUS.
Table No. 2: Association of stone expulsion rate with information of the subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stone expulsion: No. (%)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>39 (75.0) 22 (68.7)</td>
<td>0.78</td>
</tr>
<tr>
<td>Female</td>
<td>13 (25.0) 10 (31.3)</td>
<td></td>
</tr>
<tr>
<td>Biological age; groups (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19-29</td>
<td>45 (73.8) 16 (69.6)</td>
<td>0.55</td>
</tr>
<tr>
<td>30-40</td>
<td>16 (26.2) 7 (30.4)</td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms; week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;one</td>
<td>37 (77.1) 24 (66.7)</td>
<td>0.81</td>
</tr>
<tr>
<td>≥one</td>
<td>11 (22.9) 12 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Stone size; mm</td>
<td></td>
<td>0.01*</td>
</tr>
<tr>
<td>5-7</td>
<td>34 (85.0) 27 (61.4)</td>
<td></td>
</tr>
<tr>
<td>8-9</td>
<td>6 (15.0) 17 (38.6)</td>
<td></td>
</tr>
</tbody>
</table>

*significant using chi-square test at 5% level of significance

DISCUSSION

Some patients avoid to give participation consent\textsuperscript{13} self-perceiving poor prognosis in the biomedical research. On the other side, strict adherence of the subjects of present work to combination MET for LUS expulsion is exemplary. The adherence ensures quality health care.\textsuperscript{14}

Approximately double the male than female population of LUS patients remarkably differs (4:1) in a similar Pakistani study\textsuperscript{15} (4:1). The responsibility of the deviation apparently goes to differential life styles beside hereditary tendency. Male predominance also exists in hemodialysis.\textsuperscript{16} Age of a person in the close proximity of 30 years is crucial towards onset of the ureterolithiasis as endorsed by a published study\textsuperscript{5} (33 years). Finding of 8mm-sized stone on the average is frightening because some delay can shift the patients in surgical management. Generally, the combination MET fails in removal of 10mm-sized stone.\textsuperscript{17} In the presence of same-sized stone, feeling the pain with more severity than others\textsuperscript{14} seems to be a psychophysiological phenomenon.

Our finding on stone expulsion rate (73%) by Danzen DS-added tamsulosin is higher than (64-70%)\textsuperscript{5,18} while lower than (84-100%)\textsuperscript{7,15,19} using tamsulosin and a supporting drug. Adherence to therapy and reinforcing role of the supporting drug are significant determinants in this context. Moreover, combination MET is save in terms of drug tolerance just like antibiotics combination\textsuperscript{9} in the body. Significant effectivity of tamsulosin in low dose has also been reported\textsuperscript{10,20} whereas, removal of 5-9mm sized LUS through plentiful oral fluid intake is a surprising outcome.\textsuperscript{4,10,20}

Consumption of shorter stone expulsion time (i.e. on the average 11 days) than in the study by Jayant and associates is taken positive as the MET is the selection of the patients agreed to awaiting management.\textsuperscript{19,21}

Contrary to it, poor vigilance at urination for detection of the expelled stone can be held responsible for late expulsion compared to highlighted by Nadim et al.\textsuperscript{15} or Erurhan et al.\textsuperscript{18} Other combination therapy including terazosin and nifedipine has also shown efficacy (stone discharge rate = 94.5%; time = 7 days) in postoperative treatment of LUS after transurethral ureteroscopic lithotripsy.\textsuperscript{22}

Light physical activity\textsuperscript{23} by men gives difference in LUS removal rate in sexes: males/females (75/69%). Similarly, decrease in stone expulsion rate with increase in age group can be attributed to unhealthy life style in this career struggling/home establishing stage. Healthy lifestyle prevents from metabolic diseases.\textsuperscript{3,24} The higher stone expulsion rate in the patients with less than seven days of symptoms show evident coincidence with the benefits of early diagnosis. The size of the LUS matters in spontaneous\textsuperscript{25} or medicine-mediated expulsion as seen in findings of present work. No evidence of adverse effects or need of additional analgesic marks the importance of Danzen DS. Reporting of mild pain by two subjects on the scale\textsuperscript{12} makes the combination therapy, acceptable.

CONCLUSION

The MET including Danzen DS-added tamsulosin show acceptable efficacy for LUS in terms of stone expulsion rate, therapy time, significant adverse effects and pain episodes. Better outcomes are recorded against 5-7 than 8-9mm sized stones. There is need to see the therapy with the perspective of cost-effectiveness beside tailoring of dosing regimen. The findings will support the researchers to test it before recommending for clinicians in countries like Pakistan\textsuperscript{10} where MET is the only readily accessible decision for both, professionals and patients.

Author’s Contribution:
Concept & Design of Study: Khalid Saeed
Drafting: Mohammad Ayub,
Data Analysis: Shayan Rahim Kanjoo
Revisiting Critically: Khalid Saeed,
Final Approval of version: Khalid Saeed

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

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