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168 years ago, on 16th October, 1846, Sir William TG Morton did the first successful demonstration of either anaesthesia. It ranks as one of the most significant event in the history of medicine which made it possible for patients to obtain the benefits of surgical treatments without the pain associated with it. World anaesthesia day is celebrated every year on this day, to commemorate this event. Anaesthesiology has emerged as one of the most diverse specialty in medical science ranging from pre-operative care of the patient to pain management. Critical care, palliative care, labour analagesia, and emergency and trauma management. Anaesthesiologist does place a decisive role in patient management. With the advent of newer and safer drug, better drug delivery system and formulation of optimal management plans, anaesthesia has become very safe. Morality from anaesthesia is even less than that from road traffic accidents in general population. This is due to the excellent care provided by anaesthesiologist and despite this, leave alone the general population even, the surgeons still fail to acknowledge the contribution of this branch of modern medicine. Many surveys have been conducted till date to study the perception about anaesthesia and anaesthesiologist across various socio economic strata and literacy level in general population. The results have been very disappointing. Many think that the anaesthesiologists are technicians not trained doctors. Many feel that the anaesthesiologists job is done once the patient is put to sleep. Many don’t even bother who their anaesthesiologist was.

To clarify, the anaesthesiologist is the qualified MBBS Doctor who has done post graduation in anaesthesia and in some specialization like pain medicine, intensive care medicine, cardiac or neuro anaesthesia etc. similar to their surgical colleagues practicing in specialized fields. He / she is actually every patients internist and physicians to the surgeons. The professional work of anaesthesiologists can be described as providing anaesthesia for surgery and controlling / monitoring the patients vital functions, help elevate pain and anxiety in patients, caring for critical ill and be a good manager to ensure smooth functioning of the operation theaters.

The anesthetist society (TAS) and online society founded by a group of anaesthesiologist / anesthetist from all over the world, has taken important steps in formulating a questionnaire which include five must asked questions by every patient to surgeon and the hospital treating them.

The question include:

a) Will a qualified anaesthesiologist provide me anaesthesia?
b) Will the anaesthesiologist / anesthetist look after me during and after the operation?
c) Due you have all the necessary machines and monitoring to provide safe anaesthesia?
d) What different options do you provide for anaesthesia and pain relief for the operation?
e) What facilities do you have to provide safe after case if I develop complications.

This is to ensure safe anaesthesia, safe surgery and safe patient. This noble initiative of TAS is to wipe out the ignorance about anaesthesia and anaesthesiologists amongst general public, improve the image of the anaesthesiologist and to project anaesthesiologists as perioperative physicians in the eye of the general public, and the surgical specialties who use their services.
Efficacy of Epidural Tramadol as Adjuvant to Bupivacaine to Reduce Post-Anesthesia Shivering: Comparison with Intravenous Tramadol HCl in Elective Caesarian Section

Asif Nadeem¹ and Muhammad Muazzam Butt²

ABSTRACT

Objective: Central neuraxial blocks have been mainstay for elective caesarian sections. Epidural anesthesia is better tolerated haemodynamically and provides titer able analgesia and prolonged duration of analgesia. Shivering in perioperative period is reported as high as 65% in general anesthesia and 33% in central neuraxial anesthesia. Intravenous tramadol has been used for decades to treat perioperative shivering. Epidural tramadol as adjuvant to local anesthesia increases quality and duration of anesthesia. We aimed to note efficacy of epidural tramadol.

Study Design: Prospective, Randomized Control Trial study.

Place and Duration of Study: This study was conducted at the Operation theatres of Sahara Medical College, Narowal from January, 2020 to July, 2020.

Materials and Methods: Total number of 250 patients included in study randomly divided in group 1 and 2, received epidural and intravenous tramadol consecutively. SPSS software was used to analyze statistics.

Results: Group 1 resulted in 7 patients with shivering mean time to shivering was 41.42±7.29 minutes and mean APGAR was 7.56±1.14, 9.83±0.41, 9.99±0.08 at 1, 5 and 10 minutes consecutively. Group 2 resulted in 6 patients with shivering mean time to shivering was 43.66±4.27 minutes and mean APGAR was 8.48±0.85, 9.78±0.62, 9.97±0.15 at 1, 5 and 10 minutes consecutively. Shivering and time to shivering between 2 groups were insignificant with significance level of p=0.777 and p=0.524 consecutively. APGAR at 1 minute was significant with level of p< 0.001 whereas at 5 and 10 minutes improved and became insignificant with p=0.478 and p=0.315 levels consecutively. Nausea vomiting was insignificant between 2 groups p=0.856.

Conclusion: Epidural tramadol is as effective as intravenous tramadol for perioperative shivering.

Key Words: Epidural tramadol shivering.

INTRODUCTION

In elective caesarian section different methods of anesthesia has been chosen according to patient’s anxiety and preference. All methods have their own goods and bads. Traditionally spinal anesthesia when compared with general anesthesia is considered better choice for elective Caesarian section in many aspects like less postoperative nausea, vomiting, DVT, Bleeding and decreased use of opioids.

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epidural block for caesarian section randomly divided into 2 groups, group 1 received epidural tramadol and group 2 received intravenous tramadol.

**Primary outcome:**
Shivering
Time to shivering after epidural block in minutes

**Side effects like**
1. Apgar score at 0,5,10 minutes
2. Perioperative Nausea vomiting

**Inclusion criteria**
- Age between 18-35 years
- ASA 1,2
- Elective Caesarian section

**Exclusion criteria**
- Patient reluctance
- Infection of injection site
- Bleeding disorder tendency
- Previous PONV
- Preexisting neurological deficit
- PIH and GDM

**Data collection procedure:** Ethical review board allowed proceeding with our study. We conducted study on 250 patients and made sure informed consent. Patients randomly divided into 2 groups, group 1 who received 100mg tramadol epidural and group 2 received 0.5mg/kg tramadol for shivering prophylaxis. All patients received epidural anesthesia in lumbar space L3-L4-L5 by experienced anesthesiologist. After giving test dose of xylocaine with adrenaline, we injected 0.5%bupivacaine 20ml and 100mg preservative free tramadol HCl in group 1 and bupivacaine alone in group 2 patients in epidural space. Standard 1 and 2 monitoring started and continued for next 2 hours. Injection synephrine is used to maintain haemodynamics. After assessing the block level surgery started. Shivering and time to shivering noted and along with all data collected entered in Performa.

**Data analysis procedure:** SPSS Version 16 used to analyze statistics. Data collected from performa and entered in software. Descriptive statistics calculated for quantitative data like age, shivering, time to shivering, nausea vomiting as mean and standard deviation. ANNOVA test applied to determine significance of variables.

**RESULTS**

Group 1 resulted in 7 patient with shivering mean time to shivering was 41.42+7.29 minutes and mean APGAR was 7.56+1.14,9.83+0.41,9.99+0.08 at 1,5 and 10 minutes consecutively. Group 2 resulted in 6 patients with shivering mean time to shivering was 43.66+4.27 minutes and mean APGAR was 8.48+0.85,9.78+0.62,9.97+0.15 at 1,5 and 10 minutes consecutively, table 1 shows the said results. Shivering and time to shivering between 2 groups were insignificant with significance level of p=0.777 and p=0.524 consecutively. APGAR at 1 minute was significant with level of p< 0.001 whereas at 5 and 10 minutes improved and became insignificant with p=0.478 and p=0.315 levels consecutively. Table 2 shows the ANNOVA test for significance of variables.

There was no significant difference in ages of patients between two groups mean age was 26.91+4.51 and 27.91+4.74 with p=0.089. Nausea vomiting was insignificant between 2 groups p=0.856. Group 1 and 2 had mean age of 26.91+4.51, 27.91+4.74 consecutively. Pie plots total number of nausea vomiting cases included in study.

**Table No.1: Descriptive analysis of variables**

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Age of patient</th>
<th>Time to shivering in minutes</th>
<th>APGAR at 1 minute</th>
<th>APGAR at 5 minutes</th>
<th>APGAR at 10 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>group 1</td>
<td>Mean</td>
<td>26.9120</td>
<td>41.4286</td>
<td>7.5600</td>
<td>9.8320</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>125</td>
<td>7</td>
<td>125</td>
<td>125</td>
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<tr>
<td></td>
<td>Std. Deviation</td>
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<td>7.29971</td>
<td>1.14582</td>
<td>.41613</td>
</tr>
<tr>
<td>group 2</td>
<td>Mean</td>
<td>27.9120</td>
<td>43.6667</td>
<td>8.4800</td>
<td>9.7840</td>
</tr>
<tr>
<td></td>
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<td>125</td>
<td>6</td>
<td>125</td>
<td>125</td>
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<tr>
<td></td>
<td>Std. Deviation</td>
<td>4.74174</td>
<td>4.27395</td>
<td>.85760</td>
<td>.62970</td>
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<td>42.4615</td>
<td>8.0200</td>
<td>9.8080</td>
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<td>250</td>
<td>13</td>
<td>250</td>
<td>250</td>
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<tr>
<td></td>
<td>Std. Deviation</td>
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<td>5.96679</td>
<td>1.11019</td>
<td>.53317</td>
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**Figure No.1:** Pie chart for nausea vomiting

**Figure No.2:** Pie chart for nausea vomiting
### Table No.2: ANOVA for variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>Sig.</th>
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</tr>
<tr>
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<td>.004</td>
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<td>.004</td>
<td>.081</td>
<td>.777</td>
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<tr>
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<td>248</td>
<td>.050</td>
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<tr>
<td>Total</td>
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<tr>
<td>Time to shivering in minutes</td>
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<tr>
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<td>51.650</td>
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<td>.016</td>
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## DISCUSSION

Redistribution of heat due to sympatholytic vasodilation and compensatory thermal deregulation are main causes of shivering in central neuraxial anaesthesia which is worsened with cold environment, cold intravascular fluids and surgical exposure of patients. Various methods employed to decrease the incidence of perioperative shivering included pharmacological and non-pharmacological, non-pharmacological included warming patient and environment with air warmers and warm intravenous fluids. Shivering increases metabolism causing hypoxemia leading to metabolic acidosis and increases catecholamine surges.

Pharmacological interventions had been successfully employed which mostly included post shivering treatment like intravenous meperidine, clonidine, ketamine, fentanyl, magnesium, xylocaine, dexamethasone, tramadol, propofol, ketanserin and doxapram. Only few available options for prophylaxis like tramadol which is intended for different purpose but gives additional benefit of shivering prophylaxis. Masood Entezari compared dexamethasone and pethidine intravenous for prophylaxis of perioperative shivering and found that dexamethasone is more effective than pethidine in term of preventing the perioperative shivering. 47.5% placebo group, 10% dexamethasone group and 37.5% pethidine group had shivering with p=0.001. Additional benefit of dexamethasone was its anti-emetic effect while pethidine gave better analgesia postoperatively but with higher incidence of perioperative nausea vomiting. Sarmila Guha compared prophylactic use of clonidine and tramadol and concluded in favour of tramadol for lesser complications like hypotension, bradycardia and sedation but of shivering was insignificant between 2 groups. (p>0.05) Although Sarmila favoured tramadol for better analgesia but clonidine had its its own merit of patient being more calm provided blood pressure and heart rate was managed. Bahman Hasannasab in his trial compared meperidine, doxapram, ketamine groups with perioperative shivering of 2.5%,10% and 7.5% consecutively. (p=3.9). They also noticed those groups who received ketamine and meperidine required analgesia long after the procedure. (p<0.001) ketamine and meperidine group had complication like nausea vomiting and anxiety but still their effect on shivering masked their complications. Sang-Hwan Do noticed that magnesium decreases postoperative analgesic requirement and also decreases perioperative shivering. Ahmad Rastegarian first time noticed the efficiency of intrathecal meperidine and found that intrathecal...
Epidural tramadol is as effective as intravenous tramadol for perioperative shivering. (p<0.04) Meperidine intrathecal was used in lesser quantity but with better analgesic quality with additional benefit on shivering. P. Alfonsi compared intravenous lidocaine, fentanyl and meperidine. He found meperidine significantly superior to other two in terms of prophylaxis of shivering as meperidine inhibited shivering in lower body temperature. (p<0.01) In all Data available we found all medicines discussed above were effective in preventing perioperative shivering with some drug’s superiority to other due to their efficacy or their side effects. Some drugs like clonidine, doxapram etc. were solely prescribed either for prophylaxis or treatment of perioperative shivering without any other indication. Some drugs were used for other indication and they were resulted beneficiary side effect of inhibition of shivering like tramadol. There was only one study in Data showing efficacy of central neuraxial meperidine for perioperative shivering. In our settings meperidine is not available in contrast to tramadol which is freely available and being widely used as adjuvant to central neuraxial blocks for better, quick and prolonged analgesia. Tramadol is also considered as drug of choice for perioperative shivering in local practice. We took idea to study tramadol central neuraxial from its above discussed indication and it is proved to be as effective as intravenous tramadol for perioperative shivering. This way we got not only better analgesia but also had lesser shivering. Limitation of our study was that it is conducted in a specific population and in a defined period of time. We recommend more observational studies for more accurate Data.

CONCLUSION

Epidural tramadol is as effective as intravenous tramadol for perioperative shivering.

Recommendation: We recommend further studies on different populations and multi center trials as little Data is available in this regard.

Acknowledgement: We acknowledge every individual who participated and helped us to complete our trial.

Author’s Contribution:
Concept & Design of Study: Asif Nadeem
Drafting: Muhammad Muazzam Butt
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Revisiting Critically: Asif Nadeem, Muhammad Muazzam Butt
Final Approval of version: Asif Nadeem

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

REFERENCES


A Comparative Study Between Two Supraglottic Airway Devices: I Gel Vs Classic Laryngeal Mask Airway
Raza Farrukh¹, Asad Rizwan Rana² and Makhdom Ahmad Aziz Jilani²

ABSTRACT

Objective: During general anesthesia, in case of adults and children, supraglottis airway devices are good alternate to securing airway than tracheal intubation. This case study aimed at comparison between classical laryngeal mask airway (LMA) and modern i-gel with respect to adequate placement, ease of insertion of device, maintaining of parameters like ETCO2 and SPO2, intra operative and postoperative complication point of view.

Study Design: Comparative Study

Place and Duration of Study: This study was conducted at the Department of Anaesthesia DHQ Teaching Hospital, Sargodha from September 2019 to February 2020.

Materials and Methods: There was selection of 120 patients in this randomized clinical trial from age ranged from 5 to 60 years of either sex and from ASA grading ranged from I-III. These all patients were operated in supine position under general anesthesia. Anesthesia was induced to all these patients after receiving premedication. Agents that were used in anesthesia were primarily, inj. Succinylcholine 1.5-2mg/kg and inj. Propofol 2-3 mg/kg. Patient’s airway was secured with either classical LMA or i-gel in ‘sniffing air’ position. The device placement was monitored by normal chest expansion, by square wave capnography, absence of audible leak and SPO2 >95%. The patients were checked keeping in view the parameters like number of attempts, ease of insertion, hemodynamic changes preoperatively and complication involved intraoperatively as well as postoperatively

Results: Statistically, no significant difference was seen in patients of both the groups with respect to BP, SPO2 ETCO2 and heart rate, however it was observed that insertion time was greater in group classical LMA as compared to group i-gel.

Conclusion: I-gel is regarded as better and good alterative replacement device to LMA as its insertion is way easy, along with minimal complications intraoperatively as well as post operatively.

Key Words: I-gel, LMA, advantages, disadvantages.


INTRODUCTION

Endotracheal intubation was invented by Mc Evan in 1880, which was a great invention of past regarding airway management. It was a great revolutionary invention that led to the development of supraglottic airway approach. The highly professional skill and continuous training is required for proper tracheal intubation.

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In tracheal intubation, laryngoscopy is done directly that might lead to laryngopharyngeal lesions. Tracheal intubation can cause hypertension, raise in plasma catecholamine, generate reflex sympathetic stimulation, ventricular arrhythmias and finally can cause intracranial hypertension.¹

Due to multiple disadvantages of tracheal intubation, we can use device such as supraglottic airway in order to maintain the airway during anesthesia to children and adults. During the year 1981, laryngeal mask airway (LMA) that was inflatable used.² Now a day, the modern supraglottic airway device i-gel is also available. The composition of i-gel consists of transparent soft gel like material with non-inflatable cuff.

The structure and design of making of i-gel is such that it makes anatomical non inflatable seals of structures such as perilaryngeal, pharyngeal and laryngeal tissue. There are numerous advantages of i-gel such as easier insertion, lasting stability, low risk of compression of tissues and low price wise.³

The classic LMA has many disadvantages and it is inferior as compared to i-gel in a way that classic LMA
has difficult insertion method, its handling is way too tough, possibilities of tissue injuries, controlled ventilation and pulmonary aspiration risk always there while using c LMA. This case study was classically developed in order to make comparisons between both airway devices namely c LMA and i-gel. The complete evaluation, comparison and assessment was done to judge for hemodynamic parameters, intra operative and postoperative complications, insertion complications and ability of both devices to maintain ETCO₂ and SPO₂.

**MATERIALS AND METHODS**

A randomized study was conducted after taken approval from ethical committee in order to make comparison between two airway devices namely, classical LMA and i-gel. In this study, there was involvement of 120 patients that can be either male or female, with age ranged from 6 to 65 years and weight varied from 10-75 kgs and ASA grading ranged from i, ii and iii going under general anesthesia for their various surgical procedures. The few patients were excluded from study such as patients with pregnancy, full stomach, hiatus hernia, neurosurgery, emergency patients and patients that were labeled with ASA grade iv.

The complete preoperative assessment of patients were done before the surgery. Both the devices, i-gel and c LMA were readily available depending on patients weight. Patients who participated in this case study were given injections of ondansetron 0.15 mg/kg and glycopyrrolate 0.004 mg/kg preoperatively. Oxygen was given to patients for about 3 minutes as preoxygenation. All essential monitoring such as blood pressure, pulse rate, electrocardiogram and oxygen saturation were applied on all patients. Anesthesia induction was done using inj. succinylcholine 1.5-2 mg/kg and inj. propofol 2-3 mg/kg.

After achieving required anesthetic state patients were positioned in “sniffing air” position then the airway was maintained using i-gel or c LMA. So on basis of which airway device was used, we grouped patients in two categories named group i-gel and group c LMA. In group i-gel patients airway was rescued using i gel while in group c LMA, patient airway was saved using c LMA. In group i gel, gastric tube that was well lubricated was chandeliered via gastric channel into stomach.

In order to check proper placement of airway device, we used parameters like SPO₂ >95%, absence of audible leak, square wave capnography and normal expansion of chest.

There were few specific things that were noticed that include time taken for device insertion, number of failures and attempts to made device fix successfully, how comfortably device can be placed complications and difficulties during removal n insertion of device and hemodynamic changes.

Breathing circuit of anesthesia machine was attached to these airway devices. The anesthesia of patients was achieved using 50% nitrous oxide, 50% oxygen, intravenous injection of atracurium 0.5 mg/kg and isoflurane. At the end of surgical procedures there was reversal of neuro muscular blocking agent by use of inj. glycopyrrolate 0.08 mg/kg intravenously along with the dose of inj. neostigmine 0.05 mg/kg. In the end airway device was removed after attaining adequate tidal volume.

All the patients that underwent surgery were observed for complications such as hypertension/hypotension, tachycardia/ bradycardia, hypercarbia. After the operation the patients were examined for symptoms like cough, tongue numbness, breath holding, spasm of larynx, dental injuries, lip injuries and presence of blood on devices.

Complete data analysis were done by using unpaired t test was done and also p value <0.05 was taken into account by using the graph pad software and after that analyzed either significant or not.

**RESULTS**

After the observation of complete data, we came to the conclusion that there was not any statistically significant difference between the two groups regarding demographic data such as age, sex, weight, duration of surgery and ASA grading. This is shown in table 1.

**Table No.1: Demographic data**

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Group i-gel N=60 (%)</th>
<th>Group LMA N=60 (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean ± SD</td>
<td>21.09±15.0</td>
<td>21.19±17.90</td>
<td>0.579</td>
</tr>
<tr>
<td>Sex(%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>42(70%):18</td>
<td>45(75%):15</td>
<td>0.501</td>
</tr>
<tr>
<td>Female</td>
<td>(30%)</td>
<td>(25%)</td>
<td></td>
</tr>
<tr>
<td>Weight (Kg) Mean ± SD</td>
<td>44.60±19.10</td>
<td>40.54±19.31</td>
<td>0.440</td>
</tr>
<tr>
<td>ASA: Grade(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA-I</td>
<td>09(15%)</td>
<td>09(15%)</td>
<td></td>
</tr>
<tr>
<td>ASA-II</td>
<td>40(66.6%)</td>
<td>45(75%)</td>
<td>0.667</td>
</tr>
<tr>
<td>ASA-III</td>
<td>11(18.4%)</td>
<td>06(10%)</td>
<td></td>
</tr>
<tr>
<td>Duration of Surgery (Minutes) Mean ± SD</td>
<td>40.1 ± 8.11</td>
<td>42.2 ± 6.16</td>
<td>0.161</td>
</tr>
</tbody>
</table>

There was no difference regarding types of surgeries either by use of c LAM or i-gel (table 2).

In patients of both groups, there was statistically significant difference with respect to efforts for insertion, attempts in making insertion, and time taken during insertion for both c LMA and i-gel. However, i-gel seemed to be superior with respect to parameters like easy insertion and less efforts involved as compared to c LM. This comparison is shown in table 3.
Table No.2: Types of surgery

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Group i-gel</th>
<th>Group LMA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=60(%)</td>
<td>N=60(%)</td>
</tr>
<tr>
<td>Contractor Release and STG</td>
<td>18(30%)</td>
<td>21(35%)</td>
</tr>
<tr>
<td>Diagnostic scopy</td>
<td>06(10%)</td>
<td>06(10%)</td>
</tr>
<tr>
<td>Circumcision and Hypospadiasis Repair</td>
<td>12(20%)</td>
<td>05(8.3%)</td>
</tr>
<tr>
<td>Excision biopsy for Fibroadenoma</td>
<td>06(10%)</td>
<td>09(15%)</td>
</tr>
<tr>
<td>I&amp;D, Debridement, Resuturing</td>
<td>12(20%)</td>
<td>13(21.7%)</td>
</tr>
<tr>
<td>Fistulectomy, Haemorrhoidectomy</td>
<td>06(10%)</td>
<td>06(10%)</td>
</tr>
</tbody>
</table>

As far as parameters like hemodynamic were concerned, there was no statistically significant difference was seen in patients of both groups using i-gel or c LMA as shown in figure 1 and 2.

Table No.3: Comparison between i-gel and LMA with respect to different parameters of insertion

<table>
<thead>
<tr>
<th>Parameters of Insertion of device</th>
<th>Group i-gel</th>
<th>Group LMA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=60(%)</td>
<td>N=60(%)</td>
<td></td>
</tr>
<tr>
<td>Quality of Insertion</td>
<td>Easy</td>
<td>51(85%)</td>
<td>42(70%)</td>
</tr>
<tr>
<td></td>
<td>Difficult</td>
<td>09(15%)</td>
<td>18(30%)</td>
</tr>
<tr>
<td>Attempt of Insertion</td>
<td>First</td>
<td>54(90%)</td>
<td>38(63.4%)</td>
</tr>
<tr>
<td></td>
<td>Second</td>
<td>05(8.4%)</td>
<td>12(20%)</td>
</tr>
<tr>
<td></td>
<td>Third</td>
<td>01(1.6%)</td>
<td>10(16.6%)</td>
</tr>
<tr>
<td>Insertion Time (Seconds) Mean ± SD</td>
<td>51.9 ± 6.001</td>
<td>56.98 ± 9.921</td>
<td>0.004</td>
</tr>
<tr>
<td>Manipulation</td>
<td>Gentle pushing</td>
<td>02(3.4%)</td>
<td>12(20%)</td>
</tr>
<tr>
<td></td>
<td>Chin lift</td>
<td>01(1.6%)</td>
<td>08(13.4%)</td>
</tr>
<tr>
<td>During insertion</td>
<td>Gentle pushing</td>
<td>03(5%)</td>
<td>05(8.3%)</td>
</tr>
</tbody>
</table>

Table No.4: Perioperative complications

<table>
<thead>
<tr>
<th>Perioperative complications</th>
<th>Group i-gel</th>
<th>Group LMA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of Patients (%)</td>
<td>No of patients (%)</td>
</tr>
<tr>
<td>Difficulty in Removal</td>
<td>12 (20%)</td>
<td>30 (50%)</td>
</tr>
<tr>
<td>Post Exubation Cough</td>
<td>06 (10%)</td>
<td>18 (30%)</td>
</tr>
<tr>
<td>Numbness Of Tongue</td>
<td>03 (6%)</td>
<td>09 (15%)</td>
</tr>
<tr>
<td>Presence Of Blood On device</td>
<td>06 (10%)</td>
<td>10 (17%)</td>
</tr>
</tbody>
</table>

In patients who were in c LMA group during surgery, post-operative complications like cough, difficulty in removal of device, blood on removed device and tongue numbness was witnessed in greater percentage as compare to i-gel as clearly demonstrated in table 4.

DISCUSSION

Now days, there are various supraglottic devices are available for maintaining patients airway during general anesthesia. Theses supraglottic devices are far much superior as compared to conventional endotracheal tubes. There are numerous benefits of these supraglottic devices as compared to tracheal intubation such as easy insertion, avoidance of tachycardia, hypertension, better acceptance by patients, better hemodynamic parameters stability, less incidence of sore throat and cough. Moreover, supraglottic devices fit directly over peripharyhngeal seal to have perfect fit. The supraglottic device c LMA, can be blindly put into pharynx that forms seal of low pressure around the larynx and in return permit positive pressure ventilation. c LMA permits anesthetic agents inhalation with decrease in airway stimulation.4 i-gel is modern discovery and superior to c LMA in a sense that it is non-inflatable supraglottic airway device for maintaining respiratory airway. While using i-gel there is minimal risk of trauma of peripheral tissues as it fits with patients airway anatomy completely.3 i-gel has tube that allows anesthetists to have access to gastrointestinal tract without any risk of regurgitation and gastric inflation.5

In about 65 non-embalmed cadavers, Kinkle and Levitan worked on i-gel positioning with the help of video laryngoscope, radiographs of necks especially
in lateral section view and neck block dissection.\textsuperscript{6} They were surprised to find that that i-gel sits perfectly over anatomy of perilaryngeal although it has no inflatable cuff. Moreover, it attains proper position with respect to supraglottic ventilation.

Lopez-Gil et al and Keller performed four different tests to access the oropharyngeal leak pressure using c LMA.\textsuperscript{1} The assessment was done to test the audibility of noise over auscultation on the lateral side of thyroid cartilage, the audibility of noise over mouth, exhaled CO\textsubscript{2} detection by placement of gas sampling line inside oral cavity and finally the assessment of airway during respiratory valve occlude. These all four test help in a great way in assessment of leak orophargeneal pressure assessment in young children.

In some research, the placement of device was sure by Square wave capnography, chest movements, neck of audible leak, thoraco abdominal movements, lack of gastric insufflations on ventilation and leak pressure >20 cm H\textsubscript{2}O.\textsuperscript{8,13}

In our current research, the position of airway device was confirmed by parameters like adequate chest movements, SPO\textsubscript{2} ≥95% and square wave capnography. The placement of device was done effortlessly in 88% patients using i-gel while 64% of the patients using c LMA. The manipulations required in placement of i gel was 12% while in 36% patients using c LMA. These manipulations include jaw thirst and chin lift. Some studies done earlier in older times showed that placement of I gel is much more easy as compared to c LMA.\textsuperscript{13-15}

In many studies while comparing insertion of i-gel and c LMA, we came to know that insertion of i-gel was far easy as compared to c LMA while neck contracture and as well as in normal patients. Moreover, similar study was performed by Chauhan et al and Trivedi et al with respect to insertion of i-gel and c LMA and found similar results i.e i-gel was easy to inset as compared to c LMA.\textsuperscript{9,12,16,17} Moreover, Das et al did similar study and came to conclusion that i-gel insertion involve less manipulations as compared to c LMA.\textsuperscript{18}

In our current research i-gel was placed successfully in 85% patients while c LMA percentage was 75%. In group of patients that were given c LMA, about 12% of patient needed second attempt and 10% needed third. When mean insertion time was calculated for i-gel and c LMA, it came out to be 51.9 ± 6.001 seconds and 56.98 ± 9.921 seconds, respectively. Data collected from both groups was considered statistically significant regarding insertion times(p=0.0050).

Various studies were reported by Chauhan et al that clearly reported that whether its i-gel or c LMA, almost both devices took 3 attempts for successful insertion. When mean insertion time was calculated, i-gel showed significantly lowered mean t insertion time as compared to c LMA.\textsuperscript{12}

Another researcher, Wharton et al tested and evaluated the efficacy of i-gel in anesthetized patients and manikins and came to the conclusion that i-gel can befar easily and effortlessly inserted into patients airway in both anesthetized and manikins even by inexperienced person as compared to other options of supraglottic airways available.\textsuperscript{5}

A case study was performed by Jeon et al observed the attempts made for insertion of c LMA and i-gel. They found that no statistically significant difference was observed with respect to first time insertion of c LMA or i gel.\textsuperscript{14} Similarly, Das et al and Chen et al did work on this and found similar findings regarding insertion of i-gel and c LMA.\textsuperscript{18,19}

In our current Study, different parameters like diastolic blood pressure, pulse rate, ETCO\textsubscript{2} and SPO\textsubscript{2} were measured and we came to conclusion that there is no statistically significant difference in patients of both groups using i-gel or c LMA and we calculated p value >0.05. Chauhan et al, Helmy et al and Das et al did similar work regarding i-gel or c LMA.\textsuperscript{9} One study was also performed by Trivedi et al and showed that with the use if i-gel there are less changes and alteration in mean arterial pressure when compared to c LMA.\textsuperscript{12,15,17,18}

Uppal et al did research with respect to make a comparison between i-gel and endotracheal tube. On basis of this research, he found that there was increased systolic and diastolic blood pressure and heart rate intraoperatively while using endotracheal tube as compared to i-gel.\textsuperscript{9} In our current research, we found that i-gel was smoothly removed in about 80% of cases as compared to c LMA, where smoothly removal percentage was 50%. The complications such as numbness of tongue, coughing after device removal, and spotting a blood on device was higher in case of c LMA as compared to i-gel.

We observed that with the use of c LMA, we encounter complications like tongue numbness, dental trauma, lip injury, minor regurgitation, blood staining of device, GI symptoms like nausea, vomiting, major airway obstruction, sore throat and dysphagia.\textsuperscript{9,12,15,16,18,20}

CONCLUSION

The both airway devices c LMA and i-gel were able to successfully maintain the airway of patients during anesthesia and can be tolerated well by all patients. i-gel is superior than c LMA in a way that its insertion is far easy as compare to c LMA. Secondly, there is less risk of airway damage by using i-gel as compared to c LMA. Thirdly, i-gel achieves ideal position for supraglottic ventilation, and fourthly it confirms to the perilaryngeal anatomy although there is no inflatable cuff as in c LMA. So in a nutshell, i-gel is superior and much better and excellent option in comparison to c LMA whenever supraglottic airway is used.
Author’s Contribution:
Concept & Design of Study: Raza Farrukh
Drafting: Raza Farrukh, Asad Rizwan Rana
Data Analysis: Asad Rizwan Rana
Revisiting Critically: Makhdom Ahmad Aziz Jilani
Final Approval of version: Raza Farrukh

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

REFERENCES


Urethral Injuries and its Management: A Cross-sectional Study from SMBB Medical University Larkana

Riaz Hussain Mangrio\textsuperscript{1}, Sajid Ali Abbasi\textsuperscript{1}, Vijia Kumar Gemnani\textsuperscript{2}, Malik Hussain Jalbani\textsuperscript{1}, Azizullah Mirani\textsuperscript{1} and Ahsanullah Malik\textsuperscript{3}

ABSTRACT

Objective: To determine the frequency, type of urethral injury, the outcome of patients, and rate of complications in our setting.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the Urology Department, SMBB Medical University Larkana, Pakistan for 2 years from July 2018-July 2020.

Materials and Methods: A total of 40 consecutive patients were enrolled in the study. Sociodemographic profile, type of injury patterns, causes of injury, management, and outcome were recorded for study participants and also examined the complication rate.

Results: There were a total of forty patients. Common causes of urethral injuries were: pelvic fractures, iatrogenic injuries, penetrating injuries, among others. 18 out of forty (45%) patients experienced complications. The most common complication was stricture formation in 8 (44.4%), followed by extravasation or voiding difficulties in 3 (16.6%) patients, impotence, and painful ejaculation was observed in 2 (11.1%) patients, each.

Conclusion: Urethral injuries were more common in male patients. The most common cause of injury was iatrogenic, followed by blunt/crushing trauma. Education modules on urological anatomy and catheter safety along with a thorough physical examination can aid in the prompt diagnosis and prevention of such injuries.

Key Words: bulbar urethra, catheter, stricture, urological emergency, urethral injuries.


INTRODUCTION

The urethra is a very important organ of the human body. Its structure resembles that of a tube as it is responsible for emptying urine from the bladder. Although urethral trauma is a rarity they have become more common due to increasing road traffic accidents\textsuperscript{1}. These accidents often result in blunt trauma to the urethra, injuries to the pelvis, or trauma to the sexual organs\textsuperscript{2}. A quick diagnosis is required to avoid future complications such as incontinence, the stricture of the urethra, and impotence\textsuperscript{3}. Injuries to the posterior urethra are for instance linked to fractures of the pelvis in both males and females\textsuperscript{4}. These lead to breakages at the level of the prostate in males who may present with blood at the meatus, difficulty in voiding urine, fracture of the pelvis alongside hematoma of the pelvis, blood in urine, inability to insert a catheter for urine and prostate which is not palpable. In females, however, laceration or bleeding of the vagina, bleeding in the urethra, blood in urine, difficulty in urination, and swelling of the labia\textsuperscript{5}. The primary goal of the management of urethral injuries is to at first stabilize the patient presenting to the emergency room with a blunt trauma force. If there is excessive loss of blood, then it should be replaced as quickly as possible to avoid leading to complications such as shock or cardiac arrest\textsuperscript{6}. It has to be managed promptly with a well-organized team and triage should be performed. After which, the injury of urethra will be treated for. While managing injuries to the urethra, special care should be given to allow a previously well-functioning urethra to work well. The treatment for urethral trauma includes prompt management during the first 48 hours of the trauma and treatment which will be postponed between 2 to 14 days of the trauma\textsuperscript{7}. Delayed management is also considered which will be done within 3 months of the trauma due to poor resources especially in developing countries\textsuperscript{8}. The management however differs with the severity and location of the injury\textsuperscript{9}. Injuries that are not so severe can easily be treated by placing a Foley’s Catheter in the urethra for approximately 14 to 21 days. If the injury is resolved after the use of the catheter while
viewing it on an X-ray, the catheter is removed. However, in more severe cases, such as crush injuries, urethral injuries are seen alongside other injuries which makes the management all the more difficult. In severe injuries, there is a high risk of leakage of urine which can lead to infection and inflammation. Although the posterior urethral injury is considered to be more complicated, management such as drainage or primary repair is recommended to preserve the penile tissue of male patients. Disruptions can be done on the tissue such as with the use of a catheter, performing only a primary repair, or doing a suprapubic cystostomy. A follow-up would be needed after 6 months to check for the normal function of the urethra and any postoperative complications.

MATERIALS AND METHODS

An Observational, cross-sectional study was carried out at the Urology department SMBB Medical University, Larkana, Pakistan between July 2018 to July 2020 (02 years). In current study, consecutive sampling technique (non-randomized) was used to select the consented patients, and then written consent was taken from every participant. Patients were also informed about the risk associated with withdrawing blood samples such as the risk of pain, bleeding, irritation, or infection. However, they were ensured that it is a very low probability. Ethical approval was obtained from the Institutional Review Board of Chandka Medical College and Teaching Hospital, SMBBBMU, Larkana, Pakistan.

Data regarding demographic as well as other variable were collected in a proforma. The patient’s gender, age, comorbidities, site and type of injury, signs, and symptoms of trauma were observed. Urethral trauma and injuries were confirmed using urethrography and ureteroscopy.

Patients who were unable to pass urine or had a history of pelvic fractures, suprapubic cystostomy, and decompression were used to release the urine. In the case of bruising or blunt trauma, debridement was done followed with a sterile dressing. For iatrogenic injuries, mainly due to traumatic catheterization, strictures were more likely which were either treated using dilatation, urethroplasty, or urethrotomy. For superficial lacerations, primary suturing was done using prolene 3/0 stitches. For open urethral injuries, surgical exploration and debridement were needed. All patients were administered intravenous broad-spectrum antibiotics, analgesics, and fluid replacement if the patient was actively bleeding. Patients’ vitals were monitored regularly. Complete cell count of all patients were sent pre- and post-intervention. Any irregularities in the blood pressure, respiratory rate, pulse rate, oxygen saturation, and temperature were noted. Blood transfusions were done in case of very low hemoglobin level or deranged platelet counts. For observation of treatment and complication need of four week follow-up visit of patient. All data were recorded in a predefined proforma and entered into excel sheets.

A successful outcome was considered if no complications were observed in follow-up or no secondary procedure was done. An unsuccessful outcome was referred to cases that were followed up with a secondary procedure or intervention or complications were observed.

Statistical analysis: SPSS version 24 was applied for analyzing the data. Patient age, body mass index and other continuous variables were presented as mean and standard deviation. The categorical data were represented with frequency and percentage.

RESULTS

In current study, totally 40 patients were examined. Common causes of urethral injuries were: pelvic fractures, iatrogenic injuries and penetrating injuries, among others. See table.1.

Table No.1: Demographic and Clinical Profile of Patients in the Study (n=40)

<table>
<thead>
<tr>
<th>Clinical Signs and Symptoms</th>
<th>Frequency Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penile Pain in males</td>
<td>21</td>
<td>52.5%</td>
</tr>
<tr>
<td>Bleeding per urethra</td>
<td>15</td>
<td>37.5%</td>
</tr>
<tr>
<td>Swelling and edema</td>
<td>8</td>
<td>20%</td>
</tr>
<tr>
<td>Hematoma</td>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications</th>
<th>Frequency Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strictures</td>
<td>8</td>
<td>44.4%</td>
</tr>
<tr>
<td>Impotence</td>
<td>2</td>
<td>11.1%</td>
</tr>
<tr>
<td>Painful ejaculation</td>
<td>2</td>
<td>11.1%</td>
</tr>
<tr>
<td>Extravasation of Urine or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voiding difficulties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulvar edema in females</td>
<td>2</td>
<td>11.1%</td>
</tr>
<tr>
<td>Life-threatening sepsis</td>
<td>1</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Injury patterns</th>
<th>Frequency Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crushing</td>
<td>10</td>
<td>25%</td>
</tr>
<tr>
<td>Bruising</td>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>Laceration</td>
<td>8</td>
<td>20%</td>
</tr>
<tr>
<td>Hematoma</td>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>Others</td>
<td>7</td>
<td>17.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body Mass Index in kg/m²</th>
<th>Frequency Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt; 18.5)</td>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>Normal (18.5 – 24.9)</td>
<td>18</td>
<td>45%</td>
</tr>
<tr>
<td>Overweight (25.0 –29.9)</td>
<td>8</td>
<td>20%</td>
</tr>
<tr>
<td>Obese (&gt; 30.0)</td>
<td>9</td>
<td>22.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Causes of Injury</th>
<th>Frequency Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iatrogenic injuries</td>
<td>16</td>
<td>40%</td>
</tr>
<tr>
<td>Road traffic accidents</td>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>Penetrating Injuries</td>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>Others</td>
<td>7</td>
<td>17.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>34</td>
<td>85%</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>15%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean Age (SD) in years</th>
<th>35.4 (14.3)</th>
</tr>
</thead>
</table>
18 out of forty (45%) patients experienced complications. The most common complication was stricture formation in 8 (44.4%), followed by extravasation or voiding difficulties in 3 (16.6%) patients, impotence, and painful ejaculation was observed in 2 (11.1%) patients, each.

**DISCUSSION**

The male gender is 10 times more prone to suffer a urethral trauma compared to their counterparts. This predilection is a result of significantly different urologic anatomy. Females have a rather shorter and more mobile urethra which contributes to their lower chances of experiencing urethral injuries. Nevertheless, even in females, the incidence of urethral injury with pelvic fractures or blunt injuries is as high as six percent. Studies showed that significantly high prevalence rate of urethral injury was observed in male as contrast to female.

In many cases of urethral trauma, 1st stretch occur in membranous part of urethra furthermore broken occur at the junction of bulb membranous (partial or complete). Prostatic urethral to bladder neck trauma occur only in child age group. In female urethra injury mostly partially tearing of the anterior wall and not often complete tearing of urethra (proximal or distal portion).

Regarding previous studies, mostly suturing the disrupt ending of urethera resulting high rate of complication may arise such incontinence (21%) and impotence (56%) in a meta-analysis, it was concluded that primary realignment (PR) has a lower risk of stricture formation in patients with posterior urethral injuries in comparison with suprapubic cystostomy (SPC).

In male, both procedures (surgical and endoscopic) are not compete but quite balance in different treatment in different situation. Such as indwelling catheter for trauma of urethra stretch, suprapubic cystotomy or endoscopic stenting for incomplete rupture. Suprapubic cystotomy or endoscopic realignment for complete rupture (minimal distraction defect) and surgical realignment (wide distraction defect) Injuries to the bladder, neck of the bladder, or rectum dictate immediate exploration for repair, but not necessarily the location of the urethral injury. Treatment modalities for women determine the level of urethral injury, including urgent retropubic realignment or in the case of proximal injury need suturing and injury in lower part (distal) by advance transvaginal urethral process.

In female patients, it is of utmost importance to have a comprehensive physical examination to avoid misdiagnosis or delayed diagnosis. In the current study, a female patient presenting with a history of blunt trauma injury was not diagnosed until life-threatening sepsis was detected. Patients with a history of road traffic accidents, blunt, or penetrating injuries must be thoroughly examined for bleeding per urethra. In a study by Perry and Husmann, it was found that two-thirds of patients would have been promptly diagnosed if they had been examined properly.

Kashefi et al. assessed the urethral injuries in male secondary to improper insertion of a catheter. A total of 14 out of 4,310 patients suffered urethral injuries due to improper insertion of a urinary catheter. In study subjects penile pain as well as bleeding were the very important symptoms. They used an education program that was designed to promote catheter safety and basic urological anatomy. The authors then compared the pre- and post-intervention rates of urethral injuries secondary to catheterization. It was found that the post-intervention rate was significantly reduced to 0.7 per 1,000 adult males (p=0.006). Therefore, it is recommended to implement such courses in our setting as well to promote catheter safety in male patients to avoid urethral injuries.

**CONCLUSION**

Urethral injuries were more common in male patients. The most common cause of injury was iatrogenic, followed by blunt/crushing trauma. The most common post-intervention complication was stricture formation followed by extravasation or voiding difficulties. Education modules on urological anatomy and catheter safety along with a thorough physical examination can aid in the prompt diagnosis and prevention of such injuries.

**Author’s Contribution:**

Concept & Design of Study: Riaz Hussain Mangrio
Drafting: Sajid Ali Abbasi, Vijia Kumar Gennani
Data Analysis: Malik Hussain Jalbani, Azizullah Mirani,
Ahsanullah Malik
Revisiting Critically: Riaz Hussain Mangrio, Sajid Ali Abbasi
Final Approval of version: Riaz Hussain Mangrio

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

REFERENCES

Frequency of Stones, Strictures and Carcinoma Head of Pancreas in Patients with Obstructive Jaundice

Shahbaz Ahmed Qureshi¹, Sana Altaf¹, Shahnaz Noor², Sadia Bashir², Javeria Shahbaz³ and Anas Ahmed Qureshi⁴

ABSTRACT

Objective: The objective of this study is to know the frequency of choledocholithiasis, biliary stricture and carcinoma head of pancreas among patients having obstructive jaundice.

Study Design: Cross-sectional, descriptive study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, four Medical units and four Surgical units at Bahawal Victoria Hospital Bahawalpur from January 2019 to June 2019.

Materials and Methods: A total of 201 patients diagnosed as obstructive jaundice with serum bilirubin level of greater than 3 mg/dl were included. The Intra and Extra hepatic biliary channels, presence of gall stones, common bile duct and any abdominal mass were seen by ultrasonography abdomen. Endoscopic retrograde cholangiopancreatography also done in patients with obstructive jaundice. Data regarding choledocholithiasis, carcinoma head of pancreas and biliary stricture was collected.

Results: This study included age range from 40 to 70 years with mean age of 52.24 ± 5.34 years. Majority of the patients were between 51 to 60 years age groups i.e. 57.8%. Majority of patients were females (62.7%). Mean weight was 78.78 ± 12.52 Kg and mean BMI was 26.29±2.87 kg/m². The frequency of choledocholithiasis was 33.3%, carcinoma of head of pancreas 30.8% and biliary stricture was 7%.

Conclusion: The results concluded that Choledocholithiasis is the commonest benign etiology among patients with obstructive jaundice. It is more prevalent in females. This study shows that early diagnosis and intervention has significant role for the prognosis of patients with obstructive jaundice.

Key Words: Obstructive Jaundice, Choledocholithiasis, Carcinoma head of pancreas, Biliary stricture

INTRODUCTION

The deposition of bilirubin pigments in sclera, mucous membranes and skin causes yellowish discoloration known as jaundice.¹ The biliary obstruction at any level from liver up to gall bladder and small intestine results in obstructive jaundice.² Obstructive jaundice could be intra-hepatic or extra hepatic. The most common intrahepatic causes are cirrhosis, hepatitis and hepato-cellular carcinoma.³

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Printed: October, 2020

The intra-ductal and extraductal obstruction are further subdivision of the extra hepatic causes. Choledocholithiasis, biliary strictures, neoplasm, primary sclerosing cholangitis and worm infestation (parasites) can lead to intraductal obstruction. The biliary channels compression externally by pancreatitis, neoplasm and cystic duct stones with gall bladder distension consequently can cause extra ductal obstruction.⁴-⁶

Treatment of symptomatic gallstone disease by laparoscopic cholecystectomy (LC) in late 1980’s is associated with high incidence of BDIs than open cholecystectomy (OC). The incidence of BDIs shows a rise from 0.1-0.2% to as high as 0.8-1.4% in different studies.⁷ Although learning curve effect decreases the incidence of complications but it is still at least twofold compared to OC.⁸ Obstructive jaundice is concerning usually with the conditions like: Tumors (Carcinoma head pancreas, cholangiocarcinoma), Parasitic Infections (Hepato-biliary complicated hydatid disease, Ascarisis), Benign Stricture, Acute inflammation (cholangitis, Mirizzi syndrome). Congenital disease (Choledochal cyst).⁹

Pancreatic tumors that cause biliary obstruction usually arise from the head and periampullary pancreatic region due to the fact that the bile duct courses through the...
pancreatic head. The jaundice may show more advanced-stage disease due to malignancies in ampullary region which leads to biliary obstruction in 64-77% of cases.\textsuperscript{10,11} The narrowed common bile duct leads to bile duct stricture which may prevent the bile flow into the intestine. Chalya PL and his associates have found the frequency of Choledocholithiasis by 62.5%, Biliary stricture by 25% and Carcinoma head of pancreas by 64.7% in patients with obstructive jaundice.\textsuperscript{12} Another study reported by Siddique K and his associates in patients with obstructive jaundice showed that frequency of Choledocholithiasis 35%, Carcinoma head of pancreas 30% and Biliary stricture 5%.\textsuperscript{13} The data regarding the frequency of Choledocholithiasis, Biliary stricture and Carcinoma head of pancreas in Pakistani cohort studies is limited. The different causes at various centers shows a big discrepancy and it is very important to know the nature of obstruction and its existence because a bad-chosen treatment can lead to high morbidity and mortality in local population.

**MATERIALS AND METHODS**

The study was Cross-sectional and carried out in the Department of Gastroenterology, four Medical units and four Surgical units at Bahawal Victoria Hospital Bahawalpur from January 2019 to June 2019 after taking ethical approval. The calculated sample size for the study at 95% level of confidence, 5% margin of error and 5% anticipated population proportion (biliary stricture)\textsuperscript{13} was 201. Male and female patients between 25-75 years of age with clinical diagnosis of obstructive jaundice and serum bilirubin level > 3mg/dl through non-probability consecutive sampling method were included in our study. Patients with liver cirrhosis and pregnant females were excluded from the study. Data was collected by using preformed, pretested questionnaire. Demographic information of patients (name, age, gender, weight, BMI) were noted. Trans-abdominal ultrasonography carried out for all patients to look for biliary channels, common bile duct, gall stones or abdominal mass. Endoscopic retrograde cholangiopancreatography (ERCP) was performed in patients of obstructive jaundice where it was indicated. Patients with mass on ultrasound in conjunction with dilated bile ducts and serum bilirubin level >3 mg/dl were taken as cases of obstructive jaundice. The presence of echogenic rounded focus with size ranges between 2 to > 20mm in bile duct on ultrasound was taken as choledocholithiasis. The short segment Bile duct with irregular and shouldered margins along with >1.5mm thickness and on arterial and or portal venous phase enhancement of duct walls on ERCP (Endoscopic retrograde cholangiopancreatography) was taken as biliary stricture. Presence of cancerous cells in histopathology report of the pancreatic cells taken by ERCP was taken as carcinoma head of pancreas. The final diagnosis was concluded after the results of these investigations and histopathology. All procedures performed by a consultant gastroenterologist having post fellowship experience of at least 5 years. The analysis of data was done by statistical analysis program (SPSS version 22). The frequency and percentage were computed for qualitative variables like gender, different age groups, choledocholithiasis, biliary stricture and carcinoma head of pancreas. Mean ±SD was presented for quantitative variables like age, weight and BMI. Effect modifiers like age, gender and BMI were controlled by stratification. Post stratification chi square test was applied p <0.05 was considered statistically significant.

**RESULTS**

The study showed the age ranges from 40 to 70 years with mean age of 52.2±5.3 years. Most patients were between 41 to 60 years age groups i.e. 84.6%. About two third patients were females i.e. 126 (62.7%). Mean weight of the patients was 78.9±12.5 Kg and mean BMI of the respondents was 26.29±2.87 kg/m\textsuperscript{2}. Choledocholithiasis was diagnosed in 67(33.3%) patients, biliary stricture in (7%) and carcinoma head of pancreas in 62(30.8%) patients with obstructive jaundice. Stratification of choledocholithiasis, biliary stricture and carcinoma head of pancreas in respect of age groups, gender and BMI are shown in Table 2.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-40</td>
<td>12</td>
<td>5.9%</td>
</tr>
<tr>
<td>41-60</td>
<td>170</td>
<td>84.6%</td>
</tr>
<tr>
<td>61-75</td>
<td>19</td>
<td>9.5%</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>75</td>
<td>37.3%</td>
</tr>
<tr>
<td>Female</td>
<td>126</td>
<td>62.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choledocholithiasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>67</td>
<td>33.3%</td>
</tr>
<tr>
<td>No</td>
<td>134</td>
<td>66.7%</td>
</tr>
<tr>
<td>Biliary Stricture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>7.0%</td>
</tr>
<tr>
<td>No</td>
<td>187</td>
<td>93.0%</td>
</tr>
<tr>
<td>Carcinoma Head of Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62</td>
<td>30.8%</td>
</tr>
<tr>
<td>No</td>
<td>139</td>
<td>69.2%</td>
</tr>
</tbody>
</table>
BMI of patients showed a significant association with choledocholithiasis (p=0.001) and carcinoma head of pancreas (p<0.001).

Table No.3: Stratification of choledocholithiasis, biliary stricture and carcinoma head of pancreas with respect to age, gender and BMI of patients (n=201)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Choleldocholithiasis</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-40</td>
<td>06 (50%)</td>
<td>06 (50%)</td>
</tr>
<tr>
<td>41-60</td>
<td>55 (32.4%)</td>
<td>115 (67.6%)</td>
</tr>
<tr>
<td>61-75</td>
<td>6 (33.3%)</td>
<td>13 (68.4%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (25.3%)</td>
<td>56 (74.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>48 (38.1%)</td>
<td>78 (61.9%)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>02 (20%)</td>
<td>08 (80%)</td>
</tr>
<tr>
<td>20-30</td>
<td>65 (38.7%)</td>
<td>103 (61.3%)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>00 (0%)</td>
<td>23 (100%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-40</td>
<td>01 (8.3%)</td>
<td>11 (91.7%)</td>
</tr>
<tr>
<td>41-60</td>
<td>12 (7.1%)</td>
<td>158 (92.9%)</td>
</tr>
<tr>
<td>61-75</td>
<td>01 (5.3%)</td>
<td>18 (94.7%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>02 (2.7%)</td>
<td>73 (97.3%)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (9.5%)</td>
<td>114 (90.5%)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>01 (10%)</td>
<td>09 (90%)</td>
</tr>
<tr>
<td>20-30</td>
<td>13 (7.7%)</td>
<td>155 (92.3%)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>00 (0%)</td>
<td>23 (100%)</td>
</tr>
<tr>
<td><strong>Carcinoma Head of Pancreas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-40</td>
<td>04 (33.3%)</td>
<td>08 (66.7%)</td>
</tr>
<tr>
<td>41-60</td>
<td>52 (30.6%)</td>
<td>118 (69.4%)</td>
</tr>
<tr>
<td>61-75</td>
<td>06 (31.6%)</td>
<td>13 (68.4%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (34.7%)</td>
<td>49 (65.3%)</td>
</tr>
<tr>
<td>Female</td>
<td>36 (28.6%)</td>
<td>90 (71.4%)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>01 (10%)</td>
<td>09 (90%)</td>
</tr>
<tr>
<td>20-30</td>
<td>38 (22.6%)</td>
<td>130 (77.4%)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>23 (100%)</td>
<td>00 (0%)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The obstructive jaundice may lead to increase morbidity and mortality leading to a diagnostic and therapeutic challenge for gastroenterologists.\(^{14}\) In countries like Pakistan, due to limited health facilities and illiteracy patients presents very late when they develop advanced disease. Moreover, in different cities, the non-availability of advanced diagnostic modalities like ERCP, CT scan, MRCP, PTC and therapeutic facility like T-tubes is a big challenge.\(^{15}\)

The results of our study showed that the incidence in middle aged patients of obstructive jaundice was seen more commonly. The most common cause was Choledocholithiasis in 33.3% while carcinoma head of pancreas in 30.8%. Khurram et al in his study showed choledocholithiasis as most common cause of biliary obstruction.\(^{16}\)

The female gender in the study were amongst more common having stone disease; a finding similar to that of other workers.\(^{17}\) The females showed increased incidence of Obstructive jaundice because the gall stones are more commonly present among them.\(^{18,20}\)

The study done by Vargas and Astete amongst male patients undergoing ERCP showed that choledocholithiasis as first and carcinoma of common bile duct as third common diagnosis.\(^{21}\)

Malignancies leading to obstruction of biliary channels are ampullary carcinomas, tumors of gall bladder extending into CBD, tumors leading metastasis (most common from gastrointestinal tract), cholangiocarcinoma and secondary lymphadenopathy at the level of porta hepatis.\(^{22}\) Both genders are equally affected by malignancies of Biliary channels.\(^{23}\)

Choledochal cyst is the congenital cystic dilatations of either or both intra and extra-hepatic biliary channels. The high prevalent areas are in Asia, like Japan, and are more common 3 to 4 times in females.\(^{15,22}\) Our study showed that biliary strictures were present in 7% of cases. After cholecystectomy few other studies showed traumatic strictures and ligation of CBD as one of the commonest causes.\(^{24,26}\)

In developing countries like Pakistan, due to non-availability of advanced diagnostic and therapeutic modalities in every city, trans-abdominal ultrasonography is one of the non-invasive, easily available and best baseline imaging modalities in patients with obstructive jaundice because the results showed high sensitivity and specificity to find the cause.

**CONCLUSION**

It is concluded that obstructive jaundice more common in females. Choledocholithiasis was the most common cause in these patients. The results of our study suggest that early diagnosis and intervention had a significant role to reduce the morbidity and mortality along with improving the prognosis of patients with obstructive jaundice.

**Author’s Contribution:**

Concept & Design of Study: Shahbaz Ahmed Qureshi, Sana Altaf Qureshi

Drafting: Anas Ahmed Qureshi

Data Analysis: Shahnaz Noor, Javeria Shahbaz

Revisiting Critically: Sadia Bashir, Javeria Shahbaz

Final Approval of version: Shahbaz Ahmed Qureshi
Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES


Frequency of Vitamin D Deficiency in Patients with Atypical Chest Pain in Cardiac Out Patient Department

Gian Chand, Faisal Ahmed, Imran Khan Sandeelo, Nouman Kakepoto, Qaiser Aziz and Mehfooz Ali Shah

ABSTRACT

Objective: To assess the frequency of vitamin D deficiency in patients who present with atypical chest pain in cardiac OPD.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the department of Cardiology, Liaquat National Hospital, Karachi from Dec 2017 to June 2018.

Materials and Methods: Total 305 patients of either gender with age 30 to 70 years had atypical chest pain were included in the study. Demographics and clinical history were taken from patients. Blood sample for vitamin D level was taken and sent to the institutional laboratory and results were collected to assess the outcome i.e frequency of vitamin D deficiency. The confounding variables were tested by strictly following the requirements for inclusion and exclusion.

Results: There were 210 male and 95 female patients. The mean age of study subjects was 49.17±9.73 years. The vitamin D deficiency was observed in 81 (26.6%) patients. The vitamin D deficiency was significantly associated with age, sun exposure, economical status, and educational status.

Conclusion: Among patients with asymptomatic chest pain, high proportion of Vitamin D deficiency was observed. It was significantly associated with age, sun exposure, economical status and educational status.

Key Words: Vitamin D, Deficiency, Atypical Chest Pain.

INTRODUCTION

Conditions ranging from mild and self-limited (e.g. chest wall pain) to extreme (e.g. anxiety disorder) or life-threatening (e.g. dysfunctional angina, aortic dissection, pulmonary embolism) can cause chest pain. Accu-skeletal symptoms (e.g., costochondritis, Tietze syndrome, costoternal syndrome) are the least severe causes of chest pain. Accu-skeletal detection of life-threatening and significant causes of chest pain must be done without over-testing and over-treating patients with less serious causes. A longitudinal study reported 1,212 consecutive adults over 35 years of age who presented with chest pain to a primary care clinic and monitored them for six months to establish the final diagnosis.1,2

Chest pain is a leading cause of outpatient visits and accounts for more than 6 million emergency room visits in the United States.3,4 Following serious cardiopulmonary conditions, musculoskeletal pain is considered.

Vitamin D is important in bone health, but recent research also points out its essential role in extra-skeletal functions, including skeletal muscle growth, immune and cardiopulmonary functions and inflammatory modulation.5 Although there is debate about what determines deficient or optimum serum levels of 25-OHD, levels below 50 nmol / L (20 ng / mL) lead to increased bone turnover markers and increased parathyroid hormone (PTH) levels.4,6

Vitamin D plays an important role in many places throughout the body, including the development and calcification of the bones.7 Vitamin D is critical for bone and mineral metabolism, and it is established that vitamin D deficiency can cause rickets and osteomalacia.8 The adult form of rickets, Osteomalacia, may cause diffuse bone pain. Tenderness to the anterior tibia, sternum, and costochondral joints that suggest osteomalacia and vitamin D depletion.4,9 Even though bone biopsy is the gold standard for osteomalacia, it is usually not performed. Bone pain and vitamin D concentrations below 25 nmol / L (10 ng / mL) are
often appropriate for the osteomalacia clinical diagnosis. There is research performed locally and globally to determine the vitamin D deficiency in patients with atypical chest pain. The current research is designed to determine the actual prevalence of vitamin D deficiency in patients with atypical chest pain in the local population, despite the prevalence observed in these studies. The outcome of this research may be helpful in determining the current severity of vitamin D deficiency in atypical chest pain and may also be helpful for physicians / cardiologists to include vitamin D deficiency as part of the assessment when dealing with patients with atypical chest pain.

**MATERIALS AND METHODS**

This single center, non-probability consecutive, cross sectional study was conducted from Dec 2017 to June 2018. Study population in the inclusion criteria was either gender with 30 to 70 years of age, who were diagnosed cases of acute coronary syndrome and de novo lesion (> 70% lesion) in a native coronary artery after angiography, in the outpatient clinics and inpatients attending department of Cardiology at Liaquat National Hospital Karachi. Following approval by Liaquat National Hospital’s ethical committee, all qualifying patients meeting the inclusion requirements were notified and detailed procedure information was given, and a written informed consent was obtained from all patients by the principal investigator. Detailed demographics and clinical history were taken from patient by principle investigator. Was advised vitamin D level and then blood sample for vitamin D level were taken by venipuncture by a well-trained senior staff under supervision of primary investigator after that sample was sent to well-equipped laboratory and results were collected and all the data were recorded on a pre designed proforma. The confounding variables were tested by strictly following the requirements for inclusion and exclusion.

**Statistical analysis:** Patient data were compiled and analyzed through statistical package for Social Sciences (SPSS) Version 21. Frequency and percentage were computed for qualitative variables like gender, economical status, educational status, diabetes mellitus, vitamin D deficiency. Mean±SD were calculated for quantitative variable i.e. age, sun exposure and HbA1c. The stratification was done on gender, age, economical status, educational status, diabetes mellitus and sun exposure, to see the effect of these modifiers on Vitamin D Deficiency using Chi-square test. P≤0.05 was considered as significant.

**RESULTS**

The research included total patients of either gender between 30 and 70 years of age who had asymptomatic chest pain to assess the prevalence of vitamin D deficiency. SPSS used to measure the descriptive statistics. It posed qualitative variables in terms of frequency and percentages. This described quantitative variables in terms of mean and standard deviations. Stratification was performed to see the impact on outcome of the modifiers. The post-stratification chi square test was applied taken p-value <0.05 as significant.

The results showed that there were 210 male and 95 female patients. (Table-2). The mean age of study subjects was 49.17±9.73 years, with range of 40(30–70) years. The distribution of age is presented in Graph-1. The descriptive statistics of age is presented in Table-1. The mean sun exposure was 3.78±0.749 hours per day, with range of 3(2–5) hours per day (Table-1).

The mean duration of symptoms was 4.28±0.84 hours, with range of 3(3–6) hours. (Table-1). The mean HbA1c was 7.25±2.09%, with range of 8.6(4.3–12.9) %. (Table-1)

The results about economic status showed that monthly income of 27.2% patients was <25,000 rupees. 43.9% had monthly income of 25,000–50,000 rupees and it was observed >50,000 rupees in 28.9% patients. (Table-2)

The educational status showed that 7.9% patients were illiterate, 15.4% had education till primary, 30.2% had completed their education till secondary and rest of the 46.6% patients were got education till graduation. (Table-2)

Among total study subjects 211 were found diabetic and 94 were found non diabetic. (Table-2) The main outcome i.e. vitamin D deficiency was observed in 81(26.6%) patients. (Table-2) The stratification according to gender, age & sun exposure was done. Post stratification association of outcome was observed with these modifiers using chi square test considered p≤0.05 as significant. The results showed that vitamin D deficiency was significantly associated with age (p<0.01), sun exposure (p<0.01), while it was not significantly associated with gender (p=0.366). (Table-3)

| Table No.1: Descriptive statistics of age, Sun exposure, duration of symptoms, HbA1c level |
|-----------------------------------------------|-------------------|-----------------|-----------------|-----------------|
| Statistics | Age (Years) | Sun exposure (hrs/day) | Duration of symptoms (hrs) | HbA1c level (%) |
| Minimum | 30 | 2 | 3 | 4.3 |
| Maximum | 70 | 5 | 6 | 12.9 |
| Mean | 49.17 | 3.78 | 4.28 | 7.25 |
| Std. Deviation | 9.73 | 0.749 | 0.84 | 2.09 |
Table No.2: Frequency distribution of gender, economical status, educational status, diabetes mellitus, vitamin D deficiency (n=305)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency(n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>210</td>
<td>68.9%</td>
</tr>
<tr>
<td>Female</td>
<td>95</td>
<td>31.1%</td>
</tr>
<tr>
<td>Total</td>
<td>305</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Economical status</th>
<th>Frequency(n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25,000 per month</td>
<td>83</td>
<td>27.2%</td>
</tr>
<tr>
<td>25,000 – 50,000 per month</td>
<td>134</td>
<td>43.9%</td>
</tr>
<tr>
<td>&gt; 50,000 per month</td>
<td>88</td>
<td>28.9%</td>
</tr>
<tr>
<td>Total</td>
<td>305</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Educational status</th>
<th>Frequency(n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illiterate</td>
<td>24</td>
<td>7.9%</td>
</tr>
<tr>
<td>Primary</td>
<td>47</td>
<td>15.4%</td>
</tr>
<tr>
<td>Secondary</td>
<td>92</td>
<td>30.2%</td>
</tr>
<tr>
<td>Graduate</td>
<td>142</td>
<td>46.6%</td>
</tr>
<tr>
<td>Total</td>
<td>305</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diabetes mellitus</th>
<th>Frequency(n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>211</td>
<td>69.2%</td>
</tr>
<tr>
<td>No</td>
<td>94</td>
<td>30.8%</td>
</tr>
<tr>
<td>Total</td>
<td>305</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamin D deficiency</th>
<th>Frequency(n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>81</td>
<td>26.6%</td>
</tr>
<tr>
<td>No</td>
<td>224</td>
<td>73.4%</td>
</tr>
<tr>
<td>Total</td>
<td>305</td>
<td>100%</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Chest pain is a leading cause of hospital visits and accounts for over 6 million emergency room visits in the United States. Despite extreme cardiopulmonary disorder, musculoskeletal causes of chest pain, including costochondritis, are usually linked to the final diagnosis.

While there are several reports of osteomalacia and vitamin D deficiency associated with chest pain, we are not aware of any literature reports of vitamin D deficiency induced costochondritis.

Vitamin D is essential to bone health, and serum 25-OH vitamin D (25-OHD) is predictive for body stores of vitamin D. Circulating 25-hydroxyvitamin D [25(OH)D] is a robust and reliable marker of vitamin D status and has been used by numerous agencies in the establishment of vitamin D dietary requirements and for population surveillance of vitamin D deficiency or inadequacy. Although there is debate about what determines deficient or optimum serum levels of 25-OHD, levels below 50 nmol / L (20 ng / mL) contribute to increased bone turnover markers and increased parathyroid hormone (PTH) levels. Another study concluded that deficient mineralization of the bone was evident in serum 25-OHD patients less than 75 nmol / L (30 ng / mL) but none above that threshold.

Milder types of deficiency of vitamin D can cause a continuum of pain along the sternum and cost chondral junctions similar to racket and osteomalacia patients. Costochondritis remains a poorly described entity but may be a milder, earlier type of osteomalacia associated with higher 25-OHD serum levels. Importantly, the deficiency of osteomalacia and vitamin D may not be considered when a patient has symptoms consistent with costochondritis, as checking for vitamin D deficiency has not been documented in such cases, nor is it standard. An analysis of the literature showed no documented cases of vitamin D-related costochondritis, and only a few case reports of vitamin D-related chest pain.

In our study, the vitamin D deficiency was observed in 81(26.6%) patients. The male representation was more than females and hence the percentage of vitamin D deficiency was more found in males but difference was not significant. Most of the patients were of age less than or equal to 45 years. But in our study, overall more patients were of age >45 years. The vitamin D was also found deficient in patient who had sun exposure less than or equal to 3 hours. Most of the vitamin D deficient patients earning >50,000 per month and were graduates.

1,25(OH)2D regulates the development of renin, one of the most essential hormones for blood pressure regulation. There is also biological evidence that African Americans, who have been shown to be at higher risk of vitamin D deficiency, also have a higher risk of hypertension and cardiovascular disease.

Table No.3: Frequency and association of vitamin D deficiency according to gender, age groups & sun exposure (n=305)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Vitamin D deficiency</th>
<th>TOTAL</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>59</td>
<td>151</td>
<td>210</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>73</td>
<td>95</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>224</td>
<td>305</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Vitamin D deficiency</th>
<th>TOTAL</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤45 years</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>58</td>
<td>104</td>
<td>0.001</td>
</tr>
<tr>
<td>&gt;45 years</td>
<td>35</td>
<td>166</td>
<td>201</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>224</td>
<td>305</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sun exposure</th>
<th>Vitamin D deficiency</th>
<th>TOTAL</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3 Hrs/day (n=104)</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>58</td>
<td>104</td>
<td>0.001</td>
</tr>
<tr>
<td>&gt;3 Hrs/day (n=201)</td>
<td>35</td>
<td>166</td>
<td>201</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>224</td>
<td>305</td>
</tr>
</tbody>
</table>
randomized, placebo-controlled, double-blind clinical trial of 148 elderly women (mean age, 74 years) revealed vitamin D and calcium to be more effective in lowering systolic blood pressure than calcium. While this research indicates that increased vitamin D is associated with lower risk of hypertension, conflicting results have been recorded in some studies. Jorde and Bonaa recorded no correlation between intake of vitamin D and blood pressure. However, as with hypertension, conflicting results indicate that increased vitamin D may be a causative factor or have no role in cardiovascular disease. 1,25(OH)2D acts as an immunomodulatory, reducing the production of cytokines and the proliferation of lymphocytes involving the destruction of insulin-β cells in the pancreas and the development of type 1 diabetes mellitus. Moreover, β-islet cells express VDR and respond to 1,25(OH)2D by increasing the production of insulin.

A birth cohort research involving 10,366 children in Finland found that higher dietary supplementation of vitamin D was associated with a decreased risk for type 1 diabetes mellitus. Children who routinely received the required supplementary dose of 2000 IU / d of vitamin D in their first year of life had a prevalence ratio of 0.22 (range, 0.05-0.89) for type 1 diabetes mellitus relative to those who regularly received less than 2000 IU / d. Likewise, Stene et al recorded a lower risk of type 1 diabetes mellitus in children of mothers who received cod liver oil throughout pregnancy. HbA1c is believed to be an indicator of average blood glucose levels over the preceding 2 to 3 months and thus a long-term glucose homeostasis marker. Abnormalities that result from changes in insulin secretion and insulin-stimulated glucose uptake in the muscle and fat tissues. In vitro experiments and laboratory animal research indicate potential mechanisms for effects on both insulin production and insulin sensitivity of the active form of vitamin D, i.e. 1,25(OH)2D, as reviewed by Pittas and DawsonHughes.

Patients with type 2 diabetes and increased rates of HbA1c have an elevated risk of cardiovascular disease and overall mortality relative to patients with lower levels of HbA1c. Sensible exposure to the sun will provide a sufficient quantity of vitamin D3, which is retained in body fat and released in winter when vitamin D3 cannot be produced. Arms and legs exposure for 5 to 30 minutes (depending on time of day, season, latitude and pigmentation of the skin) between 10 a.m. And on 3 p.m. Twice a week, exposure to a minimum erythema dose while wearing a bathing suit is equal to ingestion of approximately 20,000 IU of vitamin D2. The skin is highly capable of producing vitamin D3, including in the elderly, to minimize the risk of fracture. The majority of tanning beds emit 2 to 6 per cent ultraviolet B radiation and are a recommended source of vitamin D3 when used in moderation.

CONCLUSION

Chest pain is a traditional symptom of presentation and is caused by cardiac and noncardiac disorders. Physicians should identify vitamin D deficiency in patients with chest pain, and elicit any risk factors for deficiency. Costochondritis patients at risk of vitamin D deficiency should be screened with a serum level of 25-OHD and treated if vitamin D deficiency is detected. In conclusion, among patients with asymptomatic chest pain, high proportion of Vitamin D deficiency was observed. It was significantly associated with age, sun exposure, economical status and educational status. Both male and female can be affected with the deficiency. Sensible sun exposure and the use of supplements are needed to fulfill the body’s vitamin D requirement.

Author’s Contribution:
Concept & Design of Study: Gian Chand
Drafting: Faisal Ahmed, Imran khan Sandeelo
Data Analysis: Nouman Kakepoto, Qaiser Aziz, Mehfooz Ali Shah
Revisiting Critically: Gian Chand, Faisal Ahmed
Final Approval of version: Gian Chand

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

REFERENCES


Alterations in Serum Creatinine and Urinary Proteins in Albino Mice After Exposure to Different Doses of Anhydrous Cadmium Chloride Via Oral and Intraperitoneal Routes
Nasim Aslam Ghumman¹, Nosheen Khurrum¹, Farwa Shamsi² and Qurrat ul Ain Javaid¹

ABSTRACT

Objective: Cadmium (Cd), a heavy metal has a potential to develop toxicity in various organs especially kidney and liver. Serious toxicity of cadmium became the centre of attention because of its association with neoplastic and non-neoplastic lesions in various organs and tissues. The objective of this study was to evaluate the detrimental effects of cadmium on kidney leading to increased urinary proteins and serum creatinine.

Study Design: An experimental study on albino mice

Place and Duration of Study: This study was conducted at the Department of Morbid Anatomy and Histopathology; University of Health Sciences, Lahore for 8 weeks in the year 2014.

Materials and Methods: Albino mice (n=72) were randomly divided in groups as control group and 5 experimental groups A, B, C, D and E with 12 mice in each group. In this experiment, cadmium was used as anhydrous cadmium chloride (CdCl₂) orally and intraperitoneally on alternate days for 8 weeks in a dose of 5mg/kg body weight. Bovine serum albumin was also used once in group D to induce serum sickness leading to development of glomerular damage.

Results: This experimental work revealed the biochemical alterations in kidney like proteinuria and serum creatinine because of cadmium. However, these biochemical changes were proportional to the dose and route of introduction of cadmium chloride.

Conclusion: Cadmium is a toxic heavy metal that can lead to progressive renal failure. Cadmium toxicity leads to progressive damage to glomeruli. In this study biochemical changes were observed that were proportional to different doses of cadmium. As this chemical is a naturally occurring toxicant that exists everywhere in air, soils, foodstuff and water, hence to control the emission of this toxicant should be of high priority for better healthcare of community.

Key Words: Nephrotoxicity, proteinuria, intraperitoneal, Bovine serum albumin, serum sickness.

INTRODUCTION

Humans frequently come across a variety of noxious substances that are probably toxic for kidney. Heavy metal noxious agents such as lead, cadmium, mercury, copper, uranium, and bismuth are some of the environmental nephrotoxins to which humans are exposed¹. Contact with heavy metals is potentially harmful.

As the kidney has the ability to reabsorb and gather metals with a valence of two, therefore kidney is the chief target organ of heavy metal toxicity². Cadmium is a momentous toxin present in our environment³. Cadmium was discovered by Friedrich Stromeyer⁴ and Karl Samuel Leberecht Hermann in 1817 in Germany as a contaminant in zinc carbonate⁵. Cadmium is enormously being utilized at conventional industrial level, as it is an essential constituent in production of batteries, predominantly in rechargeable nickel-cadmium batteries and is present in metal pigments and coatings and is commonly used in electroplating⁶. Cd is also utilized as a barricade to modulate neutrons in nuclear fission⁷. Cd and its oxides have been utilized in black and white television phosphorous and in the green and blue phosphorous for image tubes in colour television⁸.

Cadmium exists in air as fine particulate, less than 10μm in size. Cd particulate is disseminated by air and ultimately either settles down by rain or snow or as dry deposits on ground or surface water. The fine
particulate of metal may persist in air for days to weeks and are carried away for thousands of kilometers. Cd occurs either dissipated or as part of indissoluble complexes in water. Soluble form of this metal is ambulant in water and in soil. A crucial source of cadmium in soil is from the phosphate fertilizers which is used for agricultural motives. Cadmium gets accumulated in plants, in root vegetables and shoots like rice, wheat, tobacco, peanuts or cocoa and also in animals like offal, mollusks and crustaceans. Other sources are food, alcoholic beverages and cigarette smoking. Cadmium is predominantly found in fruits and vegetables due to its high rate of soil-to-plant transfer. Biological half-life of Cd is long in individuals and gets assembled in fundamental organs, principally in kidney and liver. Cd levels are elevated in mushrooms and shellfish.

On the background of the statistics procured from human occupational exposure, Cd and Cd containing complexes were classified as group one human carcinogens by the International Agency for Research on Cancer (IARC) in 1993, which is part of the World Health Organization.

The general population comes across Cd by various routes. Injection is one of the major routes. There are certain areas where soil is momentously contaminated with Cd in the Jinzu and Kakehashi river valleys in Japan. In these regions, rice absorb metal from the soil and eventually lifetime eating of these rice contaminated with Cd, can cause grievous kidney and bone disease that is known as “Itai-Itai” illness, predominantly in females. Inhalation is the predominant route of exposure in occupationally exposed population.

Data from experiments on animals demonstrates that initially after exposure, cadmium in blood is bound to albumin and is particularly taken up by the liver. Within the liver, production of metallothionein is instigated by the cadmium. Metallothionein is a protein with low molecular weight and is involved in cadmium, zinc and copper metabolism. It acts as a detoxifying agent for cadmium and plays a central role in the transportation of cadmium from liver via blood to kidneys. It has a molecular weight of around 6500Da. Metallothionein may serve in a protective way by binding cadmium in a stable bio complex. In this way interference of cadmium with other cellular components is decreased and the acute effects normally seen after larger and acute exposure can be prevented.

Cadmium exposure can lead to both acute and chronic intoxications. After ingestion of higher concentrations of cadmium, the symptoms in the gastrointestinal tract include nausea, vomiting, abdominal pain, cramps, tenesmus and diarrhea. If cadmium-contaminated air is inhaled, it can lead to damage to mucous membranes. Other serious effects like shortness of breath, pulmonary edema, pulmonary inflammation and emphysema can occur. Among smokers, development of chronic obstructive disease due to cadmium content in smoke has also been observed in various studies. Chronic inhalation of cadmium is also presumed to be a probable cause of lung carcinomas and evolution and progression of peripheral vascular disease.

Nephrotoxicity by cadmium may develop as a consequence of chronic ingestion or inhalation. In occupationally exposed population, prefatory signs of glomerular damage from cadmium are escalated elimination of high mass proteins like iron binding glycoproteins and albumin. Degree of detrimental effects on glomeruli is dose-dependent and once started, the glomerular damage is believed to be irreversible. Substantial cadmium exposure may also be a cause of diminished glomerular filtration rate and chronic renal failure. Cadmium induced nephrotoxicity has been reported in environmental pollution and industrial exposure.

Cadmium accumulates mainly in the proximal tubules of the kidney and causes kidney dysfunction after chronic exposure. The noxious effects of cadmium on the cells of proximal tubules cause decreased elimination of high mass proteins like iron binding glycoproteins and albumin. Degree of detrimental effects on glomeruli is dose-dependent and once started, the glomerular damage is believed to be irreversible. Substantial cadmium exposure may also be a cause of diminished glomerular filtration rate and chronic renal failure. Cadmium induced nephrotoxicity has been reported in environmental pollution and industrial exposure.

Cadmium accumulates mainly in the proximal tubules of the kidney and causes kidney dysfunction after chronic exposure. The noxious effects of cadmium on the cells of proximal tubules cause decreased elimination of low molecular weight proteins that ultimately results in increased excretion of these proteins in urine, so-called ‘tubular proteinuria’

MATERIALS AND METHODS

It was an experimental interventional, randomized controlled study in adult mice. Seventy-two male and female albino mice of BALB/c strain, 6-8 weeks old weighing 30 + 5g, were included in the study. Animals were separated gender wise in different cages and maintained in the Animal House of the University of Health Sciences, Lahore under controlled environment (temperature 22-25°C, humidity 65% ± 5) and light and dark cycle of 12 hours each. Albino mice were segregated in 6 groups with one control group and 5 experimental groups each comprising of 12 mice. In this foregoing experiment, cadmium was used as cadmium chloride (CdCl2) orally and intraperitoneally on alternate days for 8 weeks. According to the body weight (5mg/kg body weight) the dose was calculated and mixed with distilled water (Table 1). The control group was given normal diet and plain tap water. Serum creatinine was measured at the end of the experiment by using commercially available kits (Randox CR510, LOT: 216982). Urinary proteins were determined by strip method (Roche Diagnostic GmbH). Blood samples from each group were collected by cardiac puncture. At the commencement of the experiment, proteinuria was measured of all the animals of all six groups. All the animals showing proteinuria even in traces were rejected and those animals were selected who showed no proteinuria. During the experiment proteinuria was taken as: at the end of 3 weeks, 5 weeks and 8 weeks.
Statistical Analysis: The data was entered and analyzed using SPSS 21.0. Mean ± S.E.M was given for quantitative variables (Serum creatinine and urinary proteins). Fisher exact test was applied.

RESULTS

72 male and female albino mice of 6-8 weeks age were selected and distributed into six groups with 12 mice in each group as A, B, C, D, E and control group. The experiment was started after one week of acclimatization. Urinary proteins were checked after 3, 5 and 8 weeks of experiment. Experiment was terminated after 8 weeks. Animals were sacrificed after taking blood sample for serum creatinine via cardiac puncture. Results were analyzed using Fischer’s Exact test and P value was found to be significant (Table 2,3). Alterations in urinary proteins and S/Creatinine are shown in the tables below.

Table No.1: Groups of experimental animals

<table>
<thead>
<tr>
<th>Group</th>
<th>Mice</th>
<th>Intervention</th>
<th>Dosage/Alternate day</th>
<th>Route</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>Normal diet</td>
<td>None</td>
<td>Oral</td>
<td>8 weeks</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>CdCl₂</td>
<td>5mg/kg</td>
<td>Oral</td>
<td>8 weeks</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>CdCl₂</td>
<td>10mg/kg</td>
<td>Oral</td>
<td>8 weeks</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>CdCl₂</td>
<td>15mg/kg</td>
<td>Oral</td>
<td>8 weeks</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>BSA(singal dose)+CdCl₂</td>
<td>250mg/kg + 10mg/kg</td>
<td>Intraperitoneal + Oral</td>
<td>8 weeks</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>CdCl₂</td>
<td>10mg/kg</td>
<td>Intraperitoneal</td>
<td>8 weeks</td>
</tr>
</tbody>
</table>

Table No.2: Proteinuria(Mg/Dl) at the Start of the Experiment

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Traces</th>
<th>30</th>
<th>100</th>
<th>500</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Proteinuria (mg/dl) after 3 weeks of the experiment

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Traces</th>
<th>30</th>
<th>100</th>
<th>500</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>4(33.3)</td>
<td>0.0</td>
<td>8(66.7)</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>2(16.7)</td>
<td>1(8.3)</td>
<td>9(75.0)</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>2(16.7)</td>
<td>0(0.0)</td>
<td>10(83.3)</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>7(58.3)</td>
<td>5(41.7)</td>
<td>0.0</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>1(8.3)</td>
<td>0(0.0)</td>
<td>6(50.0)</td>
<td>5(41.7)</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>1(1.4)</td>
<td>6(50.0)</td>
<td>20(16.7)</td>
<td>10(13.9)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Proteinuria (mg/dl) after 5 weeks of the experiment

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Traces</th>
<th>30</th>
<th>100</th>
<th>500</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>0(0.0)</td>
<td>4(33.3)</td>
<td>7(58.3)</td>
<td>1(8.3)</td>
<td>0.0</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>3(25.0)</td>
<td>7(58.3)</td>
<td>0.0</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>1(8.3)</td>
<td>9(75.0)</td>
<td>0.0</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>12(100)</td>
<td>0.0</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>1(8.3)</td>
<td>11(91.7)</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>8(11.1)</td>
<td>12(16.7)</td>
<td>40(55.6)</td>
<td>0(0.0)</td>
<td>72(100)</td>
</tr>
</tbody>
</table>

Proteinuria (mg/dl) after 8 weeks of the experiment

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Traces</th>
<th>30</th>
<th>100</th>
<th>500</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>4(33.3)</td>
<td>7(58.3)</td>
<td>1(8.3)</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>4(33.3)</td>
<td>8(66.7)</td>
<td>0.0</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>8(66.7)</td>
<td>2(16.7)</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>10(83.3)</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>10(83.3)</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>10(13.9)</td>
<td>27(37.5)</td>
<td>23(31.9)</td>
<td>72(100)</td>
<td></td>
</tr>
</tbody>
</table>
Table No.3: Serum Creatinine After 8 Weeks of the Experiment

<table>
<thead>
<tr>
<th>Groups</th>
<th>0.30-0.59 mg/dl n(%)</th>
<th>1.00-1.50 mg/dl n(%)</th>
<th>1.51-2.50 mg/dl n(%)</th>
<th>Total n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12(100)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>12(100)</td>
</tr>
<tr>
<td>A</td>
<td>4(33.3)</td>
<td>7(58.3)</td>
<td>1(8.3)</td>
<td>12(100)</td>
</tr>
<tr>
<td>B</td>
<td>4(33.3)</td>
<td>8(66.7)</td>
<td>0(0.0)</td>
<td>12(100)</td>
</tr>
<tr>
<td>C</td>
<td>2(16.7)</td>
<td>8(66.7)</td>
<td>2(16.7)</td>
<td>12(100)</td>
</tr>
<tr>
<td>D</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>10(83.3)</td>
<td>12(100)</td>
</tr>
<tr>
<td>E</td>
<td>0(0.0)</td>
<td>2(16.7)</td>
<td>10(83.3)</td>
<td>12(100)</td>
</tr>
<tr>
<td>Total</td>
<td>22(30.6)</td>
<td>27(37.5)</td>
<td>33(31.9)</td>
<td>72(100)</td>
</tr>
</tbody>
</table>

Statistical Analysis: Fisher's Exact Test = 63.851; P = 0.000 (<0.001)

Table No.4: Mean ± S.E.M of Serum Creatinine

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Mean</th>
<th>Std. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>.3817</td>
<td>.03362</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>1.0417</td>
<td>.15204</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
<td>1.0825</td>
<td>.13393</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>1.3383</td>
<td>.12410</td>
</tr>
<tr>
<td>D</td>
<td>12</td>
<td>1.9358</td>
<td>.08553</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>2.0700</td>
<td>.10054</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>1.3083</td>
<td>.08079</td>
</tr>
</tbody>
</table>

Serum creatinine was also analysed using ANOVA test. P value (<0.005) was found to be significant between and within the groups showing the significant difference in values of serum creatinine (Table 3). Standard error of mean (S.E.M) is shown in the bar chart 1.

DISCUSSION

Cadmium is a toxic metal that is present throughout the environment. In humans and animals, it accumulates primarily in kidneys and liver. In mammals, diet is the major route of exposure through which they are exposed to toxic metals. Important organs significantly kidney and liver are the fundamental target sites. The current experiment was designed to appraise the biochemical effects of CdCl₂ via oral and intraperitoneal route in totally different concentrations for 8 weeks. The purpose of this study was to provide an essence to understand the similar biochemical changes in humans. In this study, significant association has been found between dose of CdCl₂ and proteinuria. Significant number of mice developed proteinuria after oral exposure that was dose dependent. After 3 weeks, 40 mice showed proteinuria of 30mg/dl and among them the majority of the mice were from group C, B and A (oral groups). After 5 weeks duration, proteinuria was found in a significant number of mice that were 40. The majority of the animals was from group D and E, including all 12 mice of group D and 11 mice of group E, followed by group C, B and A with 9, 7 and mice respectively. After 8 weeks duration of the dose of CdCl₂, proteinuria of 500mg/dl was observed in a remarkable number of mice that were 23 in a total where 27 mice showed proteinuria of 100mg/dl. Again the majority was from group D and E with 500mg/dl proteinuria having 10 mice from each group. Hence this study shows that the mice which were given intraperitoneal dose of 250mg BSA once at the start of the experiment, followed by 10mg CdCl₂/kg body weight on alternate days, developed renal damage earlier and more in severity than the other groups which were receiving oral dose only. Therefore, this experiment shows that BSA produces autoimmunity in the form of serum sickness with increased capillary permeability causing increased vulnerability of glomeruli to damage by toxicants. It was also found that group E, receiving CdCl₂ via intraperitoneal route on alternate days, developed equivocal renal damage more severe than the oral groups. Therefore, these findings...
are consistent with the other studies describing that the earlier indication of kidney devastation is generally proteinuria\textsuperscript{27}.

This study also showed that there was a significant rise in serum creatinine levels among the animals. Normal range of serum creatinine is 0.43mg/dl + 0.14mg/dl in male mice and 0.45mg/dl + 0.07mg/dl in female mice\textsuperscript{28}. Remarkable rise in serum creatinine levels were observed in animals of group D and E. Ten animals from group D and ten from group E showed serum creatinine level up to 2.50gm/dl. Although these findings are parallel to damage to glomeruli that lead to proteinuria. Elevated levels of serum creatinine after cadmium exposure were observed by Abdel-Moneim and Said\textsuperscript{29}.

**CONCLUSION**

This study suggests that cadmium is one of the noxious heavy metals that can leads to toxicity in kidneys resulting in proteinuria and raised serum creatinine levels. These biochemical changes were observed to be proportional to different doses and routes of cadmium. Since cadmium is a cumulative toxin, the most important recommendation is to minimize or avoid known sources of exposure to cadmium.

**Author’s Contribution:**

Concept & Design of Study: Nasim Aslam Ghumman
Drafting: Nosheen Khurrum, Farwa Shamsi
Data Analysis: Qurrat ul Ain Javaid
Revisiting Critically: Nasim Aslam Ghumman, Nosheen Khurrum
Final Approval of version: Nasim Aslam Ghumman

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

**REFERENCES**


Objective: To explore the perception of students regarding Team Based Learning (TBL) in Pathology at Rashid Latif Medical and Dental College, Lahore.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Rashid Latif Medical and Dental College, Lahore, in December 2019.

Materials and Methods: A total of 151 students who were present at the time of survey in pathology third year MBBS class and expressed their consent for participation were enrolled in the study. A structured validated questionnaire was used as a study tool.

Results: A total of 151 undergraduate medical students responded to the questionnaire. The perceptions regarding team based learning was very satisfactory. Majority of the student agreed that team based learning (TBL) is a better teaching methodology for learning pathology.

Conclusion: Current teaching methods in medical colleges need to be improved. Team based Learning is a student centered learning. New teaching strategies should be implemented to engage student in learning.

Key Words: Team based learning, Pathology, Students, Medical

INTRODUCTION

Pathology is a branch of medicine that deals with the precise study and diagnosis of human disease. It bridges the clinical and non-clinical subjects making pathology an essential member of the treatment team. Here we engage the students in applying their knowledge of the mechanism of disease to diagnose prevent and treat the patient. In a traditional curriculum in our country, pathology is taught for two years in medical school. Traditional teaching methods are mainly in the form of didactic lectures, tutorial and practical classes. Teaching is mainly in the form of large groups. These methods are instructor focused and consists of the teacher introducing and explaining course material to the students. There is a passive transfer of information and application chance is minimal till the exams. Many active learning strategies are currently used worldwide in different medical schools like case based group discussion, problem based learning and workshops. These teaching strategies are resource intensive.

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Contact No: 0300-4166470
Email: sofia.khan@rlmc.edu.pk

Team based learning (TBL) is a format of active learning strategy for large groups. It was developed by Dr. Larry K Michaelsen and it was started in medical education in 2001. TBL is a method which is student centered, directed instructional methodology which is not resource intensive and can easily manage in large groups by one facilitator in less time than the didactic lecture. It is based on the constructivist learning theory in which the role of a teacher is being a facilitator and it enhanced problem solving skills, promote team work and encourage critical thinking. TBL has been introduced in several basic sciences settings medical education. This methodology provides students to apply knowledge during different activities like individual work, team work, problem solving and feedback. While it has been proven that engaging students in active learning increase attention span and helps to enhance learning. In this process learners get new knowledge from the environment, experience it and reconstruct it with long term memory. According to Michaelson, TBL allows the students to recognize the need to learn and to apply reasoning skills gained through critical thinking.

MATERIALS AND METHODS

A cross sectional survey was conducted after a team based learning (TBL) session for the pathology class. Orientation session for TBL was conducted by medical education department of Rashid Latif Medical and Dental College for the students and faculty. Through Convenient sampling, 151 students who were present in
pathology third year MBBS class were selected. After taking the consent, demographic data, perception about pathology as a subject and perception about TBL were collected. Students filled the printed and validated questionnaire provided by medical education department which acquires the perception about TBL. Kaiser-Meyer-Olkin Measure of Sampling Adequacy was 0.738 and Bartlett's Test of Sphericity was significant (p-value <0.001). Cronbach's Alpha reveals high reliability 0.798. Factor analysis reveals that there were three domains in the questionnaire student motivation, student's satisfaction and subject specific. There were 10 items in the questionnaire. The responses were strongly agreeing (SA), agree (A), no opinion (NO), disagree (DA), and strongly disagree (SD). The regular pathology class for the particular topic was comprised of 540 min and the TBL session was conducted, which only last for 60 min. Groups were displayed, comprising of 4-6 students in each group and team leader was selected by intergroup voting before the session. The TBL session was structured in four phases.

In Phase 1, students were engaged in pre-class individual preparation of the material. Objectives of the topic and study material were given to students two weeks prior the session.

In phase 2, students were engaged in IRAT (individual readiness assurance test). At the time of the session the students were particularly seated as in an examination format. IRAT was conducted by giving 12 MCQ to individual student and then collected after session. In TRAT (Team readiness assurance test) students worked in predefined groups led by a team leader. In order to facilitate group discussions students were seated in a circle with facing each other. Same MCQ were given to teams and marking was done on the cards. (Fig #2) After, IRAT and TRAT session faculty moderated a review of the MCQs of all the groups, those who disagree would allow defending their answers with logic and discussion. A feedback was given by the facilitator afterwards.

During Phase 3, students were engaged in application MCQs exercise in the form of clinical scenarios displayed though multimedia. Teams were allowed to discuss and analyze simultaneously. Teams simultaneously reported their answers to the large group by showing colored cards given to them. (Fig #1)

RESULTS

Among 155 medical students, 151 students (97.4%) participated in the survey. Female students were 55% while male were 45% (Fig 3). When asked about their perceptions about pathology (Table 1) most of the student thinks that pathology is an important subject and 75% think that was quite difficult to learn. But they didn’t enjoy attending lectures and didn’t gain more information during lectures. Only 20% of students have the knowledge about TBL before the session and no one has ever participated in any TBL session before. All the students agreed that TBL improved their team working and reasoning skills and they preferred TBL on didactic lectures. Among them, 84.3% students think that this strategy gave them motivation to learn pathology. About 90% of student wanted to include TBL in their pathology curriculum (Table#2).

<table>
<thead>
<tr>
<th>Students perceptions about learning Pathology Questions</th>
<th>Students %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Think that pathology is an important for medical students</td>
<td>90%</td>
</tr>
<tr>
<td>Think that subject is difficult to learn</td>
<td>75%</td>
</tr>
<tr>
<td>Student prefer more teacher student interaction</td>
<td>62%</td>
</tr>
<tr>
<td>Student enjoy attending lectures</td>
<td>30%</td>
</tr>
<tr>
<td>Think they gain more information during lectures</td>
<td>35%</td>
</tr>
<tr>
<td>Think that the curriculum content is more</td>
<td>80%</td>
</tr>
</tbody>
</table>
It helps to improve team working skills
- - - 23.6% 76.4% - 
It motivates me to learn Pathology
- 1.1% 14.6% 42.7% 41.6% - 
TBL improve my reasoning skills
- - 3.4% 43.8% 51.7% 1.1% 
It promotes better understanding of the subject matter.
1.1% - 6.7% 38.2% 49.4% 4.5% 
TBL stimulates my thinking
- 2.2% 3.4% 36.0% 57.3% 1.1% 
TBL help to reduce my misconceptions about the topic.
- 3.4% 6.7% 44.9% 43.8% 1.1% 
This type of teaching helps me to relate pathological principles to real life situation.
5.6% 10.1% 25.8% 34.8% 21.3% 2.4% 
It helps to gain an in-depth knowledge about the subject.
- 5.6% 5.6% 52.8% 33.7% 2.2% 
I prefer this type of teaching to didactic lectures.
1.1% 4.5% 3.4% 28.1% 62.9% - 
I feel TBL should be included in pathology curriculum
1.1% 2.2% 5.6% 25.8% 65.2% -

<table>
<thead>
<tr>
<th>DISCUSSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>The teaching methodology for pathology in our college is teacher centered and majority of the content is delivered through didactic lectures. While rest by tutorials, self-directed learning (SDL) and practical. In general student preferred student centered active learning strategies they didn’t enjoy didactic lectures as reported in our study. A study by Alamoudi A (^1) also gave same results. In our study 62% of student agreed that they need better teacher and student interaction which is also reported by a study from Alamoudi A, (^1) contrast to our study their students had the experience of attending TBL sessions but in our study this was the first experience. Our students encouraged new learning strategies which engage students in team building, problem solving and reasoning skills, which is also seen in a study by Fatmi M, (^6) Hameed S et al (^12) and a study by Alwahab A, (^2) in our study all the students find that TBL help in team building skills which is contrary to a study by Alamoudi A (^1) where only 42% of students enjoy working in teams. According to Azizam NA et al (^7) TBL help students to actively participate in learning which in turn help them in acquiring knowledge which is also in accordance with our study. In TBL constructivist theory of learning is implemented which results in improved learning process and in active learning strategy teachers act as facilitators.(^8) In our study, majority of students preferred TBL method which is consistent with other studies.(^8,10) In a study from Pakistan reported by Hameed S et al (^12) also shows that TBL provide motivation to students in order to learn pathology and gave them better understanding of the subject, our results also showed similar findings but the percentage of students reported are higher as compared to the study reported by Hameed S et al (^12). In the present study, a majority of students (91%) wanted more TBL sessions organized for them. They want to add this strategy as a part of their curriculum. This is similar to other studies in which students preferred TBL as a mode of instruction(^3) In our study it was noted that students were satisfied with this strategy and their motivation to learn pathology is higher as also reported by a systematic review of TBL research published from 2003 to 2011. It is also reported that students who attended TBL session scored higher in examinations when compared by students who didn’t attend. TBL session Improved engagement during class, better content retention through active learner engagement, development of problem-solving and critical thinking skills, Team-building and development of communication skills as reported by Hameed S et al. (^12)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CONCLUSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction of TBL in pathology course has received encouraging feedback from the students. This strategy should be carried out for various courses in pathology and other subjects as well. There is a need for faculty and students orientation for the implementation of TBL. There were few limitations in our study; first we didn’t include any comparison group to assess students’ academic performance. Secondly we didn’t find out faculty perceptions about TBL. In future qualitative data is needed to find the students and faculty perceptions and its impact on academic performance.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Author’s Contribution:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concept &amp; Design of Study: Sofia Waheed Khan, Sadaf Sajid</td>
</tr>
<tr>
<td>Drafting: Sadaf Sajid, Nosheen</td>
</tr>
</tbody>
</table>
Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

Objective: To compare the outcome of the auto refraction with subjective refraction in patients.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Al-Ibrahim Eye Hospital, Karachi from March 2019 to February 2020.

Materials and Methods: A cross-sectional study was conducted on 120 patients above 15 years of age. Topcon (RM8800) was the auto refractor used to determine auto refraction, whereas subjective refraction was carried out using a trial frame in which spherical lenses were inserted. Each eye was checked monocularly, and then binocularly, with all eye measurements carried out without cycloplegia. SPSS was used to evaluate data, and for comparison, a paired t-test was applied with a P-value set at ≤0.05.

Results: The mean spherical equivalent difference between auto refraction and subjective refraction of both eyes was (±0.17D±0.12D). The p-value of the right eye and left eye between auto refraction and subjective refraction was found to be (0.033-0.088), which is statistically significant.

Conclusion: Study confirms the variation between subjective refraction and auto refraction. Auto refraction is satisfactory for preliminary refraction but is not deemed satisfactory as substitutes for conventional subjective refraction.

Key Words: Auto-refraction, subjective refraction, refractive error

INTRODUCTION

Refractive error is said to be one of the most common causes linked to visual impairment and is the second largest cause of treatable blindness after cataracts. The WHO has also further identified refractive error as the leading cause of blindness, addressing this in WHO Vision 2020 priority. According to the International Classification of Diseases, 10th revision, refractive error defines refractive error as a defect in which light is focused in front of the retina. In contrast, hyperopia is when light is focused behind the retina. However, refractive error is a widely prevalent condition; it can be easily corrected by using glasses, contact lenses, and surgery.

Unfortunately, much of the refractive error remains uncorrected, resulting in reduced educational opportunities and employment options, ultimately resulting in and impacting individuals and the community. This reduced productivity has a severe cost on the economy, estimated in the region of $269 Billion per year, all due to uncorrected refractive errors. Therefore, it is essential to diagnose and correct refractive errors in the region. Refractive errors can be detected by manual subjective refraction (SR). SR is defined as the endpoint as the combination of lenses that provides the best-corrected visual acuity to a patient with refractive error. Subjective error is considered the standard for comparing new instruments that help assess refractive errors in clinical practice. However, the procedure is subjective with many drawbacks such as patient variability in responses and inter and intra-examiner reliability, leading to limitations in preciseness and repeatability. The technology could help in increasing the efficiency in optometric practice and also prevent issues such as patient reliability and examiner reliability. Auto refractors is a widely accepted, clinically valuable tool. Auto refractors provide a rapid automated assessment of refractive errors and are now commonly used in ophthalmic practices, aiding technicians with minimal training to collect and refine refractive data.
Even though refractive error is relatively easy to avoid, the uncorrected refractive error still accounts for most of the disease burden in Pakistan\(^1\). An uncorrected refractive error must be diagnosed and corrected in the country using either subjective refraction or using Auto refractors. Therefore, a study was conducted to evaluate Auto refractors’ outcomes and subjective refractors among people age 15 and above.

**MATERIALS AND METHODS**

After taking approval from the ethical review board, a cross-sectional study was conducted in Al-Ibrahim Eye Hospital. One hundred twenty patients aged above 15 years were selected based on the non-probability sampling technique. A study took place for an entire year, in which patients with refractive errors were tested using both subjective refraction and Auto refractors. Patients were only included in the study after taking verbal consent from them. We measured the visual acuity of all the patients using the Snellen’s eye chart. Measurement of auto refraction was measured using Topcon (RM8800) on 240 eyes and compared with subjective refraction. The subjective refraction was carried out using a trial frame, in which lenses could be inserted with the highest refraction posed to the eye, with a vertex distance kept at 12mm. Precise subjective refraction was undertaken by determining the best vision sphere and using Jackson’s cross-cylinder technique. Changes to cylinder power were compensated by adjusting the sphere power. Each eye was checked for refraction monocularly, followed by binocular balancing. All refractive measurements were done without any cycloplegia. Refraction was recorded in written form on a patient prescription card and the filling of a structured questionnaire for the above variables for the study. Data, once collected, was analyzed using SPSS Version 21.0. All continuous variables were shown in mean and standard deviation, whereas categorical data were presented in frequency and percentage. For comparing results of auto refraction and subjective refraction, a paired t-test was used with statistical significance kept at P-value <0.05.

**RESULTS**

Figure 1: Shows the age groups of the patients taking part in the study in this study the age range of patient 16 to 60 years, a total of 120 patients were examined during study. Out of total number of patients, the frequency of male was 64 and female was 56.

Figure 2: Shows the mean and standard deviation between auto refraction and subjective refraction of Right and Left eye

Figure 3: Shows the age-wise comparison of Auto refraction and Subjective refraction. The Mean spherical equivalent difference of the right eyes between auto refraction and subjective refraction among the age groups of 15 to 25,26 to 35, 36 to 45, 46 to 55 and >55 years were ±0.4759D, ±0.6259D, ±0.0194D, ±0.1744D and ±0.0913D respectively. The Mean spherical equivalent difference of the left eyes between auto refraction and subjective refraction among the age groups of 15 to 25,26 to 35, 36 to 45, 46 to 55 and >55 years were ±0.5184D, ±0.3918D, ±0.1245D, ±0.4040and ±0.1167D respectively.

Figure No. 1: Shows Frequency of the patients in respect to age groups

Figure No. 2: Shows the Mean and standard deviation between auto refraction and subjective refraction of Right and Left eye

Figure No. 3: Shows the Mean value of age-wise comparison between Auto refraction and Subjective refraction of Right and Left eye
DISCUSSION

Currently, the determination of refractive error of the human eye is done in 2 steps. The first step of measuring objective refraction is done using retinoscopy, auto refraction, or aberrometry. The next step is then subjective refraction, which is still the gold standard for measuring refractive errors. Retinoscopy is one of the oldest techniques used in clinical ophthalmology; unfortunately, this technique is slower than other objective refraction measurement techniques and requires years of experience to become proficient in its use. In contrast, refractors are faster, require less clinically experienced operators. Many publications have also supported refractors to be more accurate and repeatable than retinoscopy\textsuperscript{12}. Our study used one of the ways to measure subjective refraction, which is Auto refractors, and compared it to subjective refraction. Our study demonstrated spherical equivalent (SE) difference between auto refraction and subjective refraction of the right eye (\pm 0.17D p-value = 0.033) and of the left eye, which was statistically significant. A similar study conducted also showed that SE was found to be significantly different for different auto refractors, Retinomax K plus 2, Canon RF 10 compared with monocular subjective refraction. Furthermore, Mean SE was also significantly different for Grand Seiko WR5100K than binocular subjective refraction\textsuperscript{13}. With cycloplegia, there was no significant difference in mean SE between the refraction methods. Additionally, it must be noted that Autorefractors are inadequate when it comes to measuring non-cycloplegic refractive errors, which was also seen in a study conducted by Zhao et al\textsuperscript{14}. In this circumstance, other objective refraction measurement techniques or subjective refraction should be considered. Alternatively, cycloplegic Autorefractors are deemed highly beneficial\textsuperscript{15}. The study also showed the mean difference between autorefration and subjective refraction, which was obtained between \pm 0.370D to \pm 0.438. The result difference was mean \pm 0.1728, \pm 0.1272 there were 0.2 and 0.31 according to this study, a slight difference is eradicated. Another study results also showed that the standard deviation obtained for both subjective and objective refraction measuring techniques to be were +/- 0.14 and +/- 0.18 D, indicating 95% confidence limits of +/- 0.27 and +/- 0.35 D. it also concluded that with assessment technique, a change in refractive error of +/- 0.50 D must be adopted as the minimum significant shift in refractive status\textsuperscript{16}. It was found that Auto refractors are an excellent way to provide an initial idea and are an excellent tool for preliminary refraction but are not satisfactory. Subjective refraction is still the gold standard, with the current results showing that there is variation in between auto refraction against subjective refraction. Furthermore, Auto refractors also have their drawbacks as they cannot assess the ocular media and, therefore, cannot be used for specific intents and purposes such as early diagnoses of cataracts keratoconus. However, retinoscopy and aberrometry can detect such findings\textsuperscript{17,18}. Therefore, Auto refractors should only be used for preliminary diagnosis of refractive error. Subjective refraction should still be the go-to tool for measuring precise refractive error in patients. However, auto refraction measurement can still be used reasonably well for patient screening, as this can reduce the number of patients. Further studies can also be done on aberrometry and retinoscopy, the other two methods of objective refraction, and compare them with subjective refraction to evaluate how close they are in measuring refractive errors. We also advise that clinicians have relevant skills for using a subjective method to evaluate refractive errors among patients so that accurate measurements can be made. Our study does not indicate that refractors are a better tool in measuring refractive errors over subjective refraction.

CONCLUSION

Subjective refraction is still a more accurate and reliable way to measure the refractive error in patients. However, auto refraction provides an initial idea and screening chance before commencing subjective refraction.
Author’s Contribution:
Concept & Design of Study: Israr Ahmed Bhutto
Drafting: Saima Majid, Faiza Rameez
Data Analysis: Attiya Zehra Rizvi, Umer Kazi, Bilawal Azam
Revisiting Critically: Israr Ahmed Bhutto, Saima Majid
Final Approval of version: Israr Ahmed Bhutto

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

REFERENCES
Comparison of Accuracy of Frameless Stereotactic System (Neuronavigation) Against Frame Based Stereotaxy in Deep Seated Lesion of Brain

Syed Zahid Hussain Shah¹, Shoaib Saleem Khan² and Muhammad Aamir¹

ABSTRACT

Objective: The determination of accuracy of frameless stereotactic system against frame based stereotaxy in deep seated lesion of brain.

Study Design: Randomized controlled trial study.

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

Materials and Methods: A total of 124 patients were included in the study after informed consent and eligible in accord to the inclusion and exclusion criteria. Total participants were 124 (randomized) and were divided into two randomized groups; frame-based stereotaxy group (FB) and stereotaxy group (SG) including 62 patients in each group. The angular deviation and target distance between actual and planned trajectory were the primary outcomes in this study. Independent samples were tested through 2-tailed t-tests for statistical testing. Mann-Whitney U test was performed for non-normally distributed data while for comparison of categorical variables Chi-square or Fisher tests were performed. P-value was 0.05 as a level off statistical significance. SPSS version 23 was used for statistical computations.

Results: Trajectory length and distance were 42.32±10.38 mm and 2.43±1.02 mm in FB group, while 43.45±11.65 mm and 2.59±1.06 mm in VG group, and there was no statistically significant difference in these two parameters (p value 0.570 and 0.390, respectively). Trajectory deviation was 1.85±1.28 degree in FB group and 2.63±158 degree in VG group, and the difference was statistically significant (p=0.003). Table-2.

Conclusion: Patients in which brain biopsy was done, the Varioguide system can be compared to the gold standard frame-based stereotaxy on the basis of means of trajectory accuracy, complications rate and diagnostic yield.

Key Words: Frameless Neuro-navigation, Stereotaxy, Biopsy, Brain Lesion, Magnetic Resonance Imaging

INTRODUCTION

Brain lesions are diagnosed by a routinely used procedure; Stereotactic brain biopsy¹. Frame based stereotaxy is highly précised and is a procedure of choice for biopsy and other surgical techniques of brain. On the other hand, one of its drawbacks is that it can be unpleasant for the patients and time consuming procedure when frame based stereotactic procedure with coordination frame positioned under anesthesia is used (only in few cases)²³.

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Printed: October, 2020
settings its accuracy is not yet studied as compared to laboratory setting where its accuracy was studied. Our study aimed the determination of accuracy of frameless against frame based stereotactic system in deep seated lesion of brain.

MATERIALS AND METHODS

This is a randomized controlled trial conducted in Department of Neurosurgery, Nishtar Hospital Multan from June 2019 to June 2020. The ethical approval for the study was taken from the ethical committee of Nishtar Hospital Multan. The sample size was calculated using the reference study conducted by Bardac et al. Non-probability consecutive type of sampling was used to collect the sample size. Patients with age above 18 years, willingly participating in the study, able to sign the informed consent and those with brain pathology designated to brain biopsy were included in the study. While patients with age less than 18 years, who are not able to sign the informed consent, those wanted to choose single treatment option, those with high risks to an aesthetic so were not able to undergo any procedure by anesthesia, and unable to undergo MRI. A total of 124 patients were included in the study after informed consent and eligible in accord to the inclusion and exclusion criteria. Refusal to participate and not being able to sign informed consent because of considerably altered conscious of the patients were the major cause of non-enrolment in the study. Total participants were 124 (randomized) and were divided into two randomized groups; frame-based stereotaxy group (FB) and stereotaxy group (SG) including 62 patients in each group.

Combination of Intra-op MR scan and navigation MR scan (before treatment) were imaging techniques used to measure the angular deviation and target distance, which were the primary outcomes in this study. Intra-op MR scan or after 24 hours follow-up period routine CT scan done for assessing the complications such as hemorrhage which was considered as significant if bigger than petechial hemorrhage along bionic canal, using Karnofsky Performance Scale (KPS) for measurement of clinical deterioration, total time for procedure including placement of frame, CT scan done preoperatively, surgery, anesthesia administration and intra-op MRI, diagnostic outcome of biopsy and OR duration required were the secondary outcomes of the study. A Visual Analogue Scale (VAS) with 10 grades was used for the assessment of subjective symptoms in the patients such as expected discomfort, overall pain and overall discomfort linked to the procedure. Patient must be explained about the planned procedure, an independent neurologist perform clinical (KPS) and VAS assessment for the anticipated discomfort after randomization. Same person must have done the remaining assessments on discharge day as clinical assessment. Independent samples were tested through 2-tailed t-tests for statistical testing. Mann-Whitney U test was performed for non-normally distributed data while for comparison of categorical variables Chi-square or Fisher tests were performed. P-value was 0.05 as a level off statistical significance. SPSS version 23 was used for statistical computations.

RESULTS

Mean age of the patients was 59.56±6.76 years and 59.89±6.16 years in FB and VG group, respectively (p=0.782). FB group consisted of 32 males and 30 females while VG group consisted of 28 males and 34 females (p=0.472). Preoperative KPS was 77.92±12.04 in FB group and 80.82±6.59 in VG group (p=0.098). Mean lesion volume was 13.64±6.99 ml and 11.98±5.03 ml in FB and VG group, respectively (p=0.132). Motor deficit, aphasia, intracranial HTN, and visual disturbances were present in 9, 12, 10 and 5 patients of FB group, while in 8, 10, 16 and 11 patients of VG group (p value 0.794, 0.638, 0.186, and 0.108), respectively. There was no statistically significant difference in the baseline parameters. Table-1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>FB (n=62)</th>
<th>VG (n=62)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.56±6.76</td>
<td>59.89±6.16</td>
<td>0.782</td>
</tr>
<tr>
<td>Gender</td>
<td>32/30</td>
<td>28/34</td>
<td>0.472</td>
</tr>
<tr>
<td>Pre-op KPS</td>
<td>77.92±12.04</td>
<td>80.82±6.59</td>
<td>0.098</td>
</tr>
<tr>
<td>Lesion volume, ml</td>
<td>13.64±6.99</td>
<td>11.98±5.03</td>
<td>0.132</td>
</tr>
<tr>
<td>Motor deficit</td>
<td>9</td>
<td>8</td>
<td>0.794</td>
</tr>
<tr>
<td>Aphasia</td>
<td>12</td>
<td>10</td>
<td>0.638</td>
</tr>
<tr>
<td>Intracranial HTN</td>
<td>10</td>
<td>16</td>
<td>0.186</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>5</td>
<td>11</td>
<td>0.108</td>
</tr>
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</table>

Data is as mean ±standard deviation or number

Table No.2: Trajectory data

<table>
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<th>VG (n=62)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trajectory length, mm</td>
<td>42.32±1.0</td>
<td>43.45±11.65</td>
<td>0.570</td>
</tr>
<tr>
<td>Trajectory distance, mm</td>
<td>2.43±1.0</td>
<td>2.59±1.06</td>
<td>0.390</td>
</tr>
<tr>
<td>Trajectory deviation, degree</td>
<td>1.85±1.2</td>
<td>2.63±158</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Data is as mean ±standard deviation
Table No.3: Procedural and outcome data

<table>
<thead>
<tr>
<th>Variable</th>
<th>FB (n=62)</th>
<th>VG (n=62)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure length, min</td>
<td>77.16±18.33</td>
<td>56.51±13.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgery length, min</td>
<td>42.87±8.05</td>
<td>56.51±13.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall pain</td>
<td>1.92±0.94</td>
<td>1.68±0.97</td>
<td>0.163</td>
</tr>
<tr>
<td>Overall discomfort</td>
<td>2.26±0.85</td>
<td>1.84±0.83</td>
<td>0.006</td>
</tr>
<tr>
<td>KPS on discharge</td>
<td>81.24±9.05</td>
<td>78.82±5.98</td>
<td>0.082</td>
</tr>
</tbody>
</table>

Data is as mean ± standard deviation.

Total procedure length was longer in FB group than in VG group (77.16±18.33 min vs. 56.51±13.24 min) with statistically significant difference (p<0.001). Surgery duration was significantly shorter in FB group than in VG group (42.87±8.05 min vs. 56.51±13.24 min, p<0.001). Overall pain was 1.92±0.94 and 1.68±0.97 in FB and VG group, respectively, with statistically insignificant difference (p=0.163). Overall patient discomfort was 2.26±0.85 in FB group and 1.84±0.83 in VG group, and the difference was statistically significant (p=0.006). KPS on discharge was 81.24±9.05 and 78.82±5.98 in FB and VG group, respectively, with statistically insignificant difference (p=0.082). Table 3.

**DISCUSSION**

In a previous study by Ringel et al, measurement of the accuracy of Varioguide system was done on a phantom [10]. Another study by Giese et al used specially designed agarose model for studying the Varioguide system, which was used for chemotherapy of brainstem via placement of 33 probes [11]. In this study another 32 probes were positioned into anatomical specimens. T1W MR Scan and Thin-slice CT were used for assessing the placement accuracy with mean total target deviations on CT scan and on MR scan were 3.1 ± 1.2 mm and 2.8 ± 1.2 mm respectively, in agarose model. Total target deviation in case of anatomical specimens for CT and MR scan were 1.95 ± 0.6 mm and 1.8 ± 0.7 mm respectively. Another study conducted by Bjartmarz et al used frameless and frame-based technique to compare the DBS electrode placement [12]. In their study bilateral DBS electrode placement into ventrolateral thalamus was done in 14 patients having essential tremors. The total target deviation for both the frameless technique and the frame-based technique (p<0.05) was 2.5 ± 1.4 mm and 1.2 ± 0.6 mm, respectively. Even though the difference between the deviations of both methods was considerable, due to same clinical findings, authors suggested the small difference that were observed did not affect the overall clinical results of treatment of essential tremors and both methods are feasible.

The planned targets and frame-based stereotactic system showed same deviation when Nexframe was used in 5 patients for the frameless stereotaxy use for subthalamic DBS nucleus and as accuracy of Nexframe was studied by Fukaya et al. Comparative study for Nexframe and CRW frame was conducted by the Kelman et al [13] that showed the target deviation for these methods was 2.78 ± 0.25 mm (Nexframe) and 2.65 ± 0.22 mm (CRW frame). In another study by, Konrad et al [14] over a large setting including 263 patients, a skull-fixed stereotactic system device was used for insertion of 497 DBS, showing mean target error of 1.99 ± 0.9 mm. However, the findings only included 75 patients who had post-op CT scan. The point deviation calculated by the system was only 0.52 ± 0.44 mm as concluded by Ringel’s study [10]. On the other hand, he found that there was 0.4 – 6.6 mm 12-16 of localization errors for different imaging modalities and frames in his literature review while the frameless systems were associated with an error which ranged between 0.33 and 3.86 mm [15,16,19]. Single-center nature of this study is the main limitation, along with the low number of patients being another limitation of this study. However, primary outcomes are a reason of empowerment of this study. Extremely low number of complications is the secondary outcomes of this study.

**CONCLUSION**

Patients in which brain biopsy was done, the Varioguide system can be compared to the gold standard frame-based stereotaxy on the basis of means of trajectory accuracy, complications rate and diagnostic yield. Along with this patients acceptance towards the Varioguide system is higher than frame-based stereotaxy.

**Author’s Contribution:**

*Concept & Design of Study:* Syed Zahid Hussain Shah

*Drafting:* Shoaib Saleem Khan

*Data Analysis:* Muhammad Aamir

*Revisiting Critically:* Syed Zahid Hussain Shah, Shoaib Saleem Khan

*Final Approval of version:* Syed Zahid Hussain Shah

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

**REFERENCES**


Benign and Malignant Colorectal Diseases: A Clinic Pathological View to Assess the Frequencies in Pakistani Population

Hina Wasti¹, Saleha Masood², Rashid³ and Sumayyah Shawana¹

ABSTRACT

Objective: To calculate the frequencies of various histopathological types of colorectal diseases and to assess the grade of the colorectal cancer.

Study Design: A cross sectional observational study.

Place and Duration of Study: This study was conducted at the Department of Pathology, Pakistan Navy Station Shifa Hospital Karachi from March 2016 to March 2019.

Materials and Methods: 223 colorectal specimen including, biopsies and colectomy specimen were included in the study. Paraфин embedded sections were stained with routine Hematoxylin and Eosin method. The cases were diagnosed as benign or malignant and then further sub classified. Clinical records were reviewed in order to collect data regarding age, gender, clinical diagnosis and grades of tumor. H&E slides of all diagnosed cases were reviewed by two histopathologists with the aim to collect information about histological pattern and differentiation of tumor. Data was analyzed by SPSS version 23.0. Frequencies were calculated in terms of percentage.

Results: Out of total (n=223) cases there were 77.1 % (n=172) benign and 22.86 % (n=51) malignant cases. Among the benign colorectal lesions 43.6% were diagnosed as Rectal polyps, 40.6 % as Colitis and 15.6 % were reported as Proctitis. As regards the microscopic variants, among 51 colorectal carcinomas, 32(62.7%) were diagnosed as adenocarcinoma, 16(31.4%) cases were mucinous-signet ring type carcinomas, 2(3.9%) were poorly cohesive and the remaining 1(2.0%) case showed cribriform pattern. Grade-I well differentiated tumors (62.7 %) were most frequently diagnosed. Most cases of benign diseases were diagnosed between 30-40 years and malignant between 50-59 years. Both of benign and malignant colorectal pathologies showed male preponderance and mostly involved the right colon.

Conclusion: Colorectal polyps were the most common benign colorectal pathologies followed by colorectal carcinoma. The great majority was observed as (grade -I) well differentiated adenocarcinoma.

Key Words: Colorectal polyps, Colitis, Proctitis, Colorectal carcinomas, Histological variants

INTRODUCTION

The large bowel comprises of terminal 1–1.5 m of the whole gastrointestinal tract. It starts at the terminal ileum as cecum then continues to become the left colon and terminates into the fifth part of the large intestine which is sigmoid colon. Further the sigmoid colon connects the descending colon to the rectum.¹,²

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from the colonic mucosal cells. Histopathological study of colectomy samples or biopsies is essential for the diagnosis and management of patient. The histologic tumor grading depends on glandular formation, which is characteristic of conventional adenocarcinoma. Adenocarcinoma can be divided in to three grades on the basis of cellular arrangement with regard to the degree of tubular (acinar) formation as well-differentiated tumors termed as grade- I, moderately differentiated - grade –II and poorly differentiated tumors - grade- III. As per World Health Organization (WHO) there are several histological variants of the colorectal cancers including mucinous, signet ring cell, medullary, micro papillary, serrated, adenosquamous, adenocarcinoma, cribriform comedo-type, spindle cell, and undifferentiated patterns. Colorectal cancer (CRC) is a heterogeneous disease which emerges through several important pathways. Both environmental and genetic factors are responsible for the development of the pathogenesis. However there is a continuous rise of colorectal carcinoma in those under the age of 50. Incidence of colorectal cancer in males are significantly greater than in females. Recently, a large number of developing countries have shown an acute increase in the incidence of colorectal cancer. In Pakistan CRC accounts for 52% of all gastrointestinal tumors in comparison to other countries. The estimated rates of incidence, mortality, and prevalence are consistently higher in the USA. In USA the estimated 5-year survival rate for all stages of the colorectal carcinoma being 65%. Multiple innovations have been recognized and implemented into daily practice over the last thirty years, changing the diagnostic and therapeutic options and notably improving the oncologic outcomes for CRC patients. The economic cost burden of colorectal diseases in general and carcinoma in particular has risen significantly due to availability of a variety of diagnostic and therapeutic modalities. We conducted this study in our institute to calculate the frequency of benign and malignant colorectal diseases and to assess the grade of colorectal cancer. This study will provide a base for future analytical studies and will contribute in establishing a larger data for frequencies of colorectal lesions in Pakistan.

MATERIALS AND METHODS

This cross sectional observational study was based on the analysis of colectomies and colonic biopsies received in the Department of Pathology, PNS Shifa hospital Karachi. Ethical approval was obtained from the Ethical Review Committee of Bahria University Medical and Dental College before commencement of the study. Informed consent was signed by every patient before enrollment in the study. Sample size was calculated using software G-POWER (version 3.1.9.2) by taking 95% confidence interval, 5% margin of error. During the study period, from March 2016 to March 2019, 223 colorectal samples were received at our setup. Both biopsies (n=99) and colectomy specimens (n=124) were analyzed for histopathological diagnosis. Among them 172 cases were reported as benign lesions while 51 cases were diagnosed as colorectal cancer. A Non probability convenient sampling technique was adopted for the proceedings. All colonic surgical specimens including biopsies and colectomy specimens obtained prior to therapy and patients who were willing to participate in the study were included, whereas poorly fixed tissue, inadequate material, metastatic tumors, post radiotherapy specimens as well as patients who refused to participate in the study were excluded from this research. Specimen were received in 10% buffered formalin and processed in auto processor. Paraffin embedded sections were stained with routine Hematoxylin and Eosin method. The cases were diagnosed as benign or malignant and then further sub classified. Clinical records were reviewed in order to collect data regarding age, gender, clinical diagnosis and grades of tumor. H&E slides of all diagnosed cases were reviewed by two histopathologists with the aim to collect information about histological pattern and differentiation of tumor. Data was analyzed by SPSS version 23.0 and is represented in tables.

RESULTS

In the 3-year study period, 223 cases of colorectal tissue including 124(55.6%) colectomies and 99 (44.3%) biopsy specimens were received in pathology laboratory. Out of total (n=223) cases there were 77.1 % (n=172) benign and 22.86 % (n=51) malignant cases. Among the benign colorectal lesions 43.6% (n=75) were diagnosed as Rectal polyps, 40.6 % (n=70) as Colitis and 15.6 % (n=27) were reported as Proctitis. In the present study out of 51 colorectal carcinomas, 32(62.7%) were well differentiated adenocarcinoma, 14 (27.4%) moderately differentiated and the remaining 5(9.8%) were poorly differentiated tumors. As regards the microscopic variants, out of 51 colorectal cancers, 32(62.7%) were diagnosed as adenocarcinoma, 16(31.4%) cases were mucinous-signet ring type carcinomas, 2(3.9%) were poorly cohesive and the remaining 1(2.0%) case showed cribriform pattern. For benign lesions the age of the patients ranged from 4-75 years whereas for colorectal carcinoma the age range was found to be 14-89 years. Most cases of benign diseases were diagnosed between 30-40 years and malignant between 50-59 years. In the present study out of 172 cases of benign colorectal diseases, 124(72.0%) cases were present in males, while the remaining 48(27.9%) cases of colorectal cancer were seen in females. Whereas out of 51 cases of colorectal carcinomas, 37 (72.5%) cases were present in males, while the remaining 14(27.4%) cases of colorectal cancer were seen in females.
Table No.1: Frequency of Benign Colorectal Diseases (N=172)

<table>
<thead>
<tr>
<th>Category</th>
<th>No of cases n = 172</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Polyp</td>
<td>75</td>
<td>43.6%</td>
</tr>
<tr>
<td>Colitis</td>
<td>70</td>
<td>40.6%</td>
</tr>
<tr>
<td>Proctitis</td>
<td>27</td>
<td>15.6%</td>
</tr>
</tbody>
</table>

Table No.2: Distribution of Colorectal Carcinomas According to Grades of Differentiation (N=51)

<table>
<thead>
<tr>
<th>Grade of differentiation</th>
<th>No of cases ( % of total cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well differentiated (G-I)</td>
<td>32 (62.7%)</td>
</tr>
<tr>
<td>Moderately differentiated (G-II)</td>
<td>14 (27.5%)</td>
</tr>
<tr>
<td>Poorly differentiated (G-III)</td>
<td>5 (9.8%)</td>
</tr>
</tbody>
</table>

Table No.3: Benign and Malignant Colorectal Disease According to Type of Specimen (N=223)

<table>
<thead>
<tr>
<th>Type of specimen</th>
<th>Total number ( %)</th>
<th>Benign Lesion (Polyps/Colitis/Proctitis) n (%)</th>
<th>Malignant Lesion (Colorectal Carcinoma) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colectomies</td>
<td>124(55.6%)</td>
<td>102(82.2%)</td>
<td>22(17.7%)</td>
</tr>
<tr>
<td>Biopsies</td>
<td>99(44.3%)</td>
<td>70(70.7%)</td>
<td>29(29.2%)</td>
</tr>
</tbody>
</table>

Table no. 4: Distribution of Benign and Malignant Colorectal Disease according to Clinic Pathological Features (n=223)

<table>
<thead>
<tr>
<th>Clinicopathological features</th>
<th>Total numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benign Lesions (172)</td>
</tr>
<tr>
<td>Age</td>
<td>50-59 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Male = 124(72.0%)</td>
</tr>
<tr>
<td></td>
<td>Female = 48(27.9%)</td>
</tr>
<tr>
<td>Tumor Location</td>
<td>Right-sided = 40(23.2%)</td>
</tr>
<tr>
<td></td>
<td>Left-sided = 132(76.7%)</td>
</tr>
</tbody>
</table>

Table No.5: Distribution of Colorectal Carcinomas According to Histological Variants (N=51)

<table>
<thead>
<tr>
<th>Clinicopathological features</th>
<th>No of cases</th>
<th>% of total cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glandular Adenocarcinoma</td>
<td>32</td>
<td>(62.7%)</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>16</td>
<td>31.3</td>
</tr>
<tr>
<td>Poorly cohesive</td>
<td>2</td>
<td>(3.9%)</td>
</tr>
<tr>
<td>Cribriform pattern</td>
<td>1</td>
<td>(2.0%)</td>
</tr>
</tbody>
</table>

In the present study among 172 benign colorectal diseases, 132(76.7%) cases were confined to the left side whereas 40(23.2%) cases involved the right colon. Out of 51 malignant cases, 37(72.5%) cases were localized to the ascending colon whereas 14(27.4%) cases involved the right colon. Most of the benign lesion as well as cancer of colorectal tissue was found to be in male gender as compared to females.

**DISCUSSION**

All over the world, colorectal diseases are responsible for significant morbidity and mortality among adult population with the preponderance in males. Most common benign diseases affecting parts of large intestine preferably the colon and rectum are rectal polyps. A colorectal polyp is a general term for all neoplasms that protrude into the colorectal cavity, including both neoplastic polyps and non-neoplastic polyps. Neoplastic polyps are mainly divided into (1) hyperplastic polyps (HPs), (2) sessile serrated adenoma/polyps (SSA/Ps), and (3) traditional serrated adenomas (TSAs) whereas the Non-neoplastic polyps are mainly divided into three categories: inflammatory polyps, hamartomatous polyps, juvenile polyps, Peutz–Jeghers polyps and other types of polypoidal lesions like Familial adenomatous polyposis (FAP) and Hereditary non polyposis colorectal cancer syndrome (HNPCC; Lynch syndrome). Most polyps are symptomless, but they are capable to bleed because of twisting, obstruction, changes in bowel habits or intussusception. The polyps may appear as slight elevations of the mucosa to comparatively large masses and may progress in to bulky polypoidal tumour mass as a colorectal cancer. In our study the most common benign colorectal pathologies were of polyps which constituted the largest group. This is in accordance with observations of (Said et al (2017) and Tonoloni et al (2019). Colitis (inflammation of colon) although necessary for damage repair and the battle against infections, can greatly impact proliferation, resistance to apoptosis, and cellular transformation to promote neoplasia. The inflammation in the intestine is promoted by consumption of dietary emulsifiers, a ubiquitous component of processed foods, which alter the composition of gut microbiota. The chronic gut inflammation is a foundation for tumor initiation and progression giving rise to the term "colitis-associated cancer". The development of colitis-associated cancer in patients suffering from inflammatory bowel disease is one of the best characterized examples of an association between intestinal inflammation and carcinogenesis.

In the present study the second commonest benign lesion observed was colitis with 29.16% cases. These findings are in accordance with the study conducted by Stettner n et (2018) and Yin N, et al (2016).
Being the most common malignancy of the digestive tract colorectal carcinoma constitutes the third most common tumor in term of incidence and mortality in both genders. \(^{19}\)

Estimated incidence levels in males for colorectal cancer are significantly greater than in females in significant areas of the globe. \(^{20}\) In the present study the common ages for colorectal carcinoma was found to be in 50 - 59 years whereas the benign cases were reported in comparatively younger age group 30-40 years. Similar results were reported by Hussain et al (2016) \(^{21}\), Zahir et al (2014) \(^{22}\), Tsai et al (2018). \(^{23}\) In the present study the benign colorectal lesions showed great preponderance in male gender whereas out of 51 cases of colorectal carcinomas, 37 (72.5%) cases were present in males and the remaining 14(27.4%) cases were seen in females. These findings are in accordance with the results of Elsabah and Adel (2013) \(^{24}\), Alam & Khawaja (2014). \(^{25}\)

In the present study out of 51 colorectal carcinomas, 32(62.7%) were well differentiated adenocarcinoma, 14 (27.4%) moderately differentiated and the remaining 5(9.8%) were poorly differentiated tumors. As regards the microscopic variants, out of 51 colorectal cancers, 32(62.7%) were diagnosed as adenocarcinoma, 16(31.4%) cases were mucinous-signet ring type carcinomas, 2(3.9%) were poorly cohesive and the remaining 1(2.0%) case showed cribriform pattern. Our findings correspond to the figures documented in National cancer institute Cairo University Egypt (2013) which included 26 metastatic colorectal cancer cases in one study and observed histologies included, adenocarcinoma; 22(84.6%) cases, mucinous carcinoma; 2(7.7%) cases and signet ring carcinomas; 2(7.7%) cases. These findings are in contradiction with a study in which most of the cases of colorectal cancer were identified as moderate to poorly differentiated tumors. \(^{26}\)

**CONCLUSION**

Colorectal polyps was the most common benign colorectal pathologies followed by colorectal carcinoma. Most frequently diagnosed histological grade was (grade-I, well differentiated tumors. As regards the microscopic variants, the majority of observed cases were colorectal adenocarcinoma.

**Author’s Contribution:**

Concept & Design of Study: Hina Wasti

Drafting: Hina Wasti, Saleha Masood, Rashid

Data Analysis: Saleha Masood, Rashid

Revisiting Critically: Sumayyah Shawana

Final Approval of version: Hina Wasti

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

**REFERENCES**


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, Karachi 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 molecule. Alpha chain production is controlled by two alpha genes on Chromosome 16 while non- alpha chains (beta, gamma and delta) are synthesized by beta, gamma and delta genes present on Chromosome 11. All these globin genes show an autosomal recessive transmission pattern. At birth production of gamma chains and so Hb-F gradually start decreasing and by the age of six months reaches a very low level. At the same time the production of beta globin chains and so Hb-A, start increasing and by the age of twelve months constitutes almost all the Hb in the circulation. In beta thalassemia major (BTM) there is a mutation in beta gene causing reduced or absent synthesis of beta globin chains while alpha genes are produced normally creating an imbalance between the two globin chains with a relative excess of alpha chains causing an excess of unpaired alpha chains resulting in precipitation of unpaired alpha chains in the red blood cells producing hemolysis of these cells inside the bone marrow cavity causing ineffective erythropoiesis culminating in severe anemia. Beta thalassemia major / intermedia (BTM/I) are hereditary disorders of hemoglobin synthesis with a gene carrier rate of 5-7 % in Pakistan.

In the majority of patients, it presents before completing the first year of life when Hb-F production 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 (anisocytosis) along with hypochromic microcytic red cells in the peripheral blood. There is little or no Hb-A1 with a relative increased proportion of Hb-F on a background of severe anemia. This is due to ineffective & dyserythropoietic erythropoiesis by the 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. 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. RDW can be reported statistically as coefficient of variation (CV), the term which will be used in this article or standard deviation (SD). 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.

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.

**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 RaoSoft 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 Arkray 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 35.6. When RDW & Hb-F % of group I & II were compared by t test, the value obtained was highly significant (less than 0.05).

![Figure No.1: Co-relation of RDW measurement with MCV](image)

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 thalassemia 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. 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 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. 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. 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 8 gms/dl had no significant effect on RDW-CV.

Table 1: Comparison of Age, RDW & Hemoglobin & Hb. F values among both groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>1.6</td>
<td>2.1</td>
<td>11.4</td>
<td>31</td>
<td>2.5</td>
<td>1.82</td>
<td>0</td>
<td>15.3</td>
</tr>
<tr>
<td>RDW CV%</td>
<td>30.9</td>
<td>41.8</td>
<td>31</td>
<td>2.5</td>
<td>1.82</td>
<td>0</td>
<td>15.3</td>
<td></td>
</tr>
<tr>
<td>Hb gm/dl</td>
<td>8.14</td>
<td>5.12</td>
<td>1.03</td>
<td>65</td>
<td>14</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb-F %</td>
<td>1.03</td>
<td>5.26</td>
<td>8.4</td>
<td>14</td>
<td>0.8</td>
<td>72.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>1</td>
<td>5</td>
<td>11.4</td>
<td>31</td>
<td>2.5</td>
<td>1.82</td>
<td>0</td>
<td>15.3</td>
</tr>
<tr>
<td>Maximum</td>
<td>2.6</td>
<td>1.85</td>
<td>18.5</td>
<td>35.6</td>
<td>8.14</td>
<td>5.12</td>
<td>1.03</td>
<td>65</td>
</tr>
<tr>
<td>Mean</td>
<td>2.2</td>
<td>1</td>
<td>16.9</td>
<td>35.6</td>
<td>8.7</td>
<td>5.26</td>
<td>0.8</td>
<td>72.3</td>
</tr>
<tr>
<td>Median</td>
<td>2.02</td>
<td>1.10</td>
<td>4.9</td>
<td>3.002</td>
<td>1.48</td>
<td>1.48</td>
<td>1.48</td>
<td>17.6</td>
</tr>
<tr>
<td>SD</td>
<td>2.02</td>
<td>1.10</td>
<td>4.9</td>
<td>3.002</td>
<td>1.48</td>
<td>1.48</td>
<td>1.48</td>
<td>17.6</td>
</tr>
</tbody>
</table>

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 35.6. When RDW & Hb-F % of group I & II were compared by t test, the value obtained was highly significant (less than 0.05).
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, M. Salman Zafar
Data Analysis: Imran Bakar, Iram Nazir, 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.

REFERENCES

Objective: The purpose of this study is comparison of patient satisfaction and functional treatment outcomes of parasymphysis fractures treated with two mini-plates and one mini-plate along with arch bar.

Study Design: Prospective Comparative study

Place and Duration of Study: This study was conducted at the Department of Oral & Maxillofacial Surgery, Sardar Begum Dental College and Hospital, Peshawar and Northwest General Hospital Peshawar from July to Dec. 2018.

Materials and Methods: 60 patients with diagnosed isolated parasymphysis fracture were included in the study. Two mini-plates were used for treatment in 30 patients in Group (A), while 30 patients in Group (B) were treated with one mini-plate with arch bar. The operative time and cost of the treatment was noted from start till end. Patient were checked at 15 days & 1,3 and 6-months follow up visits for effect on the quality of life by measuring the number of days missed from work, return to normal diet and duration of bed rest and was comparison was made between the two groups.

Results: The mean operating time in group A was 61.49 minutes while in group it was 47.93 minutes. The average cost of treatment in group A was 8533.33 rupees while in group B it was 4383.33 rupees. The effect on quality of life was more for patients with group B than A.

Conclusion: Patients treated with two miniplates have higher cost and greater operating than patients treated with one miniplate along arch bar but have improved quality of life than arch bar group

Key Words: Parasymphysis Fracture, Miniplate, Arch Bar, Patient Satisfaction

INTRODUCTION

In present era, there is a significant increase in the occurrence of craniofacial trauma due a mass increase in the number of vehicles and bad conditions of the roads. Due to its prominent position, mandible is the second most common fractured bone in craniofacial trauma and parasymphysis is most commonly fractured after condyle and angle. Therefore, treatment goals are aimed to improve diet, decrease joint damage to prolong immobilization, which has replaced prolong maxillomandibular fixation (MMF) with open reduction and internal fixation (ORIF) for early mobilization and early return to work.

Due to complex mandibular anatomy and the direction of forces due to muscles attachment, parasymphysis fractures are problematic during treatment because these forces separate the lower border of mandible at fracture area. Therefore, high level of torsional forces the parasymphseal region need to be balanced by two miniplates one at the inferior border and the other below the apices of the teeth to provide stable occlusion during mastication and uneventful osteogenesis of reparable bone. But placement of two miniplates in parasymphysial region results in damage to the mental nerves and roots of the teeth in many cases. Additionally the operating time and cost of the treatment is increased by using two miniplates. To eliminate the placement of second plate, alternate possibility could be placement of arch bar on mandibular teeth that acts as a tension band and thereby eliminates the necessity of upper miniplate and only lower miniplate is placed along with arch bar.

1. Department of Oral & Maxillofacial Surgery, Sardar Begum Dental College and Hospital, Peshawar.
Therefore, this study was carried out to find the effectiveness of two miniplates and one miniplate along with arch bar, in terms of patient satisfaction and functional outcome.

**MATERIALS AND METHODS**

**Study Design and Population**: After approval from the ethical committee and Research Centre, this comparative study was carried out at the Department of Oral & Maxillofacial Surgery, Sardar Begum Dental College and Hospital, Gandhara University, Peshawar, and Northwest General Hospital Peshawar from July to Dec. 2018.

A total number of 60 patients presenting with isolated parasympysis fracture in the age group of 14 to 75 years were included in the study irrespective of gender, after detail history followed by clinical and radiological examination. Patients presenting with preexisting infection, mandibular defect, edentulous mandible, parasympysis with condyle fracture, medically compromised and non-compliant patients were excluded from the study. Informed consent was taken after explaining both the risks and benefits of both procedures to all the patients. The selected sample was randomly assorted by lottery method into two equal groups (A and B), 30 patients in each group. Patients with Group A was treated with two miniplates while patients with group B was treated with one miniplate along with arch bar. The principal outlined by Chapmy for Standard miniplates system were applied in this study.

Patient satisfaction and functional outcome was measured on the basis of effect on quality of life, days missed from work, time needed to get normal diet and total cost of the procedure. All the patients were followed at 2 weeks, 1 month, 3 months and 6 months period to check the outcome measurements.

The plates used in this study was made of titanium with 2 mm AO system of plating of 1.5mm thickness and mono cortical screws with a diameter of 1.7mm. Erich arch bar were used for intermaxillary fixation in group B patients.

**Interventions**: Standardized treatment protocol was used in all patients. All patients were given intravenous antibiotics prophylaxis preoperatively with Amoxicillin 1g or Erythromycin 1gin case of Amoxicillin allergy and was continued for 3 days post operatively. Buccal sulcus approach was used for exposure of the fracture segments in all the patients under general anesthesia. Erich arch bar was applied and occlusion was achieved using intermaxillary wiring. Reduction clamps were used for anatomic alignment of the fractures segments and fixation was done with 2 titanium miniplates in Group A and 1 miniplate in group B. Intermaxillary fixation was released after repair of the soft tissues and arch as removed in patients with group A and maintained in Group for 6 weeks. The time needed for surgery completion was recorded. All the interventions were done by a single surgeon to eliminate operator dependent bias.

All the patients were kept on liquid diet for 2 weeks and then were slowly advanced to soft diet for the next 2 weeks. Thereafter, diet well tolerated were recommended for the all the patient.

**Outcome Measures**: Comparison of satisfaction of both the surgeon was done with both subjective and objective evaluation.

a. **Objective Evaluation**: Objective outcome was measured by the total time taken by the procedure for surgeon and total cost of the procedure for the patient and comparison was done in both the groups.

b. **Objective Elevation**: This was based on patient’s satisfaction in both the groups. Objective assessment was done by measuring and comparing the functional outcome in terms of Effect on the quality of life in both the groups. The effect of quality of life was measured by three variables:

1. Working days missed by the subjects from the job.
2. Bed rest of the subjects.
3. After how many days normal diet was started.

**Statistical Analysis**: All the data was calculated using SPSS version 22. Simple t-test was used for comparison of patient and surgeon satisfaction in terms of defined variable in both the groups, with a significant P value of less than 0.05. All the results were presented as Tables/Charts.

**RESULTS**

After following inclusion and exclusion criteria, 60 patient of age range from 14 to 70 years were included. The mean age for group A and B was 28.83 and 32.36 4 respectively, with a nonsignificant P value of 0.317 (p>0.05).

Both the operating time and cost of the treatment were highly significant statistically. The mean operating time in Group A was 61.49 ±12.95 minutes while Group B has mean value of 47.93 ±7.16 minutes. Group A patient was having a total cost of the treatment mean of 8533.33 ±2029.66 Rupees, While Group B with a total cost of the treatment mean of 4383.33 ±730.29 Rupees.

Details given in table.

The effect on quality of life of patients were highly significant. Mean work days missed from work in group A were 33.67days ±5.28 days, while in group it was 47.57±6.86 days reported by the patients. Patients in Group A reported with a mean bed rest of 16.63±4.18 days and group B with a mean value of 25.17± 4.39 days. Group A patients started their normal diet in a mean value of 55.73 ±11.59 days while Group B in a mean value of 73.17 ±10.17 days. So, statistical analysis of Quality of life get a highly
significant value (p=0.000) using chi square test. Details given in the table.

### Table No.1: Comparison of Group A and Group B

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean values</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td>Operating time in Minutes</td>
<td>61.49</td>
<td>47.93</td>
</tr>
<tr>
<td>Cost of treatment in Rupees</td>
<td>8533.33</td>
<td>4383.33</td>
</tr>
<tr>
<td>Work days missed</td>
<td>33.67</td>
<td>47.57</td>
</tr>
<tr>
<td>Bed Rest in days</td>
<td>16.36</td>
<td>25.17</td>
</tr>
<tr>
<td>Days after Normal diet started</td>
<td>55.73</td>
<td>73.17</td>
</tr>
</tbody>
</table>

*Chi square test

![Figure No.1 Descriptive statistics for QOL](image)

**DISCUSSION**

Treatment of mandibular fracture is the most frequent form of therapy provided by oral and maxillofacial surgeons, to restore the pre-injury form & function with least disability and shortest recovery period. Champy et al. presented the concept of 'ideal osteosynthesis lines' by the use of multi-disciplinary approach considering anatomical, biochemical and clinical factors. According to Champy, osteosynthesis plates should be fixed according to these lines to get the best results. Champy principles also stated that there are two types of forces acting in the symphysis and parasymphysis region. Tensile forces are present on the alveolar part while compressive forces are present on the inferior border of the mandible. Hence two plates should be used in area anterior to mental foramen to counteract the compressive and torsional forces, one at the lower border and the other 4 mm subapical to the roots of the anterior teeth.

Placement of two miniplates increases the total cost of the treatment for the patient and maximize the possibility of injury to the teeth roots, mental nerve injury, and also increase the operating time for the surgeon. So, if arch bar is applied in open reduction cases for mandibular fractures, then the use of lower arch bar as a tension band for para-symphysis fractures is addressed. This will eliminate the use of two miniplates in the para-symphysis region. This study was carried out to determine the functional outcome and patient satisfaction using two miniplates and one miniplate along with arch bar in para-symphysis fractures.

In this study, the mean value for patients treated with two miniplates was more than one miniplate along with arch bar. Same results were reported by Saluja et al. in his study. According to him average intra operative time for patients treated with two miniplates in mandibular parasymphysis fracture was 54.9mins and average intraoperative time for patients treated with one miniplate along with arch bar was 41.5mins. Less intra operative time is because more time is consumed in placing the upper tensionband plate in the subapical region of the teeth in mandibular parasymphysis fracture and hence easy placement of arch bar intraorally. Also it is thought that intraoperative time is operator dependant which directly relates to the expertises of the surgeon and his command of the procedure, but in this study the surgeries was done by single operator to eliminate this bias.

In our study the cost of the treatment was more for the patients with two miniplates than one miniplate along with arch bar which was highly significant statistically. Same results were reported by Hussain et al. in his study in which 2 miniplates were compared with one miniplate along with arch bar. The placement of a single miniplate followed by a relatively strong SS half round wire as dental tension band , showed upto maximize the advantages of an ORIF technique, and also it has minimized implanted material which minimises the cost effectiveness of the patients without compromising the stability of the fractured segment.

Quality of life (QOL)in medicine is specifically known as health related QOL, in which not only the evaluation of patient’s point of view is done in terms of outcome of the treatment, but it gives the clinicians valuable data about the impact of disease and their management, symptoms and side effect. It also determine the impact of illness, disease and treatment on patients. In our study effect on QOL was determined by measuring the number of days missed from job, bed rest post-operatively, and number of days after which normal diet was restarted. Mean work days missed by the subjects in group A with two miniplates were less as compared with group B in which one miniplate along with arch bar was used. Same was the case with bed rest and days after which normal diet was started. Patients with group A was having less time for bed rest and started they daily work and normal earlier than the patients with group B. The overall results were highly significant for effect on the QOL. In a study by Omeje et al. about the prospective analysis of QOL after management of fractured mandibul was done and was measured by the use of General Oral Health Assessment Index(GOHAI) and QOL score.
According to him the score declined in the initial day but it improved steadily after some days. There was no significant difference between the mean QOL of those treated by closed in comparison to those subjects treated with open reduction. In another study by Omeje et al., the which QOL were compared for mandibular fracture managed with closed reduction with open reduction and internal fixation. The results of the study showed a greater impact of treatment on QOL in terms of psychosocial, physical and pain domain differentially. Hence the results of our study don't show resemblance with above-mentioned studies. The reason behind this is the parameter used for the assessment of QOL is different in all studies.

CONCLUSION

The placement of two miniplates in the parasymphysis region is associated with greater operating time for the surgeon and more cost of the treatment for the patient as compared to one miniplate along with arch bar, but in return it increases the quality of life for the patients.

Recommendations: There is no published study on quality of life outcomes, therefore, another study with a large sample size is required to determine the effect on quality of life.

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Drafting: Amna Sarfaraz, Rabia Noreen, Nigam Sattar
Data Analysis: Mohammad Umar, Mohammad Sulaiman
Revisiting Critically:
Final Approval of version: Mohammad Umar

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

REFERENCES

Clinicopathological Characteristics of Basal Cell Carcinoma of the Head and Neck in Tertiary Care Hospital in Rawalpindi, Pakistan

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ABSTRACT

Objective: Clinicopathological Characteristics of Basal Cell Carcinoma of the Head and Neck in Tertiary Care Hospital in Rawalpindi, Pakistan.

Study Design: Randomized control trial study.

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

Materials and Methods: Clinicopathological analysis is done using H and E staining technique. A sample of 114 patients were selected. Cases were recuperated from the Data on age, gender, location of tumor and histopathological variant was collected and analyzed using SPSS version.

Results: BCC is common in males above 50 years of age comprising M: F ratio of 2.5:1 with nose been the most common anatomical site followed by the eye. Most common histopathological subtype include nodular variant followed by adenoid variant.

Conclusion: Nose been the most common clinical site instituted along with nodular variant as most common histopathological subtype of BCC in head and neck region.

Key Words: BCC, Malignancy, site, variant, morbidity


INTRODUCTION

Basal Cell carcinoma is commonest malignant tumor found locally destructive in nature with no metastasis but considerable morbidity. Major contributing factors include Sunlight and UV exposure. Certain international studies on BCC statistics, with less emphasis at national level is witnessed. Early in the nineteenth century in 1827, term “rodent ulcer” was used initially by Jacob Arthur, later known as BCC\textsuperscript{1}. It is the commonest cancer affecting humans\textsuperscript{2}. Its incidence is rising and it will exceed all other tumors in some years\textsuperscript{3}. BCC comes under the umbrella of NMSC and account for 75-80% of NMSC\textsuperscript{4,5}. It has varying incidence according to different geographical location. The incidence of BCC patients in UK and Australia ranges between 18% and 40%.

In North America the incidence of BCC is increasing at a rate of 10 % resulting in lifetime risk of 30% of developing BCC\textsuperscript{7}. According to another Australian study done in the year 2002 the incidence of BCC is (male/female) 1041/1745 per 100 000 per year\textsuperscript{8}. In Queensland, Australia the incidence of BCC is 2000 per 100,000 population\textsuperscript{9}. In United Kingdom 75000 new cases of BCC are annually diagnosed with increasing incidence by year 2040. As BCC cases are not entered in the skin cancer registries in UK, their incidence is still miscalculated\textsuperscript{10}. In South Wales the incidence is recorded to be 114.2 per 100000 population. In Minnesota, USA it is reported to be 146 per 100,000 population\textsuperscript{7}. According to a study in our setup at AFIP Rawalpindi, Pakistan, 7.2% of the cases reported were skin cancers and 33% out of these were BCC\textsuperscript{11}. Another study from Pakistan reported that skin malignancies comprised of 0.04% cases out of which 40 % cases were BCC\textsuperscript{12}. Exposure to ultraviolet radiation during childhood is a significant factor in development of BCC. Adult exposure to ultraviolet radiation does not seem to have the same impact as in younger ages. Intermittent sunlight exposure as compared to continuous exposure has much more importance in development of BCC. Wavelengths of 293, 354 and 380 nm of UV have been linked to its pathogenesis. Development of malignant melanoma and NMSCs is linked with 2 vitamin D polymorphism. Patients on immunosuppressive therapy are also more prone to the development of BCC as well.
as SCC. Xeroderma pigmentosum, Gorlin syndrome, Rasmussen Syndrome, Rombo syndrome, and albinism are allied to augment risk factor of SCC. Gorlin syndrome or the nevoid BCC syndrome is caused by mutation in PTCH gene the Hedge Hog pathway. The incidence of BCC increases with age and it is commonly diagnosed after 40 years of age. According to WHO, the incidence of BCC is greater in older age groups, with higher frequency in men than women. However, in younger age group, there is a greater incidence in women than men due to the use of indoor tanning and smoking.

It has been documented that BCC is slightly more common in Pakistani males as compared to females. The M: F ratio ranging from 1.2 - 1.4:1.14,15 Most common sites for BCC in Pakistani population is head and neck (93.5%), particularly nose, forehead, periorcular areas and cheek among which nose and cheek been the most common sites. Basal cell carcinoma is defined as locally destructive slow epidermal tumor. Histologically, BCC is characterized by proliferating strands of uniform, hyperchromatic basophilic cells with scant cytoplasm and oval nuclei. The islands and cords have peripheral palisading that looks similar to the basal layer of the epidermis. WHO defines basal cell carcinoma as “A group of malignant cutaneous tumors characterized by the presence of lobules, columns, bands or cords of basaloid cells (germinative cells)”.

BCC is classified into different variants. The common morphological feature present between these variant is the presence of lobules, columns, bands and cords of basaloid cells characterized by a scant cytoplasm, loose fibromucinous stroma and retraction artifacts. The retraction artifacts arise due to the lack of hemidesmosomes that attaches the overlying epidermis to the underlying dermis.

**Nodular Basal Cell Carcinoma:** It consists of well demarcated lobules and nests of basaloid cells that seem to originate from the basal / germinative layer of the overlying epidermis reach up to the reticular layer of the dermis. The basaloid epithelial cells of the nests and strands show peripheral palisading. Cleft like spaces called retraction artifacts are seen between the tumor nests and the surrounding adjacent connective tissue.

**Superficial BCC:** It is a tumor which consists of nests of basaloid cells which project from the epidermis and extend up to the papillary layer of the dermis.

**Micronodular Basal Cell Carcinoma:** It comprises of small nodules that seem to be separated by normal collagen in between them. Associated with perineural invasion most of the time.

**Infiltrating Basal Cell Carcinoma:** It consists of very fine thin strands, cord like arrangement of basaloid (germinative) cells that infiltrate between the collagen bundles into the underlying dermis. This variant usually does not show peripheral palisading and artifactual retraction.

**Fibroepithelial Basal Cell Carcinoma:** It consists of interconnecting network of cords and strands of basaloid cells that extend downwards from the overlying epidermis. These strands of germinative cells are surrounded by fibrous stroma containing blood vessels with indolent clinical course.

**Basal Cell Carcinoma with adnexal differentiation:** It is composed of BCC with the presence of adnexal differentiation. It may have trichilemmal, sebaceous, ductal and follicular elements. Sometimes eccrine and apocrine differentiation is also seen in this variant.

**Basosquamous Carcinoma:** The presence of BCC with histopathological features of SCC was first hypothesized in the year 1922. They represent a continuum which extends from a BCC at one and SCC at the other end. This aggressive variant is characterized by BCC with squamous differentiation. The epithelial cells have higher degree of keratinization. Peripheral palisading is lost in some areas and the cells tend to have a vesicular chromatin and varying degrees of pleomorphic can be seen. It has a tendency to metastasize unlike a typical BCC which is locally destructive.

**Keratotic Basal Cell Carcinoma:** This variant has the typical features of a nodular BCC which is composed of basaloid tumor cells with deeply stained basophilic nucleus, scant cytoplasm, peripheral palisading and retraction artifacts, along with horn cysts in between the tumor nests.

### MATERIALS AND METHODS

Data of all the malignant skin tumors was retrieved from the records during January and June 2016 and only BCC in head and neck were included in the study. Hematoxylin and Eosin slides were prepared, diagnosis and reconfirmed in consultation with a senior pathologist. The clinical data was obtained from record files of Histopathology Department of Armed Institute of Pathology. Data such as age, gender, anatomical location and histopathological variant was collected. The BCC cases included different variants of BCC classified according to WHO Fascicle of Skin Tumors. Variables (quantitative) such as age mean ± SD was calculated. Variables (qualitative) such as gender, site of biopsy, histopathological variant, frequency and percentages were calculated.

### RESULTS

From the results following observations were made. According to the 114 studied BCC cases the mean age calculated was 63.18 ± 14.41 years with a minimum age of 33 and maximum age of 86 years. 33 (28.94%) out of 114 cases were in range of 33 to 50 years and the remainder cases 81(71.05%) were above 50 years shown in figure 1. Among these cases female patients...
are 33 (28.94%) whereas 81 (71.05%) were male with ratio of male to female is 2.5:1. Out of the 114 cases patients, 72 (63.16%) cases of BCC were Nodular variant, 18 (15.79%) Adenoid variant, 12 cases (10.53%) Infiltrating variant, 6 case (5.26%), Micro nodular variant, 3(2.63%) Fibro epithelial variant and 3 (2.63%) Pigmented variant shown in figure 3. Highest proportion of tumors was on the nose among total 114 cases that is 51 out of 114 (44.74%). Another common site eye having 27 (23.68%) cases. Cheek comprises 18 (15.79%) cases and neck, scalp and forehead comprises the remainder 15 (13.16%) illustrated in figure 2.

**DISCUSSION**

Basal Cell Carcinoma is non melanoma skin cancer with increasing incidence globally due to increased ultraviolet exposure and the depletion of ozone layer in certain areas because of pollution and environmental hazards. Ultraviolet radiation causes damage to DNA leading to subsequently development of BCC. Immunosuppressed and transplant patients are more likely to develop BCC. BCC development is also seen in Neviod Basal Cell Carcinoma Syndrome, Rasmussen syndrome, Darier’s disease, Bazex syndrome and Rombo syndrome as they share the same Sonic Hedgehog pathway Mutation genetic mutation. Although, BCC is an indolent tumor and does not metastasize but it is the most common non melanoma skin cancer and causes considerable local destruction and morbidity and is a huge financial burden on the economy.

In present study, BCC has a prediction towards elders. 63.18 ± 14.41 years is mean age. >50 years comprises 71.05% cases. Age range between 33 to 50yrs comprises 28.94% cases, first 3 decades of life comprises nil cases. 8th decade of life comprises peak incidence. In another study done in our institute by Asif et al the mean age of patients with BCC was 60.04 years and two third of the patients were from the sixth decade of life. Peak prevalence was seen in the seventh and eight decade of life. Wehshah et al also reported the tumor to be the most frequent in age group between 60-69 years. The trend of BCC in older age could be attributed to the decreased regenerative and corrected potential of the DNA to correct the genetic damage caused by ultraviolet sun radiations.

According to our study the majority of patients with BCC were male 71.05%, as compared to female 28.94%. The male to female ratio is 2.5:1. Similar trend is seen in a study by Asif et al in which males account for 53.2% cases with 1.2:1 ratio of male to female. The male predilection for BCC is most likely linked to their outdoor occupations and subsequent increased UV light exposure as compared to females in our part of the globe.

After analysis for the anatomical site for occurrence of BCC, it was found out that nose is the most common site accounting for 44.74%. Eyes being 2nd common site with 23.68% cases. 15.79% cases from cheek with neck, scalp and forehead consisting of 13.16% case. Similar trend is seen in a study by Asif et al in which common site in head and neck comprise of nose and cheek. Janjua et al carried out an analysis on 171 cases of BCC in the head which they reported that the nose was the most anatomical common site for BCC in this region and accounted for 31.5% of their total cases. According to their results second most common location was the cheek accounting for 26.9% of their cases. Afridi et al also observed that the nose was the

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**Figure No.1:** Age Distribution of BCC cases (n=38)

**Figure No.2:** Site distribution - Basal Cell Carcinoma (n=38)

**Figure No. 3:** Variants of BCC (n=38)
most common site for BCC (45.9%) followed by periocular (28%) and cheek (15.6%). Results from other Asian countries are also similar to my results and support my finding for the nose being most common BCC site.

The information about the lesion size was also collected and analyzed. It was found out that at the time of presentation most of the lesions ranged between 0.2- to 9cm. The mean size at the time of presentation was 20mm. In an Italian study Cigna et al reported mean size of lesion at the time presentation to be 12mm which is smaller than our study. In third world developing countries like Pakistan, late presentation is a common finding due to lack of a preventive public awareness programs which results in considerable morbidity and huge financial burden on the patient.

Histopathological pattern of the tumor was analyzed and assessed in our study and in this regard nodular variant is the most common histopathological subtype of BCC in the head and neck region accounting for 63.13% cases followed by adenoid variant accounting for 15.79%. Similar trend is seen in a study by Gundalli et al and McGuire et al in which nodular variant has been reported as the most common histopathological subtype of BCC in the head and neck region. Aandani and Ganatra and Cigna et al in their respective studies have supported the similar trend.

CONCLUSION

BCC is fairly common malignant skin tumor in our society. BCC is common in older age group above 50 years and is uncommon in younger age. Nose is the most common site followed by the eye. BCC is more common in males than females more likely due to outdoor sun exposure. Nodular variant followed by the adenoid variant are the two most common histopathological subtypes in the head and neck region.

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Data Analysis: Maria Ilyas, Misbah
Revisiting Critically: Maria Ilyas, Misbah
Final Approval of version: Maria Ilyas

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

REFERENCES
Post-Operative Depression in Rhinoplasty Patients
Osman Bashir Tahir, Muhammad Abbas, Nauman Mazhar and Aysha Butt

ABSTRACT

Objective: To explore the development of depression in patients undergoing rhinoplasty.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Halcyon Medical Centre Lahore, July 2018 to March 2020.

Materials and Methods: It is a cross-sectional study consisting of 38 patients. Out of these 10 patients were male and 28 females. 35% patients went through this surgery for medical reasons while remaining for aesthetic purposes. Follow up plan for rhinoplasty patients already in place at our Halcyon Medical Centre Lahore. All the patients coming for follow up after rhinoplasty were properly assessed for the complications one can have after rhinoplasty. Patients who showed signs and symptoms of major depression were assessed in detail for early identification and management.

Results: Out of 38 patients undergoing rhinoplasty, only 5 patients showed signs of major depression. Four of these were females and one male. Total percentage of affected individuals was 13 % which might not be clinically significant but it seems to be more common among females as compare to men.

Conclusion: Depression might not be a clinically significant post-operative complication of Rhinoplasty but still it can be troublesome for patients, their families and carers.

Key Words: Rhinoplasty, Plastic surgery, Depression, Psychiatry.

Citation of article: Tahir OB, Abbas M, Mazhar N, Butt A. Post-Operative Depression in Rhinoplasty Patients. Med Forum 2020;31(10):61-64.

INTRODUCTION

Plastic surgery has emerged as an advancing field for the last few decades. The continuous advancement of medical equipment and techniques in this field have had an effect on the surgical as well as pharmaceutical development. One of the important change seen in this regard is the rising trend of aesthetic surgery. Despite risk of complications, many people undergo cosmetic surgery. Like other surgeries, plastic surgeries also accompany post-operative complications which may be physical or psychological in nature. The most significant complications are scarring, keloids, organ damage, dissatisfaction and depression. Rhinoplasty is a surgery designed to change the shape of nose.

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Printed: October, 2020
MATERIALS AND METHODS
This cross-sectional study was conducted on Rhinoplasty patients at Halcyon Medical Centre, Lahore between July 2018 to March 2020. The study included 38 patients, out of which ten were males and 28 females. The study included two types of patients:

1: Patients with aesthetic motives.
2: Patients with functional motives, most commonly being the breathing problems.

Data regarding these two sets of individuals was collected from the clinic. ICD-10 criterion was used for diagnosis of depression. For the collection of data, these patients were briefly explained regarding the research, its objectives and clinical goals. Period of recovery is sometimes greater than expected in some cases and for the psychological parameters evaluation, a proper follow up is vital. One of the most important things to be done is the assessment of the patient before the surgery to rule out any prior depressive symptoms.

Inclusion Criteria: We included adult patients who went through rhinoplasty in this period i.e. between July 2018 to March 2020. Otherwise Healthy individuals who were not on any antidepressants prior to undergoing surgery were included in the study.

Exclusion Criteria: Patients suffering from depression or on antidepressant medication were excluded from the study. Each individual was called for a follow up according to protocol of our medical centre. Every patient with rhinoplasty was free to discuss any concern postoperatively. However, patients who showed signs and symptoms of major depression were given necessary care and proper management if they had any problem. All of their concerns were noted down and explained to them.

All the data collected from these individuals was analyzed. SPSS Software version 16 was used for data entry, analysis and compilation. For qualitative variables, frequency and percentage distribution tables were generated. Mean and standard deviation were calculated for quantitative variables. P value of 0.05 was taken as significant.

RESULTS
It is usually noted that women have more interest in cosmetics and aesthetics than men. Same is the case in our study. There were total of 38 patients out of which 26% were men and 74% women. It is given in tabular form as follows.

Table No.1: Gender detail with percentage

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>10</td>
<td>26%</td>
</tr>
<tr>
<td>Female</td>
<td>28</td>
<td>74%</td>
</tr>
</tbody>
</table>

For procedure such as Rhinoplasty there can be two motives. One is Medical or Functional motive. The other reason is cosmetics. Most of the patients arriving in plastic surgery clinics have cosmetic motive. Our results also show that most of the patients had cosmetic reasons to undergo Nose Reshaping procedure.

Table No.2: Motive of surgery of patients with percentage

<table>
<thead>
<tr>
<th>Motive of Surgery</th>
<th>% age of patients</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Reasons</td>
<td>34%</td>
<td>13</td>
</tr>
<tr>
<td>Cosmetic Motive</td>
<td>66%</td>
<td>25</td>
</tr>
</tbody>
</table>

Patients with medical reasons were mostly men and with cosmetic motive were mostly women. Personal satisfaction is an important parameter when considering the results of a cosmetic surgery. In case of Rhinoplasty, nose reshaping is a useful procedure for cosmetic reasons, but the results are not always satisfactory. Following data describes the personal satisfaction in first 2 months after rhinoplasty.

Table No.3: Gender-wise personal satisfaction of patients

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of Satisfied Patients</th>
<th>No. of unsatisfied Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>09 (23.68%)</td>
<td>01 (2.63%)</td>
</tr>
<tr>
<td>Females</td>
<td>24 (63.15%)</td>
<td>04 (10.52%)</td>
</tr>
</tbody>
</table>

Depression after the surgery was analysed. Following information was gathered in these individuals.

Table No.4: Depression after surgery detail

<table>
<thead>
<tr>
<th>Category-1 without Depression</th>
<th>Category-2 with Depression</th>
<th>Total</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-1 Males</td>
<td>09</td>
<td>01</td>
<td>10</td>
</tr>
<tr>
<td>Group-2 Females</td>
<td>24</td>
<td>04</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>05</td>
<td>38</td>
</tr>
</tbody>
</table>

As depicted in the above data, P value is greater than optimal value of 0.05.

Number of patients who visited the clinic and went through the procedure of Rhinoplasty were mostly women. Ratio of men to women was 1:3. The basic motive of surgery in these cases was for cosmetic reasons. Most of the patients who had gone surgery for...
medical reasons were satisfied with the results. Dissatisfaction and psychological issues were seen in patients more concerned with cosmetic reasons. 04 out of 05 patients who were not satisfied with the results were female and their motive was cosmetic improvement. There were total 5 patients who developed major depression. Out of these 04 (80%) were females and 01 patients (20%) was male. This makes a total percentage of 13 % patients who presented with Post-Operative Major Depression.

**DISCUSSION**

This study was conducted to evaluate post-operative depression in Rhinoplasty patients. Demographic details are important when evaluating cause and response of patients undergoing cosmetic surgery. Pakistan being developing country doesn’t report many cases of cosmetic surgery as compare to developed countries. Cultural norms and social behaviour are usual barriers to cosmetic surgeries. Besides aesthetic motives, functional causes are probable causes of surgeries such as Rhinoplasty. The number of female patients visiting the clinic for aesthetic reasons is greater than the number of male patients. Functional reasons may be similar in both males and females but aesthetic motive is greater in females. In western population, cosmetic surgery has increased in the last decade. Similarly, our results show that mostly females went through Rhinoplasty and the number of females going through this procedure for medical reasons was less than those due to cosmetic reasons.

Rhinoplasty patients can also present with breathing problems which might have better prognosis. In our study, five patients showed signs and symptoms of major depression. One was male and four females. Most of the patients were satisfied after one month of surgery. Four female patients who showed symptoms of depression were not satisfied with the results initially. “P” value for both male and females was much greater than 0.05. Therefore, our results show that post-operative depression is not statistically significant. However, major depression can be a very serious health problem which should be dealt carefully and plastic surgeon should get the help of psychiatrist or psychologist if needed. We noticed that our patients were reluctant to visit psychiatrist or psychologist due to stigma. This can improve by proper awareness & psycho education.

Naraghi, M, et al, conducted a research and they concluded that depression is not clinically significant in Rhinoplasty patients. Only a few patients showed post-operative depression in their research and few of these already had some psychological complications prior to surgery. The main reason of this insignificance is success of surgery and alleviation of any breathing problem associated. If any post-operative depression was observed in these patients, it was treated within a short period of time. Both psychotherapy and antidepressants proved to be effective in such cases. Patient satisfaction is an important concern which cannot be ignored. Our research shows similar results. Focus of our research was major depression though statistically insignificant but can be a major health problem for the patients and challenging for treating doctor as well.

**CONCLUSION**

The findings of our research suggest that the level of satisfaction among patients undergoing rhinoplasty was high, with rather little or no complications of psychological nature. Though Depression was not statistically significant Post-Operative complication of Rhinoplasty in our study, it cannot be ignored. It was more common among females especially those undergoing surgery for cosmetic reason. Major depression is a serious health condition and even if it happens in a few patients, it can be very disturbing for the patient and family as well.

**Recommendations:** We suggest that the patient undergoing surgery should be carefully evaluated for any major psychiatric illness before the procedure and patients for rhinoplasty with cosmetic indications should be selected very carefully. Collaboration between Plastic surgery, psychology and psychiatry teams will go a long way in improving the outcome of our patients.

**Acknowledgements:** We are thankful for contributing in data processing, references and final manuscript revisions to Dr. Fatima Aziz Chaudhry, Research Intern. Department of Psychiatry & Behavioral Sciences, SIMS/ Services Hospital Lahore / Haleyon Medical Centre, Lahore and Sania Shaukat, Clinical Psychologist, Lahore.

**Author’s Contribution:**

- Concept & Design of Study: Osman Bashir Tahir
- Drafting: Osman Bashir Tahir, Muhammad Abbas, Nauman Mazhar, Aysha Butt
- Data Analysis: - all above -
- Revisiting Critically: - all above -
- Final Approval of version: Osman Bashir Tahir

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

**REFERENCES**

Pattern of Developmental Dental Anomalies in Patients Visiting Sardar Begum Dental College, Peshawar

Sana Naem¹, Farzana Kalsoom¹, Saifullah Khalil², Tehmina Marwat³, Muhammad Sheraz Alam¹ and Amin Jan⁴

ABSTRACT

Objective: To determine the pattern of developmental dental anomalies, compare age and to identify the most common anomaly.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Sardar Begum Dental College, Ghandhara University, Peshawar during six months period in the year 2016.

Materials and Methods: This study was carried out on 350 patients with developmental dental anomalies. Preoperative data were collected through history and clinical examination. Each patient was evaluated for dental anomalies to identify the pattern, most common anomaly and compare the age distribution of anomalies. Statistical analysis included descriptive statistics and χ² test. Results were considered significant if P<0.05.

Results: The age range was 8-20 years and maximum number of patients presented in 17-20 years age group (46%). The commonest anomaly was rotation (28%) followed by cusp of Carabelli (14.3%). Rotation was most common in 17-20 years age group. Cusp of Carabelli was most common in 13-16 group and in 8-12 years age group microdontia.

Conclusion: Early detection of anomalies is important to prevent complications.

Key Words: Developmental dental anomaly, Pattern, Rotation, Hyperdontia, Cusp of Carabelli, Microdontia.


INTRODUCTION

Developmental dental anomalies are variations from the normal, size, shape structure, number and position¹. These anomalies are caused by myriad of genetic/hereditary/ acquired, local as well as systemic factors, influencing either the deciduous or permanent teeth before or after birth²-³. Globally, the frequency ranges from 1.7% to 5.5%⁴,⁵. It is reported that these anomalies variate in number (hyperdontia, hypodontia) predominates than variation in size and shape⁶. Few studies have been done in Pakistan to document dental anomalies in population, which shows varied results ranges from 1.4% to 7.8%,⁶,⁷,⁸

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The rationale is to identify the frequency of these anomalies in population adding more data to the literature for future comparisons. This study will also help to generate population characteristics databases which could be used for personal identification purposes like forensic odontology and will also help in the early identification of these anomalies. Once the problem is identified, it will be convenient for healthcare provider to plan comprehensive management for the condition and prevent future complications.

MATERIALS AND METHODS

Data Collection Procedure: Informed consent was taken from the patient/guardians accordingly. Patients were examined thoroughly clinically for any developmental dental anomaly/anomalies. Supplemented by detailed history and radiographic study (Periapical and OPG). The data collected were entered in a pre-formed proforma.

Data Analysis: The data were analyzed by applying descriptive statistics and chi- square test and was then calculated by using Statistical Package for Social Sciences (SPSS) version 16. For age distribution age range, mean ±SD and percentages of age groups were computed and represented in the form of graph using Microsoft Excel. Similarly, frequencies and percentages were computed for pattern of anomalies, distribution according to age groups. Tabulated and graphic analysis
of the data was performed. Data were compared calculating \( \chi^2 \) and \( p \) values. The level of significance was set at \( p < 0.05 \).

**RESULTS**

The age range was 8-20 years, with a mean value 14.5 ± 5.5 years. Maximum number of patients presented in 17-20 years age group (46 %) followed by 13-16 years (39%). Detail data is given in figure 1. The most common anomaly was rotation (28%) followed by cusp of Carabelli (14.3%), while the least common was anodontia (0%) followed by gemination (0.3%). Rest of the detail is given in figure 2 and table 1.

Rotation was most common in 17-20 years age group (n=43). While cusp of Carabelli was common in 13-16 group and in 8-12 years age group microdontia was more prevalent. More detail is given in table 2.

![Graph showing distribution of anomalies according to age groups](Image)

**Figure No. 1: Developmental dental anomalies according to age Group**

**Table No. 2: Distribution of anomalies according to age groups**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Type of anomalies</th>
<th>Age Groups</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>8-12</td>
<td>13-16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>1</td>
<td>Microdontia</td>
<td>3(0.8%)</td>
<td>2(0.6%)</td>
</tr>
<tr>
<td>2</td>
<td>Macrodontia</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>3</td>
<td>Gemination</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>4</td>
<td>Fusion</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>5</td>
<td>Concrescence</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>6</td>
<td>Talon cusp</td>
<td>1(0.3%)</td>
<td>1(0.3%)</td>
</tr>
<tr>
<td>7</td>
<td>Cusp of Carabelli</td>
<td>3(0.9%)</td>
<td>4(1.14%)</td>
</tr>
<tr>
<td>8</td>
<td>Dens Evaginatus</td>
<td>0(0%)</td>
<td>1(0.3%)</td>
</tr>
<tr>
<td>9</td>
<td>Dens Invaginatus</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>10</td>
<td>Taurodontism</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>11</td>
<td>Amelogenesis Imperfecta</td>
<td>1(0.3%)</td>
<td>2(0.6%)</td>
</tr>
<tr>
<td>12</td>
<td>Dentinogenesis Imperfecta</td>
<td>0(0%)</td>
<td>1(0.3%)</td>
</tr>
<tr>
<td>13</td>
<td>Anodontia</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>14</td>
<td>Hypodontia</td>
<td>3(0.9%)</td>
<td>3(0.9%)</td>
</tr>
<tr>
<td>15</td>
<td>Oligodontia</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>16</td>
<td>Hyperdontia</td>
<td>1(0.3%)</td>
<td>2(0.6%)</td>
</tr>
<tr>
<td>17</td>
<td>Ectopic Eruption</td>
<td>2(0.6%)</td>
<td>3(0.9%)</td>
</tr>
<tr>
<td>18</td>
<td>Rotation</td>
<td>7(2%)</td>
<td>9(2.6%)</td>
</tr>
<tr>
<td>19</td>
<td>Impaction</td>
<td>2(0.6%)</td>
<td>3(0.9%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>23(6.5%)</td>
<td>31(8.8%)</td>
</tr>
</tbody>
</table>
DISCUSSION

During routine clinical examination of oral cavity these developmental dental anomalies are noted in clinical practice. A plethora of epidemiological studies, which have been conducted across the globe. Unfortunately, few studies have been conducted in Pakistan about the pattern and prevalence of dental anomalies.

Microdontia: The prevalence ranges from 0.8% to 8.4% in various populations. In this study microdontia was noted in 8.2% of total patients, while Backman et al\(^9\) had recorded lower percentages in their study.

Macrodontia: Only two patients presented with macrodontia. Macrodontia is much less common than microdontia.\(^10\),\(^11\),\(^12\),\(^13\)

Macrodontia is noted 0.6% in the present study. Similarly, Patil S\(^14\) gave 0.2% in his study.

Gemination: Gemination is defined as an incomplete division of one tooth germ. It has prevalence of 0.1% in permanent dentition.\(^15\) 0.3% of total cases was found in the present study. Similar findings had been given by Guttal KS\(^1\)(0.28%) and Altug-Atac AT et al\(^16\)(0.07%).

Fusion: In the present study 0.6% fusion cases was found. The tooth may be of normal size or larger than normal. The prevalence ranges from 0.02% to 5% based on geographic, racial or genetic factors.\(^17\),\(^18\),\(^19\),\(^20\) Nearly similar results were given regarding the fusion 0.7% by Kositbowornchai S\(^21\), 0.23% by Altug-Atac AT et al.\(^16\)

Concrescence: In the present study, only two patients had concrescence constituting 0.6% of all the dental anomalies. Guttal KS\(^1\) had reported 1.4%.

Talon Cusp: During the present study 3.7% talon cusp occurred. Guttal KS\(^1\) had reported 4.28%. Overall talon cusp ranges from less than 8% in different populations.\(^3\),\(^21\),\(^22\),\(^23\)

Cusp of Carabelli: The cusp of Carabelli reported in this study is 14.3%. It was seen in 2.17% by Najm MJ et al\(^24\) and by Falomo O in Nigeria which was 17.43%.

Dens Evaginatus: In the present study, dens evaginatus comprised 2.6% of the total dental anomalies. Guttal KS et al\(^3\) had reported 2.85%. These results are in accordance with results of the current study. In two successive surveys of over 1,000 Chinese subjects 1.3% and 1.5%, were affected by dens evaginatus.\(^25\),\(^26\) A slightly higher prevalence figure of 4.3% was reported in several Indian studies.\(^3\),\(^22\),\(^27\),\(^28\)

Dens Invaginatus: In the present study the percentages of dens invaginatus was 3.12%. The incidence among several population groups ranged from 0.25 to 5.1%.\(^29\),\(^30\)

Taurodontism: Taurodontism is 0.6% in this study Its prevalence has been reported to range between 1.67% and 16%. In study of Guttal KS\(^1\), it accounted for 18% and Gupta SK et al\(^22\) reported 2.49%.

Amelogenesis Imperfecta (AI): It is 3.9% in present study and its prevalence varies from 0.7% to 4% according to the populations studied. The sample of Sener S et al\(^23\) included two cases (0.2%), which is comparatively lower than the present study. Najm MJ et al\(^24\) reported 2.04% and 7.72% in the study of Ezoddini AF et al.\(^10\)

Dentinogenesis Imperfecta: In this study, DI was found to be 1.4%. 1 case was reported only (0.09%), making it the rarest anomaly.\(^22\)

Anodontia: No case of anodontia was noted in the present study.

Hypodontia: Current study showed 9.7%. The recorded prevalence rates of different studies ranges from 0.1% to 11.2%. Tofangchiha M\(^3\) and coworkers reported a prevalence rate of 9.7%. Figures about hypodontia are in line with the results obtained from studies in Japan\(^3\) 9.40% and Saudi Arabia\(^3\) 9.41%, while several other studies showed in little bit lower prevalence rates of 6.5%, 7.9%, 7.25%, 6.9%, 7.68% respectively.\(^21\),\(^23\),\(^34\),\(^35\)

Oligodontia: This study showed 0.9% oligodontia. It is relatively rare condition with the prevalence reported to vary from 0.08% to 8%. Altug-Atac AT et al\(^16\) had found 0.13%, Backman 1.9%, while Thongudomporn U et al\(^17\) a higher percentage (8.1%) in their studies.

Hyperodontia (Supernumerary Teeth): This study recorded 5.5% hyperodontia. The prevalence ranges from 0.3% to 6.5% in various populations.\(^3\),\(^33\),\(^34\),\(^35\) In Caucasians they range from 0.4% to 2.1%; while they are 3.4% for Japanese and 6% for American Blacks.\(^3\)

Ectopic Eruption: This study recorded 7.95%, which is similar to Gupta SK\(^4\) study. A very high percentage had been recorded in Pakistan by Abbas Q et al\(^6\) with 21.3% of ectopic eruption. This difference is due to the selected orthodontic patients.

Rotation: 28% rotation is noted in this study. Gupta SK\(^4\) showed that rotations occurred 10.24%. In the present study high prevalence of rotation is due to the fact that 45° and 90° rotations were included.

Impaction: 8.5% impactions were present in this study. Ezoddini et al\(^10\) and Thongudomporn and Freer also found a somewhat similar prevalence of respectively 8.3% and 9.9% in non-orthodontic patients.\(^27\)

Figure No. 2: Distribution of type and number of anomalies according to age group
CONCLUSION

The age range was 8-20 years and maximum number of patients presented in 17-20 years.
The most common anomaly was rotation followed by cusp of Carabelli, while the least common was anodontia. Rotation was most common in 17-20 years age group, while cusp of Carabelli was most common in 13-16 and microdontia in 8-12 years.

Various anomalies are noted. The presence of such anomalies suggests a complete evaluation of the patient to rule out any syndrome and initiate treatment earlier.

Recommendations: Young patients are psychologically more conscious about their esthetics and these anomalies may disturb their psychosocial behavior:
1. To reduce the complications in affected patients, it is recommended that dental and radiographic examination must be carried out routinely.
2. More studies are required in rural and urban hospital from all districts of Khyber Pakhtunkhwa to assess and adopt earlier management.
3. Public dental health services may be initiated in the province.

Author's Contribution:
Concept & Design of Study: Sana Naeem
Drafting: Farzana Kalsoom, Saifullah Khalil
Data Analysis: Tehmina Marwat, Muhammad Sheraz Alam, Amin Jan
Revisiting Critically: Sana Naeem, Farzana Kalsoom
Final Approval of version: Sana Naeem

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

REFERENCES


A Comparative Observational Study Signifying the Diversity of Clinical Features in Patients having Tuberculosis with and Without Renal Failure

Mahnoor Khalil¹, Syed Muhammad Baquar Raza¹, Ajmaal Jami³, Syed Mubarak Ali², Yumna Ahmed¹ and Siraj Us Salkeen¹

ABSTRACT

Objective: Renal failure has in recent period exposed a shocking augmentation globally and there are increasing facts demonstrating that it can affect presentation and results of treatment in patient of TB disease. This study was performed to study the differences in presentation of pulmonary tuberculosis in patients who present with renal failure and who present without renal failure.

Study Design: Comparative Observational Study

Place and Duration of Study: This study was conducted at the Dept. of Medicine, Abbasi Shaheed Hospital, Karachi from May 2018 to September 2019.

Materials and Methods: The study comprised of a total of 107 patients. All the patients who were diagnosed cases of pulmonary tuberculosis were chosen for this study and on the basis of the data patients were allotted to two groups. The patients of tuberculosis who were found to have renal failure were kept in Group one and other group had patients of tuberculosis without renal failure. Data was analyzed using SPSS version 20.0. Quantitative data was presented as mean ± SD while qualitative was presented as frequency (%). T-test and chi-square test were used to assess the significance and p-value was set at 0.05.

Results: In a total of 107 patients 62 (58%) were males and 45 (42%) were females divided into 2 groups. The mean age of patients was 64.56±8.77 years in renal failure group and 38.25±12.70 years in without renal failure group. Substantial differences were observed between the 2 groups with respect to not only the laboratory values such as lymphocytes, neutrophils and protein but also with regards the clinical features (p<0.001).

Conclusion: The present study concluded that a significant difference existed regarding the clinical indices of TB patients with renal failure and without renal failure in the patients. The features including shortness of breath, productive cough, chest pain, hemoptysis, pleural effusion and diabetes mellitus were observed to be more common in renal failure group while night sweats, fever, and fatigue were more common in the non-renal failure group.

Key Words: Pulmonary Tuberculosis, renal failure, non-renal failure.


INTRODUCTION

An airborne infection having high mortality as well as morbidity rates globally is the tuberculosis of the lungs or pulmonary tuberculosis (TB). Although advancements have been achieved in anti-tuberculous (anti- TB) medicines as well as the utilization of directly observed treatment short course (DOTS) therapy has been prescribed for many decades. However, the mortality of tuberculosis still remains at a greater level in many parts of the world, especially developing ones¹,² Worldwide estimates of death due to tuberculosis are at about 1.7 million per annum, approximately 3 deaths per minute³. In order to manage the patients of TB, it is of prime importance to investigate the clinical features linked with mortality of TB. Nevertheless, more intense and aggressive treatment can be provided by clinicians to patients through early identification as well as stratification of patients to prevent its spread. Increasing age associated with underlying co-morbid conditions is often regarded to be independent morality predictors in TB⁴. In contrast, extensive presentation radio-logically as well as bacterial load in sputum is less likely to be regarded as an independent risk factor⁵. Researches evaluating
drug safety profiles on mortality have shown to report controversial results, and many of the morality predictors are non-modifiable.

Susceptibility to tuberculosis (TB) is highly increased in patients having chronic kidney disease (CKD) / renal failure in comparison with patients having normal kidney function. Impairment of cell-mediated immunity, human immunodeficiency virus (HIV) co-infection, and renal failure associated diabetes mellitus (DM) and immunosuppressive medicines are some of the chief reasons for TB infection in CKD / renal failure patients. It has been reported that patients belonging to ethnic minorities have shown to be particularly at higher risk for CKD and TB development. However, in CKD/ renal failure patients, diagnosing TB becomes a challenge as well as delayed because of presentation of non-specific symptoms plus a high involvement of extra pulmonary TB. As stated above, since patients with TB are at increased risk for developing renal disease, especially in patients belonging to ethnic minority groups who have been reported to be at a particular risk of developing active TB infection plus also have a high prevalence of CKD and renal failure. The dilemma exists in a way that no guidelines have investigated and / or treated TB disease with renal failure in such population. Even though it is established for the medical treatment and duration of TB that different views exist with respect to its dosing in renal failure patients. Almost no trial has been carried out in TB patients having renal failure, especially in dealing with immune suppression as well as transplantation. Even limited evidence is present for screening as well as treating latent infections and shows variations in practicing of approach in order to prevent reactivation.

The reasons for the cause of increased susceptibility to TB with regards to CKD/ renal failure and with patients on dialysis or post transplantation are; patients born in foreign countries that have visited UK in the last 5 years, having Asian, African, East European or South American ethnicity or with a history of contact with positive smear T.b infection. Approximately half of the patients with CKD show a decreased sensitivity to tuberculin skin test; therefore, cure from TB cannot be confirmed by a negative tuberculin skin test in a TB patient with renal disease.

The objective of this study was to investigate the association and features of renal failure with clinical presentation of TB patients in Pakistan, since very few studies done here have evaluated this association. Therefore, this study was conducted in order to explore the role of renal failure on clinical presentations of patients diagnosed with TB.

MATERIALS AND METHODS

This was a cross sectional observational study through non probability convenient sampling technique carried out for a period of May 2018 to September 2019 in Dept. of Medicine, Abbasi Shaheed Hospital, Karachi. Ethical permission was taken from the Institutional review board of the hospital.

One hundred and seven in-patients who were diagnosed to have pulmonary tuberculosis were chosen for this study and were divided into two groups’ i.e. one group with renal failure and other group without renal failure. Patients with age between 20 to 70 years, new onset of respiratory symptoms, non-smokers, not associated with acute illness, raised ADA level on pleural D/R, chest radiographic findings of patchy infiltrates, bilateral or unilateral hilar lymphadenopathy, cavitations, homogenous patch & pleural effusion and known cases of renal failure with respiratory complaints were included in this study. Patients with multiple co-morbid, mass lesion on chest x-ray, smokers, with known respiratory illness, no positive sputum or pleural fluid findings and with extra pulmonary tuberculous symptoms were excluded. Informed consent was taken from the patients with complete concealment of the data. All patients were examining for respiratory symptoms and investigated with chest X-ray, Sputum studies, pleural fluid studies (D/R, C/S, and Gene Expert plus ADA levels), HbA1C and ultrasound kidney ureter and bladder. All patients were started on Anti Tuberculous Therapy on the basis of radiographic findings, sputum studies, or pleural fluid studies and those who responded to the treatment within 3 weeks were taken as subjects.

Data Analysis: For analysis of data the statistical software SPSS version 20.0 was used. Quantitative data was presented as mean ± SD while qualitative was presented as frequency (%). T-test and chi-square test were used to assess the significance and p-value was set at 0.05.

RESULTS

Total 107 diagnosed cases of tuberculosis were taken who were divided into 41 patients with renal failure (24 males while 17 females) and 66 patients without renal failure (38 males while 28 females) patients. Mean age of patients with renal failure was 64.56± 8.77 years while that of patients without renal failure was 38.25±12.70 years. Significant differences were observed in specific gravity, lymphocytes, neutrophils, low density lipoprotein, proteins and creatinine levels in renal failure and without renal failure group. (Table-1)

Night sweat was present in 03 (7.3%) patients with renal failure whereas it was present in 52 (78.8%) patients without renal failure with significant difference (p<0.001). Fever was present in 10 (24.4%) patients with renal failure whereas it was present in 60 (90.9%) patients without renal failure with significant difference (p<0.001). Fatigue was present in 25 (61%) patients with renal failure whereas it was present in 53 (80.3%) patients without renal failure with a significant
Shortness of breath was present in 39 (95.1%) patients with renal failure whereas it was present in 19 (28.8%) patients without renal failure with significant difference (p<0.001). Productive cough was present in 40 (97.6%) patient with renal failure whereas it was present in 28 (42.4%) patients without renal failure with significant difference (p<0.001). Chest pain was present in 37 (90.2%) patients with renal failure whereas it was present in 18 (27.3%) patients without renal failure with significant difference (p<0.001).

Table No.1: Comparison of quantitative variables in renal and non-renal failure TB patients

<table>
<thead>
<tr>
<th>Variables n=107</th>
<th>Renal failure (n=41)</th>
<th>Non renal failure (n=66)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>64.56±8.77</td>
<td>38.25±12.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urine Specific Gravity (%)</td>
<td>1.03±0.16</td>
<td>0.46±0.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>69.67±9.22</td>
<td>77.55±10.65</td>
<td>0.002</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>29.22±11.06</td>
<td>18.86±10.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low Density Lipoproteins</td>
<td>874.56±410.67</td>
<td>328.24±459.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proteins</td>
<td>7.13±0.95</td>
<td>2.77±3.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine Clearance</td>
<td>46.63±7.31</td>
<td>57.86±7.80</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table No.2: Association of clinical features in two groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Renal failure (n=41)</th>
<th>Non renal failure (n=66)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender Male</td>
<td>24(58.5%)</td>
<td>38(57.6%)</td>
<td>0.922</td>
</tr>
<tr>
<td>Night Sweats</td>
<td>Yes</td>
<td>31(73.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes</td>
<td>36(87.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Yes</td>
<td>25(61.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>Yes</td>
<td>39(95.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Productive Cough</td>
<td>Yes</td>
<td>40(97.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>Yes</td>
<td>37(90.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hemoptysis</td>
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<td>22(53.7%)</td>
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<tr>
<td>Effusion</td>
<td>Yes</td>
<td>31(75.6%)</td>
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<td>History of Diabetes</td>
<td>Yes</td>
<td>32(78.0%)</td>
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</tr>
<tr>
<td>Mellitus</td>
<td>Yes</td>
<td>9(22.0%)</td>
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</table>

DISCUSSION

Substantial differences were observed in our study in pulmonary tuberculosis patients with or without renal failure with regards to TB specific as well as non-specific symptoms. Symptoms such as fever, fatigue, night sweats, shortness of breath, productive cough, chest pain, hemoptysis, pleural effusion all were reported to have significant differences.

In a study by Moran et al, 68 cases of active TB were identified. Incidence was lowest in those with stage 1 or 2 renal failure/ CKD and was recorded highest in patient-years in those having renal replacement therapy. Almost half of the cases (48%) were pulmonary TB and 87% of which were TB patients that reported an ethnicity of either being Black / Black British or Asian/Asian British, substantially higher than in non-TB with renal failure group.

In another study by Vikrant reported that about 68.7% of patients with TB in their study had chronic kidney disease. 20% of patients among them were on hemodialysis. 75% of the patients had extra-pulmonary TB. Pleuro-pulmonary (41.8%), kidney and urinary tract (20%), abdominal and lymph node (13% each) were most commonly noted site of TB. The chief clinical presentation of TB was: fever / pyrexia of unknown origin (24.3%), constitutional symptoms like anorexia, fever, night sweats, and weight loss (27.8%), abnormal chest radiograph in 31.2%, ascites/peritonitis in 13.9%, pleural effusion in 25.2%, lymphadenopathy in 20%, and sterile pyuria/hematuria/chronic pyelonephritis in 13%. In comparison to the above study, our study only included pulmonary tuberculosis patients with or without renal failure. Even though fever was present in a similar frequency in patients, i.e., 24.4% of TB patients having renal failure however a higher incidence of pleural effusion was observed in our study, i.e., in 75.6% of patients having concomitant renal failure possibly due to the fact that only pulmonary tuberculosis patients were selected in our study.

In a study by Chuang et al, on tuberculosis patients having renal failure and on hemodialysis, the mean age of patients at diagnosis was 57.41 years (ranging from 34 to 75 years). The presenting symptoms were fever (35.3%), abdominal fullness (35.3%), and disturbances in consciousness (11.8%), cervical lymphadenopathy (11.8%), abdominal pain (5.9%), bone pain (11.8%), chest pain (5.9%), and skin rash (5.9%). Laboratory studies showed hypercalcemia (64.7%), hypoalbuminemia (47.1%) and leukocytosis (35.3%).
mean serum-calcium level was 10.71.7mg/dl (range from 8.3 to 13.4mg %). The mean serum albumin was 2.80.6g/dl (range from 1.5 to 3.6). The mean peripheral-leukocyte count was 11,423 /mm3. In our study the mean age in TB patients with renal failure was 64.56±8.77 years and without renal failure were 38.25±12.70 years. Fever was present in 24.4% with renal failure and in 90.9% without failure. Hypoalbuminemia was observed in patients without renal failure. Lymphocytosis was reported in our study in which majority of the patients were those without renal failure.

Out of 304 positive cases for TB, Narain et al reported the mean age of patients with TB was 54.40 + 06.04 years with majority males (68%) and females (32%). The reported symptoms were weight loss 86.8%, anorexia 80%, and fever 55%, vomiting 13.8% and headache 7.2%. In our study the mean age in TB patients with renal failure was 64.56±8.77 years and without renal failure were 38.25±12.70 years. Fever was present in 24.4% with renal failure and in 90.9% without failure. Since in our study, newly diagnosed cases were selected, therefore decreased frequency of weight, anorexia was reported.

During a study done by Venkata et al, from over 900 renal failure patients, only 04% were reported to have TB. In majority of the TB patients (69.4%), TB was observed in association with end stage renal failure. Ranges of age were 25 - 77 years, male: female ratios were 33: 3. Fever, malaise and weight loss were the most common symptoms observed at presentation. Extra-pulmonary tuberculosis (23 patients, 63.8%) predominated over pulmonary tuberculosis (10 patients, 36.1%)20. In our study, only pulmonary tuberculosis patients were enrolled in order to report the presence of renal failure only in pulmonary tuberculosis patients and not in patients with extra-pulmonary tuberculosis, since the rate of pulmonary tuberculosis is very high in Pakistan as compared with extra pulmonary tuberculosis.

The associations between TB and CKD/ renal failure have been known for over 40 years, but interactions in-between these 2 diseases have not been completely understood. The association was initially reported in a case series in the 1970’s which involved TB patients on dialysis due to renal failure after which many studies carried out in different parts of the world on renal failure patients that had developed TB. With the extent of current knowledge, almost none of the studies have reported the demographic incidence of TB and risk of TB in population in renal failure patients not needing dialysis21. The qualitative way of our study has certainly evaluated the wide range of clinical features of tuberculosis patients with and without renal failure. However, the study might be having the observer and reporting bias. Relating the interpretation of our study and to what range these clinical features might be constant with other comorbid in patients would be helpful to discover more facts about the clinical features of tuberculosis.

CONCLUSION

The present study reported that a substantial difference existed regarding the clinical features of Tuberculosis patients with and without renal failure. The features including shortness of breath, productive cough, chest pain, hemoptysis, pleural effusion and diabetes mellitus were observed to be more common in renal failure group while night sweats, fever, and fatigue in non-renal failure group.

Author’s Contribution:

Concept & Design of Study: Mahnoor Khalil
Drafting: Syed Muhammad Baquar Raza, Ajmaal Jamil
Data Analysis: Syed Mubarak Ali, Yumna Ahmed, Siraj Us Salkeen
Revisiting Critically: Mahnoor Khalil, Syed Muhammad Baquar
Final Approval of version: Mahnoor Khalil

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

REFERENCES

Early Neonatal Morbidities in Late Preterm Neonates

Nasir Khan¹, Khyal Muhammad², Fiaz Ahmed³, Zaheer Abbas³, Rifayat Ullah Afridi⁴ and Ejaz Hussain²

ABSTRACT

Objective: To determine the distribution of early neonatal morbidities in late preterm infants.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the department of Pediatrics and Neonatology Ayub teaching hospital, Abbottabad from May 2018 to December 2019.

Materials and Methods: After taking approval from ethical committee, data was collected from all neonates admitted to department of neonatology, who were born late preterm with gestation of less than 37 weeks but with 34 completed weeks. Total 147 neonates were included in this study. In all neonates who were included in this study, morbidities were evaluated from birth till 7th day of life through clinical examination and relevant investigations and were recorded on proforma.

Results: Mean neonatal age was 4 days with SD ± 3.74. Fifty-six percent neonates were male and 44% neonates were female. More over 25% neonates had hyperbilirubinemia, 28% neonates had sepsis, 20% neonates had intrauterine growth restriction, 4% neonates had transient tachypnea of newborn, 15% neonates had hypoglycemia, 16% neonates had respiratory distress syndromes and 13% neonates had apnea.

Conclusion: Our study concludes neonatal morbidities like hyperbilirubinemia, sepsis, intrauterine growth restriction, transient tachypnea of newborn; hypoglycemia, respiratory distress syndromes, and apnea are associated with late preterm births.

Key Words: Early neonatal morbidities, late preterm, infants

INTRODUCTION

Preterm delivery is one of the most significant cause of neonatal morbidity and mortality.¹ Globally preterm deliveries are occurring due to various medical and obstetrical conditions mostly occurring in the late preterm period that results in morbidities of the newborn.² Late preterm neonates, born with period of gestation less than 37 weeks but 34 completed weeks are considered normal newborns and are kept in well-infant nursery units under the similar protocols as that of the term infants and sent home before sufficient observational period.³,⁴ Late preterm babies are not physiologically as full-grown as term babies so should not be considered functionally term in any aspect.⁵

Late preterm infants are at high threat of morbidity and endangered outcome.⁶ These babies are at notably high short and long term unfavorable outcomes compare to term babies with a list of neonatal problems documented in literature.⁷ Some of these problems include feeding difficulties, hypoglycemia, respiratory distress syndromes (RDS), intrauterine growth retardation, sepsis, apnea, jaundice (hyperbilirubinemia) and transient tachypnea of the newborn.⁸,¹⁰

In a study in Pakistan by Haroon et al.¹¹ the Respiratory distress syndrome was documented as 16.5%. High level of bilirubin of 37.9%, Hypoglycemia was reported about 5.2%. Growth retardation was 24.8%. Sepsis was documented about 4.9%. Transient tachypnea of newborn was reported in 7.0%. Apnea was documented about 15.3 in a Pakistani.

As the late preterm group is associated with greater morbidity compare to term neonates so this study is undertaken to identify the early neonatal morbidities in later preterm babies. Prior awareness of the morbidities associated with late preterm bodies is helpful for the health care provides to anticipate and manage potential complications in late preterm infants. Accurate estimate of the risks of morbidities is required to enable healthcare provider to take timely measures to improve the outcome.

MATERIALS AND METHODS

After taking hospital ethics committee approval this descriptive study was conducted at Pediatric...
Department, Ayub Teaching Hospital Abbottabad from May 2018 to December 2019. Sample size of 147 was calculated using previous study. Sampling technique applied was Consecutive non-probability sampling. All the late preterm (34 to 36 weeks of gestation) infants of both genders and of age up to 7 days admitted to neonatology unit of Ayub Teaching Hospital, Abbottabad were included while the term infants, infants with congenital anomalies, syndromes, early preterm, multiple births and surgical conditions were excluded. Pretest counseling was given to parents. After written consent from the parents, those neonates fulfilling the above mentioned criteria were assessed for gestational age by menstrual period. In every baby who had receive admission to neonates unit from birth to first 7 days of life, morbidities such as respiratory distress syndrome, hypoglycemia, sepsis, transient high respiratory rate of newborn, apnea and jaundice were evaluated. Infants were evaluated daily till 7 days of life through clinical examination or investigation for development of any of the morbidities mentioned above. Any of the predefined medical conditions resulting in post-delivery inpatient hospital observation and admission were assessed by physical examination as well as through relevant investigations. All the observations were done under supervision of an experience pediatrician.

All the above mentioned information including name, age, gender and address were recorded on a pre-designed proforma.

Data was analyzed using SPSS version 21. Quantitative variables like age, gestation (weeks), weight were described in terms of mean ± standard deviation. Categorical data like gender and early neonatal morbidities (hyperbilirubinemia, sepsis, intrauterine growth restriction, transient tachypnea of newborn, hypoglycemia, respiratory distress syndrome and apnea) were described in the terms of frequency and percentages. All results were presented as tables and diagrams. Data was stratified by gender, age, gestation (weeks) & weight in term of neonatal morbidities. Post stratification chi -square test was used at 5% level of significance.

RESULTS

Table No 1. Neonatal morbidity (n = 147)

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<tr>
<th>Morbidity</th>
<th>Frequency</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Hyperbilirubinemia</td>
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<td>25%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>41</td>
<td>28%</td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>29</td>
<td>20%</td>
</tr>
<tr>
<td>Transient tachypnea of newborn</td>
<td>6</td>
<td>4%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>22</td>
<td>15%</td>
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<tr>
<td>Respiratory distress Syndrome</td>
<td>24</td>
<td>16%</td>
</tr>
<tr>
<td>Apnea</td>
<td>19</td>
<td>13%</td>
</tr>
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Table No 2. Stratification of neonatal morbidity w.r.t age distribution

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<tr>
<th>Morbidity</th>
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<th>4-7 days</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
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<tr>
<td></td>
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<td></td>
</tr>
<tr>
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<td>13</td>
<td>41</td>
</tr>
<tr>
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<td>46</td>
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<td></td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>Yes</td>
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<td>9</td>
<td>29</td>
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<tr>
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<td>6</td>
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<tr>
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Table No 3: Stratification of neonatal morbidity w.r.t. gender distribution

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<td>65</td>
<td>147</td>
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<tr>
<td>Intrauterine growth restriction</td>
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<td>65</td>
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<td>Transient tachypnea of newborn</td>
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</tbody>
</table>

In this study age distribution among 147 neonates was analyzed as 101(69%) neonates were in age range 1-4 days, 46(31%) neonates were in age range 4-7 days. Mean age was 4 days with SD ± 3.74 Gender distribution among 147 neonates was analyzed as 82(56%) neonates were male and 65(44%) neonates were female. Gestational weeks among 147 neonates were analyzed as 56(38%) neonates had 35 weeks of gestation while 91(62%) neonates had 36 weeks of
Neonatal morbidity among 147 neonates was analyzed as 37 (25%) neonates had hyperbilirubinemia, 41 (28%) neonates had sepsis, 29 (20%) neonates had intrauterine growth restriction, 6 (4%) neonates had transient tachypnea of newborn, 22 (15%) neonates had hypoglycemia, and 24 (16%) neonates had respiratory distress syndromes while 19 (13%) neonates had Apnea. (Table 1).

**DISCUSSION**

There has been a concomitant rise in the rate of morbidities among newborn delivered as preterm gestation. Our study showed that among 147 neonates 69% neonates were in age range 1-4 days, 31% neonates were in age range 4-7 days. Mean neonatal age was 4 days with SD ± 3.74. Fifty six percent neonates were male and 44% neonates were female. Thirty eight percent neonates had 35 weeks of gestation while 62% neonates had 36 weeks of gestation. Mean Gestational weeks was 36 weeks with SD ± 2.341. Eighteen percent neonates had weight <1.5 kg while 106 (72%) neonates had weight range 1.5-2.5 Kg. Mean weight was 1.7 kg with SD ± 1.116.

**Table No. 4: Stratification of neonatal morbidity w.r.t gestational week**

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Status 35 weeks</th>
<th>Status 36 weeks</th>
<th>Total</th>
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</thead>
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<td>23</td>
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<tr>
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<td>No</td>
<td>42</td>
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<td>110</td>
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<td>91</td>
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</tr>
<tr>
<td>Sepsis</td>
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<td>16</td>
<td>25</td>
<td>41</td>
</tr>
<tr>
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<td>No</td>
<td>40</td>
<td>66</td>
<td>106</td>
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<tr>
<td>Total</td>
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<td>147</td>
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</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>Yes</td>
<td>11</td>
<td>18</td>
<td>29</td>
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<tr>
<td></td>
<td>No</td>
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<td>73</td>
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<tr>
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<td>147</td>
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<tr>
<td>Transient tachypnea of newborn</td>
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<td>9</td>
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<tr>
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<td>123</td>
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<td>Total</td>
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<td>Respiratory distress syndrome</td>
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<td>7</td>
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**Table No. 5: Stratification of neonatal morbidity w.r.t weight**

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<th>Status 36 weeks</th>
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<tr>
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<tr>
<td>Total</td>
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<td></td>
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<tr>
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<td>Yes</td>
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<td>29</td>
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<td></td>
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<td>147</td>
<td></td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>Yes</td>
<td>9</td>
<td>15</td>
<td>24</td>
</tr>
<tr>
<td></td>
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<td>123</td>
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<tr>
<td>Total</td>
<td>56</td>
<td>91</td>
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<tr>
<td>Apnea</td>
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<td>7</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
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<td>No</td>
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<td>128</td>
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<tr>
<td>Total</td>
<td>56</td>
<td>91</td>
<td>147</td>
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</table>

In another study conducted by Femitha P et al in which respiratory distress syndrome was 12.4%, hyperbilirubinemia was 28.7%, sepsis was 20.8%, and Hypoglycemia was 5.2%. while in a study at Brazil the growth retardation was 26.1%, transient tachypnoea was 25.9% and apnoea was 6.3% while 30% sepsis, hypoglycemia in 10.3% and feeding difficulty in 15.8% late preterm neonates were recorded in Jordan. Tiwari et al reported that among late preterm 13.06% developed respiratory distress 52.56% late preterm had jaundice, 10.99% episodes of hypoglycemia, Hypothermia occurred in 7.94% late preterm neonates, 4.24% late preterm experienced one or more episodes of apnea. 18.06% late preterm babies had feeding problems, 9.79% term babies had confirmed sepsis. In a study conducted by Binarnabi P et al, hypothermia was noted in 14.5% of late preterm neonates and feeding difficulty in 19.1% in late preterm. Ligginc GC et al observed that incidence of
apnea in 6% late preterm babies. In another study\(^8\) the incidence of sepsis in late preterm was 10.3%. This variation may be due to climatic condition of study places, difference in cut off temperature for consideration of hypothermia or differences in timing of study.

**CONCLUSION**

Our study concludes that the frequency of early neonatal morbidities like hyperbilirubinemia, sepsis, intrapartne growth restriction, transient tachypnea of newborn, hypoglycemia, respiratory distress syndromes, apnea are associated in late preterm infants. Prior awareness of the morbidities associated with late preterm bodies is helpful for the health care provides to anticipate and manage potential complications in late preterm infants. Accurate estimate of the risks of morbidities is required to enable healthcare provider to take timely measures to improve the outcome.

**Author’s Contribution:**

<table>
<thead>
<tr>
<th>Concept &amp; Design of Study</th>
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<td>Khyal Muhammad, Fiaz Ahmed</td>
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<td>Zaheer Abbas, Rifayat Ullah Afridi, Ejaz Hussain</td>
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<tr>
<td>Revisiting Critically</td>
<td>Nasir Khan, Khyal Muhammad</td>
</tr>
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<td>Final Approval of version</td>
<td>Nasir Khan</td>
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

**REFERENCES**

Frequency of Cardiac Anomalies in Patients of High and Low Variety Anorectal Malformation (ARM)

Abdul Latif¹, Mahreen Zahra², Ikramullah², Shehnab Ahmed², Shakeel Ahmed² and Matee-Ullah¹

ABSTRACT

Objective: To study the frequency of cardiac anomalies in patients of high and low variety anorectal malformation (ARM)

Study Design: Prospective Observational study

Place and Duration of Study: This study was conducted at the Inpatient Department of Pediatric Surgery, Nishtar Hospital, Multan and Children Hospital and Institute of Child Health Multan for 06 months from July, 2019 to January, 2020.

Materials and Methods: After the approval of ethical committee, parental informed consent was taken from the parents before the commencement of study. All the neonates that presented with absent anus, had undergone Invertogram study and were classified as low or high ARM. Echocardiography was performed in all patients to diagnose cardiac anomalies. Data was collected on a predesigned performa and analyzed statistically on SPSS version 20.

Results: Out of 121 patients, 83 (68.6 %) were male patients while 38 (31.4 %) were female patients. Mean age of our study cases was 1.23 ± 0.513 days. Those who belonged to rural areas were 74 (61.2 %) and 47 (38.8 %) belonged to urban areas. Mean gestational age of these children was 38.14 ± 1.29 weeks and 106 (87.6%) had gestational age more than 36 weeks. Regarding mode of delivery, 99 (81.8%) were born vaginally and 22 (18.2%) through cesarean section. Positive family history of anorectal malformations was noted in 9 (7.4%) whereas 89 (73.6%) mothers were illiterate. Low variety ARM was found in 59 (48.8%) cases and high variety ARM in 62 (51.2%) while cardiac anomalies were noted in 40 (33.8%).

Conclusion: Very high frequency of cardiac anomalies was noted in our study among neonates presenting with anorectal malformation. Cardiac anomalies were significantly associated with gender, family history of anorectal malformation and high variety of ARM. Such patients can be helped by early diagnosis and timely management to decrease burden of related morbidity and mortality.

Key Words: Anorectal malformation, Cardiac anomalies, Congenital anomalies.


INTRODUCTION

In pediatric surgical practice Anorectal Malformation (ARM) is one of the most frequently presenting congenital anomaly.¹ The neonate is born without a normal anal opening.

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ARM is responsible to cause neonatal intestinal obstruction, which is usually diagnosed by the absence, or ectopic location of the anus and delayed passage of meconium.² One of every 4000 to 5000 infants is affected by ARM although this condition is more common in certain geographic areas and it is slightly more common in males³ while annual report of international Clearing house for Birth Defects Surveillance (2011) revealed incidence ARM is approximately 1 to 3 in every 5000 live births.⁴ There are several forms of imperforate anus and anorectal malformations. The new classification is in relation to the type of associated fistula. The classical Wingspread classification was in low and high anomalies: A low variety ARM, in which the colon remains close to the skin. A high variety ARM, in which the colon is higher up in the pelvis and there is a fistula connecting the rectum and the bladder, urethra or the vagina.
Patients with these malformations often have other associated congenital anomalies. About 20-80% patient of ARM have different anomalies including cardiovascular, genitourinary, gastrointestinal, neurological and musculoskeletal anomalies. Although it is difficult to directly compare the types of associated anomalies because of their varied nature. The diagnosis of these anomalies on early stage is very important, because correct operative approach may be planned and prognosis for the infant may be assessed, second reason is that the mortality and morbidity among infants with cardiac anomalies is directly related to the nature and severity of other associated anomalies. Associated anomalies such as congenital heart disease, are present in a high percentage of patients with ARM. These associated anomalies are serious and have long term prognosis. Different studies reported that prognosis of child with ARM more often depend on extent of these associated anomalies than on ARM itself. The frequency and types of such associated anomalies different among various reported studies, ranging among 20% to 70%. A study conducted in India by Ratan et al has reported 10% cardiac anomalies in ARM while cardiac anomalies proportion in high variety was 85% (n = 34/40) and in low variety it was 15% (n= 6/40) showing cardiac anomalies were significantly more prevalent in high variety (p=0.01). Owing to the scarcity of local data from Pakistan on this topic, this study has been proposed to ascertain current magnitude of the problem to give baseline information which will help clinicians to diagnose cardiac anomalies at early stage, followed by timely management. This will improve quality of life of such patients in terms of disease related morbidities leading to severe hospital admissions. It will also help hospital authorities in terms of extra financial burden.

MATERIALS AND METHODS

It was a prospective observational study, carried out at Department of Pediatric Surgery, Nishtar Medical University Hospital, Multan during July 2019 to January 2020. Sampling technique was non–Probability Consecutive sampling. In this study 121 cases of both gender (male and female) having age up to 28 days of life presented with ARM, were included. If parents are not giving consent, it was the only exclusion criteria. Sample size was n= 121, P1 = 85% (cardiac anomalies with high velocity), P2 = 15% (cardiac anomalies with low variety), d = 0.09 and confidence level = 95%

The study was started after approval from ethical committee of Nishtar Medical University and children hospital and institute of child health (CHICH) Multan. Consecutive (n = 121) patients meeting inclusion criteria of our study were recruited from the emergency Department of Pediatric Surgery, Nishtar Hospital and CHICH Multan. Informed consent was taken from parents after briefing them about the objectives and procedures of this study. Baseline characteristics including age, gender, gestational age, mode of delivery (Vaginal / Cesarean section), previous sibling with ARM and maternal education were noted. All the neonates had undergone Cross-table lateral radiograph study and were classified as low or high variety ARM. Echocardiography was performed by pediatric cardiologist in all patients included in study to diagnose cardiac anomalies and type of cardiac anomaly as defined in operational definitions.

Data was entered and analyzed by SPSS version 22. Mean and standard deviation were calculated for quantitative data like age of the patient and gestational age. Frequency and percentage was calculated for gender, age groups, residential status, Mode of delivery (Vaginal / Cesarean section), Variety of ARM, family history, maternal education and cardiac anomalies. Frequency of cardiac anomalies in high and low variety ARM was compared by chi-square test and p-value of ≤ 0.05 was taken as significant.

Effect modifiers like age, gender, residential status, Mode of delivery (Vaginal / Cesarean section) Variety of ARM, family history of cardiac diseases, maternal education and gestational age were controlled by stratification. Post stratification Chi-Square test was applied to see the effect on frequency of cardiac anomalies in high and low variety ARM and p-value of ≤ 0.05 was taken as significant.

RESULTS

Our study comprised of a total of 121 patients meeting inclusion criteria of our study. Of these 121 study cases, 83 (68.6 %) were male patients while 38 (31.4%) were female patients. (Figure No. 1). Mean age was 1.23 ± 0.513 days (with minimum age of 1 day to 3 days). Majority of the cases i.e. 93 (81.0 %) were aged up to 24 hours.

Figure No.1: Gender distribution of ARM Patients

Mean gestational age of these children was 38.14 ± 1.29 weeks and 106 (87.6%) had gestational age more than 36 weeks. Majority of these 99 (81.8%) were born vaginally and 22 (18.2%) through cesarean section. Positive family history of anorectal malformations was
noted in 9 (7.4%) whereas 89 (73.6%) mothers were illiterate. It was found that 74 (61.2 %) belonged to rural areas and 47 (38.8 %) belonged to urban areas. Low variety anorectal malformations were noted in 59 (48.8%) and high variety anorectal malformation was noted in 62 (51.2%). Cardiac anomalies were noted in 40 (33.8%) and these cardiac anomalies were stratified with regards to gender, age, residential status, gestational age, mode of delivery, family history, maternal literacy and variety of ARM. (Tables 1 - 2).

**Table No.1: Stratification of Cardiac Anomalies with regards to gender**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Cardiac Anomalies (n=121)</th>
<th>P – value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n=83)</td>
<td>Yes(n=40)</td>
<td>No(n=81)</td>
</tr>
<tr>
<td>Female (n=38)</td>
<td>Yes(n=121)</td>
<td>No(n=81)</td>
</tr>
</tbody>
</table>

**Table No.2: Stratification of Cardiac Anomalies with regards to variety of ARM**

<table>
<thead>
<tr>
<th>Variety</th>
<th>Cardiac Anomalies (n=121)</th>
<th>P – value</th>
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</thead>
<tbody>
<tr>
<td>Low variety</td>
<td>Yes(n=40)</td>
<td>No(n=81)</td>
</tr>
<tr>
<td>High Variety</td>
<td>Yes(n=62)</td>
<td>No(n=81)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Anorectal malformations occur approximately in 1/1,500 to 1/5,000 live births. They may occur alone, but they can commonly have other associated anomalies or occur as a part of the combined anomaly. The treatment involved may be complicated by a need to address the associated anomalies, in addition to the anorectal malformations. Furthermore, the problems of these associated anomalies could have more of an impact on the morbidity and mortality before and after surgical treatment. The surgical and medical management of patients with these malformations can be complex, especially when one considers the high frequency of concomitant anomalies that occur with ARMs. This frequency of additional anomalies in patients with ARMs ranges from 40% to 70%. Thorough evaluation of patients with ARMs is essential because it is these coexisting anomalies that account for most of the morbidity and mortality that is associated with this condition.

The frequency of associated anomalies in other organs is known to be approximately 40-70% in the decreasing order of urogenital system, musculoskeletal system, and cardiovascular system. In addition, anomaly in other parts of the gastrointestinal system can occur concomitantly, and a prompt treatment is required in such situations when the neonate's life is threatened. In particular, when an esophageal atresia accompanies the anorectal malformations, the complex of surgical procedure and the difficulty of situational postoperative management must be considered.

Our study found that 83 (68.6 %) were male patients while 38 (31.4 %) were female patients. A study conducted by Khawaja et al from Lahore had found 79 % male gender predominance. Qazi et al had reported 68 % male gender predominance and study conducted by Byun et al reported 12 : 1 male to female ratio in ARM, were found in compliance with our study results. Similar results were also found by Mirza et al and by Cho et al with 67 % male gender predominance.

Mean age of our study cases was 1.23 ± 0.513 days years (with minimum age of our study cases was 1 day to 3 days). It was also indicated that majority of our study cases i.e. 93 (81.0 %) were aged up to 24 hours. A study conducted by Qazi et al had also reported that majority of patients presenting within 24 hours while study by Mirza et al had reported 3.4 days mean age. Mean gestational age of these children was 38.14± 1.29 weeks and 106 (87.6%) had gestational age more than 36 weeks which coincides with the study conducted by Byun et al.

It was noted that patients with low variety anorectal malformations were 59 (48.8%) and high variety anorectal malformation was noted in 62 (51.2%). Byun et al has indicated 54.9 % high variety ARM which is close to our results. A study conducted in USA by Cho et al has also reported 58 % high variety ARM.

In this study, cardiac anomalies were found in 40 (33.8%). Qazi et al and Byun et al had described 38 % and 39.6% cardiac anomalies in anorectal malformation respectively, while Mirza et al had reported 8 % cardiac anomalies which is quite lower frequency than our study. Cho et al had reported 27% cardiac anomalies in USA.

Our study had few limitations. Individual cardiac anomalies were not studied which may further elaborate the severity of cardiac anomalies in terms of survival and mortality. There are many studies which classify the cardiac anomalies associated with GI malformations. A study done by Goroko et al in 2004 indicated that The most common CHD was isolated atrial septal defect (ASD) (73%), followed by ASD + ventricular septal defect (VSD) + patent ductus arteriosus (PDA) (7.6%), ASD + VSD (3.8%), ASD + PDA (3.8%), VSD (3.8%), PDA (3.8%), and coarctation of the aorta (3.8%). Similar study was also done by Teixeira et al to find the prevalence of cardiac anomalies with low variety anorectal malformation. Similar studies performed in Saudi Arabia showed the cardiac anomalies with type of ARM associated. Other GI anomalies were also discussed in this study.

Anorectal malformations are associated with VACTERAL which provides a vast scope of research. Regarding Cardiac anomalies the survival of the
patients can be assessed to plan single or staged procedure for correction of ARM.\(^\text{19,20}\)

**CONCLUSION**

Very high frequency of cardiac anomalies was noted in our study among neonates presenting with anorectal malformation. Cardiac anomalies were significantly associated with gender, family history of anorectal malformation and high variety of ARM. All clinicians treating ARM patients should anticipate cardiac anomalies in these patients for early diagnosis and timely management which will decrease burden of related morbidities and mortalities.

**Acknowledgement:** We acknowledge the technical support by Pediatric Cardiology Department the Children’s hospital & The Institute of Child Health, Multan for Echocardiography of all patients included in the study.

**Author’s Contribution:**

Concept & Design of Study: Abdul Latif

Drafting: Mahreen Zahra, Ikramullah, Shehna Ahmed

Data Analysis: Shakeel Ahmed, Matee-Ullah, Muhammad Kashif

Revisiting Critically: Abdul Latif, Mahreen Zahra

Final Approval of version: Abdul Latif

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

**REFERENCES**

Impact of Ascites in Pulmonary Function of Patients with Portal Hypertension
Muhammad Mahboob Alam1, Umar Usman2, Umair Ahmad3, Muhammad Arif4, Saqib Musharraf5 and Noor ul Huda Mehboob6

ABSTRACT

Objective: To evaluate the pulmonary function of patients having portal hypertension with altered volume of ascites.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pulmonology, Faisalabad Medical University, Faisalabad and Abwa Hospital / Research centre Faisalabad from July, 2019 to December, 2019.

Materials and Methods: Fifteen patients with portal hypertension and ascites underwent pulmonary function tests, consisting of spirometry and arterial blood gases, before and after reducing the volume of ascites. The parameters analyzed were: forced vital capacity (FVC); expiratory reserve in the first second (FEV1); force expiratory volume 6(FEV6); FEF25-75%; Force expiratory volume 6(FEV6); FEV1 ratio/ FVC; PEF, arterial oxygen pressure (PaO2), carbon dioxide arterial pressure (PaCO2) and oxygen saturation (SaO2).

Results: There was a significant improvement in the lung volumes analyzed after decreasing ascites with diuretic treatment associated or not with paracentesis.

Conclusion: We conclude that in patients with portal hypertension and ascites, there is a decrease in lung volumes in relation to the predicted values, with significant improvement after a decrease in ascites. Likewise, we observed an increase in PaO2 and SaO2.

Key Words: Ascites, Portal hypertension, Pulmonary function tests, Compensated cirrhosis, Hypoxemia


INTRODUCTION
Liver cirrhosis is the main cause of portal hypertension and ascites, which in turn is the main complication found in cirrhotic patients after approximately ten years of diagnosis of compensated cirrhosis, affecting 50% of patients 1-13.

Several changes can be detected by pulmonary function tests in patients with chronic liver disease, especially in those with cirrhosis. These changes, which together characterize the "hepatopulmonary syndrome", cause hypoxemia and occur in one third of patients with cirrhosis 4. Inadequate oxygenation in patients with cirrhosis is caused by several pathophysiological mechanisms, such as inadequate vascular tone, pulmonary vasodilation, altered ventilation-perfusion ratio (V/Q), increased arteriovenous shunts and changes in the diffusion-perfusion ratio 5-9.

In addition to the changes already expected in cirrhotics, when ascites occurs, we can observe restrictive and obstructive changes in pulmonary function tests with decreased lung volumes & hypoxemia, that improve after reducing ascites 10-14.

The increase in volume and intra-abdominal pressure resulting from ascites leads to a decrease in lung expansion, with consequent hypoventilation, especially in the lung bases. Along with the interstitial edema present in cirrhotic patients, there may be alveolar collapse and micro atelectasis that may explain the spirometric and gasometric changes found. Therefore, ascites, especially when high in volume, impairs the pulmonary function of patients with portal hypertension of different etiologies in a variable way, especially when associated with cirrhosis 15. This work aims to evaluate and quantify the influence of reduction in the volume of ascitic fluid on the pulmonary function of patients with portal hypertension.

MATERIALS AND METHODS
We analyzed lung function using spirometry and measurement of arterial gases in adult patients, of both sexes, diagnosed with portal hypertension and ascites, admitted to the Department of Pulmonology, Faisalabad Medical University, Faisalabad and Abwa Hospital /
Resarch centre Faisalabad for the period from 1st July, 2019 to 31st December, 2019. All participants included after being properly informed about proposed treatment and having agreed to the spirometry and arterial blood gas tests.

Exclusion Criteria: Those having previous cardiac and pulmonary diseases, hemodynamic instability, neoplasms, renal failure with serum creatinine >3.5mg/dl, gastrointestinal hemorrhage, encephalopathy, bacterial peritonitis and difficulty in breathing presented ascites with signs and symptoms of previous pulmonary involvement.

Ches radiographs were found to be within normal limits, with a decrease in lung expansibility as a consequence of the large abdominal volume presented by the patients. The cirrhotic patients classified according to the Child-Pugh criteria for establishing severity of the disease Pic 1. The patients had moderate to severe ascites, which was characterized by data from the physical and ultrasound examination: high-volume ascites, by simple inspection of the abdomen; ascites with increased abdominal wall tension, as evidenced by palpation; ascites which, due to its proportion, caused respiratory distress to the patient, especially when in the supine position; and ultrasound showing massive ascites.

All patients underwent a pulmonary function study before starting treatment for ascites. The clinical treatment consisted of a prescription for rest, a diet with 2.0 g of salt and diuretics. The diuretic used was spironolactone, associated or not with furosemide. The patients were not submitted to pulmonary physiotherapy. Therapeutic paracentesis was indicated in patients who presented ascites with signs and symptoms of abdominal and respiratory discomfort or in patients who were not responding satisfactorily to clinical treatment with diuretics (continuous weight loss of about 500 g / day).

An average of 6.5 liters of ascitic fluid was removed per patient, with parenteral replacement of a plasma unit (300 ml) for every liters of ascitic fluid drained. After paracentesis, patients were submitted to spirometry, performed the day after the procedure. The spirometric tests were performed at the Pulmonology Department of DHQ Hospital Faisalabad with devices:MIR spirolabIII version 3.1.

The technique used to perform the exam and the parameters obtained and analyzed are in accordance with American Thoracic Society(ATS). The parameters analyzed were: FVC (forced vital capacity); FEV 1 (expiratory volume in the first second); FEF 25-75% (forced expiratory flow between 25 and 75% of FVC); force expiratory volume 6(FEV6), peak expiratory flow (PEF) and FEV 1 / FVC ratio. The slow vital capacity curve (VCC) evaluated lung volumes and capacities and the predicted values adopted were those of Crapo. The volume-time curve (forced spirometry) was performed according to the acceptance and reproducibility criteria of curves recommended by the American Thoracic Society, and the best of three acceptable curves, of eight performed, was chosen. The predicted values were those of Wang WT. Patients undergoing arterial blood gas analysis were analyzed for their arterial oxygen pressure (PaO2), arterial carbon dioxide pressure (PaCO2) and arterial oxygen saturation (SaO2). The results of the variables found were analyzed by the Student's t test for paired data. Statistically significant differences were considered when p<0.050(5%).

RESULTS

We analyzed 15 patients with portal hypertension and ascites, 9(60%) were male and 6(40%) were females, with ages ranging from 31 to 67 years and mean of 51 ± 9.5 years old. A higher prevalence of patients with diagnosis of liver cirrhosis was observed in 33.33% cases. Portal hypertension associated with hepatitis B or C virus, had a prevalence of 60% (Table-1). Ten patients had a history of Hepatitis C (67%) and 5 patients were smokers (33.3%).

Figure No.1: Child Pugh Score

Table No.1: Distribution according to the frequency of etiological diagnosis of patient

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patient</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis with hep c</td>
<td>5</td>
<td>33.33%</td>
</tr>
<tr>
<td>Cirrhosis with hep b</td>
<td>2</td>
<td>13.33%</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>1</td>
<td>6.66%</td>
</tr>
<tr>
<td>Hep b with hep c</td>
<td>2</td>
<td>13.33%</td>
</tr>
<tr>
<td>Hepb with alcoholism</td>
<td>1</td>
<td>6.66%</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>1</td>
<td>6.66%</td>
</tr>
<tr>
<td>Hep c with alcoholism</td>
<td>2</td>
<td>13.33%</td>
</tr>
<tr>
<td>Portal vein thrombosis with hep-c</td>
<td>1</td>
<td>6.33%</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100%</td>
</tr>
</tbody>
</table>

According to Child-Pugh criteria, applied to 13 patients, except for patients 1 and 3, with cryptogenic cirrhosis, our group was formed mostly by patients with score B (11 patients / 84.6%), with only 2 patients had a C score (15.4%) and no patient had an A score.
Twelve patients underwent therapeutic paracentesis, with removal of 6.5 liters of ascitic fluid and an average loss of 6.9 kg of weight. Three patients showed an excellent response to clinical treatment, with a significant decrease in abdominal volume, with an average loss of 6.4 kg of weight, and were then referred to a new spirometry without undergoing therapeutic paracentesis. The spirometric diagnoses found in the patients analyzed are shown in Table-2.

### Table No.2: Spirometry Results Obtained Pre & Post Paracentesis and Clinical Treatment of Ascities Patients

<table>
<thead>
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<th>Sr.no.</th>
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<th>Post treatment</th>
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<tr>
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<td>OVDSA</td>
<td>OVDSA</td>
</tr>
<tr>
<td>2</td>
<td>OVDSA</td>
<td>NL</td>
</tr>
<tr>
<td>3</td>
<td>OVDSA</td>
<td>OVDSA</td>
</tr>
<tr>
<td>4</td>
<td>NL</td>
<td>NL</td>
</tr>
<tr>
<td>5</td>
<td>MVD</td>
<td>NL</td>
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<td>6</td>
<td>MOVD</td>
<td>LOVD</td>
</tr>
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<td>7</td>
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<td>8</td>
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<tr>
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<td>LOVD</td>
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<tr>
<td>10</td>
<td>MVD</td>
<td>MVD</td>
</tr>
<tr>
<td>11</td>
<td>RVD</td>
<td>NL</td>
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<tr>
<td>12</td>
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<tr>
<td>15</td>
<td>NL</td>
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</tr>
</tbody>
</table>

OVDSA= Obstructive ventilatory disorder of small airway, LOVD= mild obstructive ventilatory disorder, RVD= restrictive ventilatory disorder, MOVD= moderate obstructive ventilatory disorder, MVD= mixed ventilatory disorder, NL= normal.

Our patients, before paracentesis and / or clinical treatment of ascites, presented FVC results below the expected average measurements and obtained a significant improvement in this parameter after treatment. FEV1 values were also reduced before ascites treatment and improved after paracentesis and / or clinical treatment. The FEV 1 ratio / FVC showed no statistically significant difference after treatment. The FEF values 25-75% before paracentesis and / or clinical treatment of ascites were also reduced in relation to the predicted average.

Although we observed an increase after treatment, it was not statistically significant. We can observe that there was an improvement in the FEV6 and PEF after reduction of ascites, with statistical significance. The results in Table 3 briefly demonstrate all the main variables analyzed by us and their degree of significance for the study in question.

Six patients underwent arterial blood gas analysis. Before paracentesis, the mean values found in these patients were: PaO₂ = 68 ± 17mmHg; PaCO₂ = 32 ± 17mmHg; and SaO₂ = 92 ± 6%. After paracentesis, the means were: PaO₂ = 76 ± 17mmHg; PaCO₂ = 29 ± 5mmHg and SaO₂ = 94 ± 4%.

The increase in values of PaO₂ and SaO₂ showed statistical significance (Table 3).

### Table No.3: Comparison of spirometric variables and air gases pre and post paracentesis and clinical treatment of ascities

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-paracentesis</th>
<th>Post paracentesis</th>
<th>Significance (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC(L)</td>
<td>2.67±0.67</td>
<td>3.13±0.83</td>
<td>*&lt;0.002</td>
</tr>
<tr>
<td>FVC(%)</td>
<td>82.4±17.00</td>
<td>97.53±12.51</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>FEV1(L)</td>
<td>2.10±0.53</td>
<td>2.45±0.61</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>FEV1(%)</td>
<td>78.33±19.59</td>
<td>93.80±16.74</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>FEV/FVC (%)</td>
<td>78.07±10.02</td>
<td>78.40±7.58</td>
<td>0.727</td>
</tr>
<tr>
<td>FEF 25-75(L/S)</td>
<td>2.12±1.00</td>
<td>2.35±0.85</td>
<td>0.127</td>
</tr>
<tr>
<td>FEF 25-75 (%)</td>
<td>75.4±38.94</td>
<td>83.87±33.43</td>
<td>0.170</td>
</tr>
<tr>
<td>FEV6(L)</td>
<td>0.73±0.34</td>
<td>1.0±0.50</td>
<td>0.019</td>
</tr>
<tr>
<td>PEF(L/S)</td>
<td>73.27±40.60</td>
<td>100.0±37.42</td>
<td>0.033</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>68.25±16.63</td>
<td>75.84±17.01</td>
<td>*&lt;0.027</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>31.95±7.89</td>
<td>28.70±4.59</td>
<td>0.217</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>91.71±5.99</td>
<td>94.3±4.18</td>
<td>*&lt;0.032</td>
</tr>
</tbody>
</table>

FEV=forced expiratory volume FVC=forced vital capacity FEF= Forced expiratory flow PaO₂=partial pressure of oxygen PaCO₂=partial pressure of carbon dioxide SaO₂=oxygen saturation PEF=peak expiratory flow FEV6=forced expiratory flow in 6 seconds.

### DISCUSSION

According to other studies, the pulmonary changes found in cirrhotic patients are closely related to the degree of impaired liver function. This data is important for the interpretation of the results of our work, since our patients were mostly cirrhotic (60%) with a moderate to advanced degree of disease (Child-Pugh B or C in 86.66% of the cases -13 patients), and may present pulmonary manifestations resulting from their underlying disease, in addition to those caused by increased intra-abdominal pressure as a consequence of ascites. We observed a higher prevalence of obstructive ventilatory disorder (eight patients-53.32%), and in the literature the reports point to a higher prevalence of restrictive ventilatory disorder.

As in our work, Zampiet al reported the presence of obstructive ventilatory disorder and concluded that this finding could be related to the degree of hepatic impairment of the patients analyzed. In patients with more advanced liver disease, there would be greater pulmonary interstitial edema and, therefore, greater involvement of the alveoli and bronchioles, causing early closure of the airways on expiration and obstructive disorders.

According to Ramalingam et al, the effects of ascites on the respiratory system are probably mediated by the hydrostatic pressure exerted on the diaphragm and the
severity of the damage caused by gas exchange is closely related to the decrease in lung volumes that occurs in these circumstances. We were unable to establish a relationship between smoking and obstructive ventilatory disorder, as only three patients, out of eight with an obstructive pattern, were smokers. We believe, like other authors, that decrease in intra-abdominal pressure due to reduced volume of ascites, was responsible for the improvement. Some studies found hypoxemia in ascitic patients before treatment and reported a significant increase in PaO₂ after diuretic therapy. Possibly the use of diuretics, according to the authors, reduced pulmonary interstitial edema, leading to a more favorable ventilation/perfusion ratio.

A study conducted by Yigit et al. documented the presence of a restrictive pattern, with increased in FEV6 and PEF in the pulmonary functional assessment, in cirrhotic patients with and without ascites. They found a decrease in the parameters analyzed when measuring respiratory muscle strength in patients with and without ascites, indicating less effectiveness of the rib cage muscles, which could contribute to the functional changes found. In most of reviewed studies, it was observed, like us, a decrease in FVC, FEV1, FEV1, in addition to PEF before, and significant increases after paracentesis.

We observed that several patients had a normal spirometric examination after clinical treatment with diuretics, or after paracentesis, showing an evident improvement in respiratory parameters by decreasing the volume of ascites. The FEV1/FVC ratio did not show significant differences before and after treatment, which shows that the increases in FEV1 were proportional to the FVC increases, being very close to the 80% expected for the relationship. The decrease in FEV1 and FVC with maintenance of the predicted values for the FEV1/FVC ratio is found in restrictive pulmonary disorders, which may therefore be associated with the observed obstructive disorders. The small decrease in FEF25-75% found before treatment may be associated with bronchiolar involvement and pulmonary compression with early closure of the small airways, which can occur in patients with liver disease with ascites. The FEV6 and PEF was significantly reduced in our study before the treatment of ascites with significant improvement after its treatment, in agreement with the reviewed studies.

In the present study, we found mild hypoxemia in our patients with improvement after treatment. SaO² also improved after reducing ascites, but we did not see the same when assessing PaCO2. Probably the improvement in lung volumes, with a consequent improvement in pulmonary ventilation, contributed to better oxygenation. As all patients used diuretics during the study, this may have contributed to an improvement in PaO₂.

CONCLUSION
Reduced ascites volume significantly improves pulmonary ventilation and therapeutic paracentesis seems to be a treatment alternative for rapid relief of symptoms of dyspnea and abdominal discomfort, or for cases in which therapy diuretics is not entirely satisfactory. We concluded that in patients with portal hypertension and ascites, there is a decrease in lung volumes in relation to the predicted values, with significant improvement after a decrease in ascites.

Author’s Contribution:
Concept & Design of Muhammad Mahboob Alam
Drafting: Umar Usman, Umair Ahmad
Data Analysis: Muhammad Arif, Saqib Musharraf and Noor ul Huda Mehoob
Revisiting Critically: Muhammad Mahboob Alam, Umar Usman
Final Approval of version: Muhammad Mahboob Alam

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

REFERENCES
Accuracy of Automated Blood Pressure Assessment Device Confirmed by Mercury Sphygmomanometer

Muhammad Shafiq¹, Irfan Ullah¹, Irfan Khan¹, Khalid Khan¹, Khalil Ahmad² and Waseem Ur Rahman³

ABSTRACT

Objective: To determine the accuracy of automated blood pressure assessment device confirmed by mercury sphygmomanometer.

Study Design: Cross sectional study

Place and Duration of study: This study was conducted at Pediatric department Qazi Hussain Ahmad Medical Complex Nowshera from July 2019 to December 2019.

Materials and Methods: In this study a total of 212 patients were observed. All the children were put on an examination bed over 45 degree angle and a rest period was allotted of approximately 5 minutes. After rest period, the BP both systolic and diastolic was measured using Omron HEM-907XL automated BP measuring device. From each patient, three readings were obtained and an average of these three readings was recorded for further analysis. After BP measured with automated device, another rest period of 5 minutes was give to each participant of the study before measuring the BP using standard mercury sphygmomanometer.

Results: The mean age of patients was 10 ± 7.53 years. There were 56% males and 44% female children. Mean BMI was 25Kg/m² with SD ± 4.463. More over automated BP was accurate in 72% patients and was not accurate in 28%.

Conclusion: Our study concludes that the accuracy of automated BP measuring device was 72% confirmed by mercury sphygmomanometer.

Key Words: accuracy, automated blood pressure, mercury sphygmomanometer

INTRODUCTION

Raised BP or hypertension is one of the most leading cause of mortality all over the world. It may cause about 12.8% of all the deaths occurring around the world, including 51% deaths related to stroke and 45% deaths related to the of coronary artery disease. Increasing age is a major non-modifiable factor that leads to hypertension; as 90% individuals can develop certainly develop hypertension in their lives after the age of fifty five years.¹,³

The increase in the incidence of hypertension in young adults is alarming. The Bogalusa Heart Study and Patho-biological Determinates of Atherosclerosis in Youth study determined that among autopsies, the increased atherosclerosis was the reason for elevated blood pressure in young individuals. Consequently, the accurate measurement of blood pressure and proper treatment of this elevated blood pressure in pediatrics age group and in adolescence is necessary to prevent the development of cardiovascular diseases. It has been suggested that the ambulatory monitoring of blood pressure can be a better prognostic than clinical assessment for the prediction of cardiovascular complications and deaths in adult individuals. Thus, the use of ambulatory blood pressure monitoring is increasing for evaluation of hypertension and the risk of end-organ impairment in adults.⁴,⁸

But there are some problems with ambulatory blood pressure monitoring that must be taken into consideration. Several automated ambulatory blood pressure devices depend on oscillometric method, which is observed to have less accuracy than examining the diastolic blood pressure (DBP) than systolic blood pressure (SBP). However, this may be false for many devices. Alternatively, all the indirect methods for assessment of blood pressure are less accurate for

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Printed: October, 2020
determination of both SBP & DBP as compared to direct intra-arterial measurements. New tools for the assessment of blood pressure including the automatic oscillometric blood pressure devices are replacing the gold standard tool i.e. mercury sphygmomanometer in numerous clinical set-ups. But, there are the circumstances where the replacement of oscillometric for auscultator devices could have mostly severe ramifications for patients, like when patient have either hypertension or hypotension. Though, further studies are warranted regarding the use of aneroid sphygmomanometer as the improved replacement of mercury device. In a study, the accuracy of oscillometric blood pressure device was 81% that measure the blood pressure accurately, while it as reported as 70.28% in the other study.

The present study was designed to determine the accuracy of automated BP monitoring devices compared to the mercury sphygmomanometer. As mentioned above, there is a threat of rise in the cardiovascular diseases among pediatric population and there are a No of devices which run on automated oscillometric principles for measuring the BP. This study would be very useful in determining the accuracy of automated BP measuring devices which are commonly used for BP monitoring for children at homes and clinics. This study will give us local statistics about the accuracy of these devices and on the basis of results of this study, we will formulate future research recommendations which will help us in efficient monitoring of BP of children at homes and at clinics.

MATERIALS AND METHODS

The cross sectional study was done at pediatric department Qazi Hussain Ahmad medical complex Nowshera. Sample size was 212 keeping 70.28% proportion of accuracy (sensitivity) of automated BP measuring device, 95% confidence level and 6% margin of error using WHO sample size formula. Sampling technique used was consecutive (non probability) sampling. Children of age 3-18 years of both gender were included while children with diagnosed hypertension, history of any type of cardiovascular abnormality, congenital heart problems were excluded. All the children who fulfilled the selection criteria were enrolled from the OPD. Consent form was taken from parents or guardians attending the child. Then detailed history and clinical examination was done in all children. All the children were put on an examination bed over 45° angle and a rest period was allotted of approximately 5 minutes. After rest period, the BP both systolic and diastolic was measured using Omron HEM-907XL automated BP measuring device. From each patient, three readings were obtained and an average of these three readings was recorded for further analysis. After BP measured with automated device, another rest period of 5 minutes was given to each participant of the study before measuring the BP using standard mercury sphygmomanometer. Accuracy was determined in terms of number of patients having automated device measured systolic BP+ 5mmHg and Diastolic BP+ 3mmHg as confirmed by mercury sphygmomanometer. Data was entered and analyzed via SPSS v. 20. Mean + SD was calculated for numerical variables like age, Systolic BP, Diastolic BP, height, weight & BMI. Frequency & percentage were calculated for categorical variables like gender, true positive, false negative & sensitivity.

RESULTS

The mean age of children included in the study was 10 ± 7.53 years. There were 89 (42%) children of age 3-10 years, while 123 (58%) children were of age range 11-18 years. Out of 212 children, there were 119(56%) males and 93(44%) females. The mean systolic BP was 110 ± 12.56, mean diastolic BP was 80 ± 12.56, mean height was 1.3 ± 1.102 meters and mean weight was 30 ± 6.271 Kg. BMI distribution among 212 patients was analyzed as 187(88%) patients had BMI ≤25 Kg/m² and 25(12%) patients had BMI >25% Kg/m². Mean BMI was 25 ± 4.46 Kg/m². (table no 1)

Accuracy of the automated BP assessment device among 212 candidates was analyzed as the measurement of automated BP device was accurate in 152 (73.1%) patients. (Table no 2)

<table>
<thead>
<tr>
<th>Table No. 1. Demographics of patients</th>
<th>N</th>
<th>212</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>10 ± 7.53</td>
<td></td>
</tr>
<tr>
<td>3-10 Years</td>
<td>89 (42%)</td>
<td></td>
</tr>
<tr>
<td>11-18 years</td>
<td>123 (58%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>119 (56%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>93 (44%)</td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>110 ± 12.56</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>80 ± 8.81</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>1.3 ± 1.10</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>30 ± 6.27</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>25 ± 4.46</td>
<td></td>
</tr>
<tr>
<td>≤25 Kg/m²</td>
<td>187 (88%)</td>
<td></td>
</tr>
<tr>
<td>&gt;25 Kg/m²</td>
<td>25 (12%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No. 2: Accuracy (Sensitivity) of automated BP measuring device confirmed by mercury sphygmomanometer.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension on</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Automated device</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Sensitivity = 73.1%
Kappa = 0.062
DISCUSSION

Hypertension or elevated BP is normally observed in aged candidate, and this rise usually occur after age of 40-50 years, and about 90% individuals develop hypertension after age of 55 years. But elevated BP has also been observed pediatric population also.1,3 Our study concludes that mean age of candidates was 10 ± 7.55 years. There were 56% males and 44% females. Mean BMI was 25Kg/m² with SD ± 4.463. Moreover, automated BP was accurate in 72% cases. Similar findings were reported by another research done by Ostechaga et al. They presented the accuracy of oscillometric BP instruments for accurately measuring the BP was recorded in 81% of participants and it was reported as 70.28%.14

Similar finding were noticed in previous studies. A study by Natalie et al., found the validity of device in 61% studies which used as standard protocol. Only 34% studies where the device was effectively confirmed were executed without violation in protocols.15

In another study Mansoor et al., had conducted a study on 200 individuals. The mean difference in SBP was 8.54 ± 9.38 mmHg while the mean difference in DBP was 4.21 ± 7.88 mmHg. Eighty nine individuals have already known hypertension; and the difference of mean SBP was 9.43 ± 9.89 mmHg (p-value = 0.000) and difference in mean DBP was 4.26 ± 7.35 (p-value = 0.000).16

In another study Lim et al., conducted a study on 454 patients with the mean age of 50.7± 15.4 years. The mean SBPs was 119.8 ± 139 mmHg on the MM while 119.5 ± 13.6 mmHg on AD in males, whereas among females, the mean SBPs was 115.0±16.8 mmHg on MM and 111.6±15.7 mmHg on AD. The mean DBP among males was 77.7±10.4 mmHg on MM while 74.7±10.4 mmHg on AD, whereas among females, the mean BDP was 73.2±9.3 mmHg on MM and 69.9±10.3 mmHg on AD. The kappa statistics was0.6538 (0.5436–0.7641) for detection of hypertension. The diagnostic sensitivity for hypertension was 59.0%.17

CONCLUSION

Our study concludes that the diagnostic accuracy of the automated BP assessment device was 72% confirmed by mercury sphygmomanometer.

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

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12. Urbina EM, Khoury PR, McCoy CE, Daniels SR, Dolan LM, Kimball TR. Comparison of mercury blood pressure readings to oscillometric and central
Association Between Serum Ferritin Levels and Lung Functions Among Iron Deficient Anemic Adults

Aliya Waseem¹, Mohammad Saleh Soomro², Shahjabeen³, Syed Adnan Ahmed¹ and Saba Abrar⁴ and Tabinda¹

ABSTRACT

Objective: Assessment of association between Serum Ferritin levels and lung function tests (FVC, FEV₁, FEV₁/FVC Ratio) in iron deficient anemic adults. Comparison of correlation between Serum Ferritin levels and Lung functions among iron deficient 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 Hospital, 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 also 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 iron deficiency anemia (IDA) was rechecked and confirmed by further tests like serum iron, serum ferritin, serum Total iron binding capacity (TIBC) levels by Enzyme linked immunosorbent assay (ELISA), Pulmonary function tests(PFTs) i.e. Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1st second (FEV₁) were measured by Digital Spirometer in all anemic patients and lung functions were compared with lung functions of non-anemic healthy individuals.

Results: There was significant reduction (p<0.05) in FVC and FEV₁ in male and female iron deficient anemic cases than 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. Mean value of serum ferritin in male and female iron deficient anemic subjects were significantly lower (p<0.05) than in male and female controls respectively. Positive association between serum ferritin levels and lung function changes were found in the anemic group. While the non-anemic healthy participants showed no abnormal lung functions.

Conclusion: The results showed restrictive lung function changes in iron deficient anemic group. Positive association was observed between serum ferritin levels and lung function changes in the anemic subjects. No abnormal changes in lung functions were found in healthy controls.

Key Words: Hemoglobin, Iron Deficiency Anemia, Serum Ferritin, Pulmonary function tests, Forced Vital Capacity, Forced Expiratory Volume in 1st second.


INTRODUCTION

Our body stores iron primarily in the form of ferritin. Ferritin is secreted into the plasma in small amounts. In absence of inflammation, the size of the total body iron stores is positively correlated with concentration of plasma (serum) ferritin. Normal ferritin concentrations vary by age and sex. Normal range of serum Ferritin in adult males is 40-340 microgram/liter. For adult females normal range of serum Ferritin is 14-150 microgram/liter¹. Ferritin is a positive acute phase response protein. Its concentration increase during inflammation and thereby no longer correlate with the size of the iron store. Therefore, the interpretation of normal or high serum ferritin values become difficult in areas of widespread inflammation or infection². Iron overload is indicated by high serum ferritin concentrations in the absence of liver disease or inflammation. Ferritin is typically assessed in serum or plasma with ELISA after venous blood collection³.

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While the link between poor neurodevelopmental outcomes and iron deficiency has been observed, association between iron status and pulmonary disease remains relatively unexplored. Lung cells must acquire enough iron for their survival like other cells in the body. Certain markers of iron homeostasis were associated with critical parameters of lung function (forced vital capacity and forced expiratory capacity) in a recent large cohort study. Obstructive lung diseases include but is not limited to asthma, acute and chronic bronchitis, emphysema, bronchiectasis, cystic fibrosis, and bronchiolitis. The forced expiratory flow at any given lung volume is reduced in obstructive lung diseases. The spirometric abnormality identified by the use of the predicted lower limit of normal for that individual based on the sex, age, height, and ethnicity is the recommended practice. Both the NHANES and GLI reference equations provide lower limits of normal for spirometric parameter. According to American Thoracic Society, a restrictive pattern is defined by Lower limit of normal (LLN) criteria as FEV1/FVC > LLN and FVC < LLN. Decreased lung compliance and distensibility, low lung volumes and increased lung recoil are characteristic features of restrictive diseases are characterized by decreased lung compliance, low lung volumes and increased lung recoil. Therefore, increased work of breathing is required in these diseases. Pneumonia, atelectasis, Adult Respiratory Distress Syndrome, Pulmonary edema, Pulmonary Embolism and Interstitial Lung Diseases are included in restrictive intrinsic pulmonary disorders. Restrictive Extra pulmonary Conditions include Pleural Effusion, Pneumothorax, Hemothorax and Empyema etc. There is no increase in airway resistance and measures of airflow are within normal limits in restrictive pulmonary diseases.

Rational of Study: By knowing the effects of iron deficiency anemia on lung functions, understanding of iron transport and storage in the lung and its role in lung disease onset and progression will improve. Also by knowing blood hemoglobin levels/ serum iron indices levels of a person, indirect assessment of functioning of lungs could be made and early detection of any impairment in function of lungs in anemic adults will help in its treatment. This knowledge will help us to improve interventional modification of iron homeostasis and prevent the progression of lung diseases.

MATERIALS AND METHODS

This case control study was carried at Fatima Hospital, Baqai Medical University Hospital 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. Sample size: 100 anemic male and 100 anemic female patients with age range from 18 to 45 years were included. Also 50 healthy adult males and 50 healthy adult females with age range from 18 to 45 years were included. 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.

Inclusion Criteria: Diagnosed iron deficient anemic patients confirmed by blood Hb, serum Iron, serum Ferritin, serum TIBC and serum % transferrin saturation levels were included.

Exclusion Criteria: The patients with any other diseases like cardiac, lung diseases, any infectious diseases, and any inflammatory disorders were excluded. Patients with back, chest deformities and other types of anemia were excluded. Active smokers and pregnant women were also excluded.

Methods: 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. Digital spirometer was used to measure FVC and FEV1 in all anemic patients and lung functions were compared with lung functions of non-anemic healthy individuals. Serum ferritin levels were measured by ELISA. In the first step approximately 35 μl serum are added to each well followed by the same volume of BSA-buffer(bovine serum albumin). The wells are aspirated and rinsed 3 times with PBS (phosphate-buffered saline) after the plates were kept at room temperature for 15 minutes. In the second step of the assay, 4 drops conjugated antiferritin are placed in each well and the plates allowed to stand for 15 minutes. The wells are again aspirated and after rinsing again with PBS, a substrate solution containing p-nitrophenylphosphate (PNP) is added to each well. Finally, 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. The intensity of the yellow color in each well is estimated visually against a white background. The color intensity in the screening test with each sample was 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. A series of at least 3 acceptable forced expiratory readings were taken. The best value was selected. Subjects were given a rest of 2-3 minutes between the tests. Nose clips were used in the present 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 serum ferritin levels and lung functions in both gender.

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 male and the same number of females.

Comparison of serum ferritin levels in Table I showed that serum ferritin levels were significantly lower (p<0.05) in anemic male and female cases than in non-anemic controls of both genders. Mean value of serum ferritin 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 cases was 8.0±1.14 µg/L and the t-values and p-values are 39.12 and 0.0001 respectively. Comparison of PFTs in Table II showed that The FVC and FEV1 in male and female cases were significantly lower (p<0.05) than in male and female controls respectively. 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 cases were 2.40±0.59 Liters and the t-values and p-values are 10.54 and 0.01 respectively. 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 cases were 2.24±0.58 Liters and the t-values and p-values are 3.62 and 0.01 respectively. FEV1/FVC 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 are -2.51 and 0.01 respectively. FEV1/FVC ratio in female controls was 0.80±0.04 % and FEV1/FVC ratio in female cases was 0.92±0.25 % and the t-values and p-values are -3.36 and 0.01 respectively.

Table No.1: Comparison of serum ferritin levels among cases & controls of both genders

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gender</th>
<th>Control</th>
<th>Cases</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>96.34</td>
<td>22.60</td>
<td>8.0</td>
<td>1.14</td>
</tr>
</tbody>
</table>

p-value <0.05 significant  
p-value>0.05 non-significant

FEV1/FVC ratio was significantly increased (p<0.05) in male and female cases. Therefore, restrictive lung disease was observed in anemic subjects. Positive significant correlation (p<0.05) of serum ferritin levels with lung function tests was found among male control & cases in Table 3. Positive significant correlation (p<0.05) was observed between serum ferritin levels and lung function tests among control & cases in females in Table 4.

Table No.2: Comparison of Pulmonary Functions Among Control & Cases of Both Genders

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gender</th>
<th>Control</th>
<th>Cases</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>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>3.34</td>
<td>0.31</td>
<td>2.40</td>
<td>0.59</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>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2.70</td>
<td>0.97</td>
<td>2.24</td>
<td>0.58</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>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>0.80</td>
<td>0.04</td>
<td>0.92</td>
<td>0.25</td>
</tr>
</tbody>
</table>

p-value<0.05 significant  
p-value>0.05 non-significant

Table No.3: Correlation of Serum Ferritin levels with Lung function tests among control & cases in males (n=150)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>R-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC(Liters)</td>
<td>0.67</td>
<td>0.01*</td>
</tr>
<tr>
<td>FEV1(Liters)</td>
<td>0.68</td>
<td>0.01*</td>
</tr>
<tr>
<td>FEV1/FVC(%)</td>
<td>-0.12</td>
<td>0.11</td>
</tr>
</tbody>
</table>

*p<0.05 was considered significant for Correlation  
p>0.05 was considered non-significant for Correlation

Table No.4: Correlation of Serum Ferritin (µg/l) with Lung function tests among control & cases in females (n=150)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>R-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC(Liters)</td>
<td>0.74</td>
<td>0.01*</td>
</tr>
<tr>
<td>FEV1(Liters)</td>
<td>0.86</td>
<td>0.01*</td>
</tr>
<tr>
<td>FEV1/FVC(%)</td>
<td>-0.78</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

*p-value<0.05 was considered significant for correlation  
p-value>0.05 was considered non-significant for correlation

DISCUSSION

Lower serum ferritin levels have been associated with poor lung functions in iron deficient anemic patients15. A study conducted in Indus Medical College, Sindh, Pakistan reported high frequency of low serum ferritin levels in young iron deficient anemic medical students in comparison to non-anemic students.16. The same significant effect(p<0.05) was observed in the current study (Table 1).

In a study conducted in Korea, the subject’s PFTs declined with reduction in concentration of serum ferritin levels17. Similar significant positive (p<0.05)
association was found in the present study between serum ferritin levels and PFTs in anemic adults (Table 2). An Austrian based cohort study also revealed positive correlation between serum iron indices and FEV1. In another Korean study, higher serum ferritin levels were not associated with better lung function, and instead were associated with a lower FVC in men. The results of the current research are in contradiction to the Korean study as significant (p<0.05) positive association between serum ferritin levels and lung function changes was observed in the present study in men (Table 3).

In a US study, researchers found that higher serum ferritin was associated with lower prevalence of asthma among adult anemic women. The results showed the same significant (p<0.05) effect in the present study in relation to association between serum ferritin levels and PFTs in anemic adults in women (Table 4).

A case control study was conducted in the outpatient department of Enam Medical College & Hospital, Dhaka, Bangladesh. Asthma cases had lower serum ferritin levels as compared to controls. The present study also showed the same significant (p<0.05) in women (Table 4).

CONCLUSION

Restrictive lung function changes were found in IDA subjects in the present study. Positive association was observed between PFTs and serum ferritin levels in subjects with IDA. While no positive correlation was found in non-anemic controls. Early detection and correction of IDA in patients with reduced pulmonary functions are recommended. Development of respiratory diseases can thus be prevented by these measures.

Author's Contribution:  
Concept & Design of Study:  Aliya Waseem  
Drafting:  Mohammad Saleh Soomro, Shahjabeen  
Data Analysis:  Syed Adnan Ahmed, Saba Abrar, Tabinda  
Revisiting Critically:  Aliya Waseem, Mohammad Saleh Soomro  
Final Approval of version:  Aliya Waseem  

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

REFERENCES

Relation of Liver Fibrosis Assessed by Elastography with Glycemia in Chronic Hepatitis C Patients

Talat Samreen¹, Sagheer Ahmed², Syed Munawer Alam³ and Syeda Asia Perveen¹

ABSTRACT

Objective: HCV infection is a major cause of liver fibrosis that may leads to glucose dysregulation. Elastography is a relatively new, non-invasive technique for assessment of liver stiffness. Present study aimed to find out the correlation of degree of liver stiffness with glycemia in chronic HCV patients.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Institute of Basic Medical Sciences of Dow University of Health Sciences, Karachi for one year.

Materials and Methods: Patients were recruited by convenient sampling technique from the hepatitis clinic and medical ward of Ruth Pfau Civil Hospital, Karachi. A total of ninety participants were inducted. Among them, sixty were HCV related chronic liver disease patients (Group B) of 30-60 years of age of either gender while thirty were age and sex matched healthy control subjects (Group A). Patients not fulfilling the inclusion criteria or not willing to participate were excluded. Fasting blood glucose all participants were estimated. Based on Elastography findings HCV patients were sub-grouped into B1 (METAVIR grade F1 and F2) and B2 (MATAVIR grade F3 and F4). Data entered and analyzed by SPSS version 20.0. and presented as frequency (n; %) and mean ±SD. One-way ANOVA, Post Hoc Tuckey’s test and Pearson’s correlation test were applied where appropriate. A p-value of <0.05 was considered as statistically significant.

Results: Demographic and anthropometric characteristics of the study participants showed non-significant difference compared to control. Liver stiffness was found to be significant raised in advance fibrosis compared to control and early fibrosis group. Patients with advanced fibrosis had significant raised FBG compared to control (p = 0.002) and early fibrosis patients (p = 0.004). Pearson’s correlation test revealed significant moderate positive relation (r=0.393, R²=0.155) of FBG with liver fibrosis (p= 0.000).

Conclusion: Liver stiffness as assessed by elastography has significant positive correlation with glycaemia in chronic HCV patients.

Key Words: Chronic Hepatitis C, Liver Fibrosis, Shear wave Elastography

INTRODUCTION

Revalence of hepatitis C infection is increasing at an alarming rate effecting nearly 185 million people worldwide¹. HCV infection rate in Pakistan has also reached an epidemic proportion with nearly 10 million people in the country lived with this virus.

According to an estimate of WHO, Pakistan stands second after Egypt according to number of people infected with this virus². HCV once considered as hepatotropic virus affecting and limited to the liver, growing body of evidences now pointed out role of this virus in manifestation of certain extra hepatic diseases³. Though exact prevalence of these extra hepatic manifestation was not known, Gill K et al, reported nearly 40-74% of HCV patients had some of the extrahepatic manifestations ranging from severe fatigue to certain form of lymphoma³.

Dysregulation of blood glucose is one of the extra hepatic manifestations of CHC⁴. Epidemiological studies reported nearly 14-33% of CHC patients developed type 2 diabetes (T2DM)⁵. Numerous mechanisms have been suggested for T2DM development in CHC patients that ranges from direct infection of beta cells of pancreas to the development of insulin resistance due to hepatic fibrosis and cirrhosis⁶. Studies reported increased frequency of T2DM with every rise in fibrosis score of HCV patients with an OR

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of 3.83. Cirrhosis is the final stage of liver fibrosis and liver inflammation, may reduce uptake of glucose by hepatic cells thus affects the glucose metabolism.

There are various methods for evaluating and grading liver fibrosis. It ranges from invasive procedure like liver biopsy to non-invasive evaluation of fibrosis by serological panels, mathematical calculations of certain serum fibrosis markers and clinical data to imaging techniques.

In contrast to liver biopsy which is painful and determine very small volume of hepatic parenchyma with inter and intra observer variability, SWE is one of the non-invasive modality for the assessment of liver fibrosis and can examine 100 times bigger volume of liver tissue. Meta-analysis conducted on diagnostic accuracy of noninvasive modalities suggested high accuracy of SWE and clinically useful for fibrosis F≥2 and identical for liver cirrhosis as compared to other non-invasive modalities such as RTE, ARFI, TE. Furthermore, unlike transient elastography, which consists of a vibrator producing shear waves, the latter can perform a conventional ultrasound at the same time. Therefore, shear wave elastography (SWE) may be preferred, because sensitivity and specificity for diagnosing hepatic cirrhosis was nearly 90% and for hepatic fibrosis it was 70-80%.

Present study thus evaluated the relation of serum glucose with severity of liver fibrosis as assessed by SWE in order to validate the findings of earlier studies in which liver fibrosis was graded by other modalities. SWE Elastography is a new technique for measuring the liver stiffness in Kpa and graded according to META VIR classification in to F1, F2, F3 and F4. Present study thus aimed to find out the correlation of liver stiffness/fibrosis as assessed by SWE elastography with glycemic status of non-diabetic chronic HCV patients.

MATERIALS AND METHODS

This descriptive, cross sectional study was conducted in the Institute of Basic Medical Sciences of Dow University of Health Sciences. Study was conducted after ethical approval from the institutional review board of DUHS. Patients were selected from the hepatitis clinic and medical ward of Ruth Pfau Civil Hospital, Karachi. Sample size was calculated by PASS version II sample size calculator taking confidence interval and power 99%. A total of ninety (n=90) participants were inducted in this study by convenient sampling technique. Among them, sixty (n=60) were HCV related chronic liver disease patients (Group B) of 30-60 years of age of both gender while thirty (n=30) were age and sex matched healthy subjects (Group A). Subjects with history of hypertension, smoking, alcohol, ascites, pregnancy, co-infection with other types of hepatitis viruses, patients with history of thyroid diseases and persons not willing to participate were excluded. Elastography of the selected patients (n=60) and controls (n=30) were performed in the radiology department of Ruth Pfau Civil Hospital, Karachi. Liver stiffness was expressed in Kpa and grouped according to META VIR classification. According to liver stiffness value patients were graded into gradeI; 6.2Kpa (5.3-7.1), grade II; 7.6Kpa (7.0-8.5), grade III; 10.0Kpa (9.5-11.6) and grade IV; 15.6Kpa (13.1-18.8). These patients were further sub grouped into B1 (patients with elastography META VIR fibrosis grade F1 and F2) and Group B2 patients with elastography META VIR fibrosis grade F3 and F4. Blood samples from each participant were collected after 12 hours of fasting for estimation of fasting blood glucose level. Elastography was done after blood collection. Data was entered and analyzed by SPSS version 20.0. and presented as frequency (n; %) and mean ±SD. One-way ANOVA was applied to compare the mean (±SD) among group variable with significant difference in ANOVA was analyzed by Post Hoc Tuckey’s test. Pearson’s correlation test was performed by to find out the association of liver stiffness with glycemic status. A p-value of <0.05 was considered as statistically significant.

RESULTS

A total of ninety participants including thirty control (n=30) and sixty (n=60) known HCV patients were inducted in the study. Demographic and anthropometric characteristics of the study participants are shown in table 1. Comparison among groups revealed non-significant difference in demographic and anthropometric characteristics of HCV patients compared to control.

Mean (±SD) values of liver fibrosis among hepatitis C patients in group B1 and B2 and control were assessed by shear wave ultrasound and categorized according to META VIR classification. A significant difference in mean (±SD) of liver fibrosis among group was observed by application of one way ANOVA test (Figure 1). Posthoc Tuckey’s test revealed significant difference in mean ±SD of liver fibrosis in late fibrosis group compared to control (group A) and patients in early fibrosis group (group B1).

Liver stiffness among the study groups by Shear wave
Elastography (mean±SD)
A significant difference in fasting blood glucose (FBG) was observed by application of ANOVA test revealed significant p-value = 0.001, as shown in Table 2. Application of Post Hoc Tukey’s test revealed patients in early fibrosis (group B1) had non-significant difference (p= 0.954) whereas patients in late fibrosis (group B2) had significant raised FBG compared to group A (p = 0.002). Late fibrosis patients (group B2) had significantly raised level of fasting blood glucose compared to early fibrosis (Group B1), (p = 0.004)

Table No.2: Comparison of (mean ±SD) FBS Level among study groups by one-way ANOVA and Pot Hoc Tuckey’s test

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A Control (n=30)</th>
<th>Group B 1 Early Fibrosis F1+F2 (n=29)</th>
<th>Group B 2 Late Fibrosis F3+F4 (n=31)</th>
<th>F-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>88.1±21.6</td>
<td>90.2±20.3</td>
<td>113.0±35.6</td>
<td>7.97</td>
<td>0.001</td>
</tr>
</tbody>
</table>

p-value < 0.05 is significant

The correlation between FBS level and liver fibrosis (shear wave average) shown in table 3 revealed significant moderate positive relation (r=0.393, R²=0.155) with p-value 0.000. R² shows 15% variation in FBS was explained by liver fibrosis as shown table 3.

Table No.3: Correlation of FBS in HCV infected patients with liver Fibrosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r-value</th>
<th>R² Value</th>
<th>% of determination</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS mg/dl</td>
<td>0.393</td>
<td>0.155</td>
<td>15%</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

DISCUSSION

DM and Hepatitis C are chronic diseases, prevalent throughout the world1. Present study revealed the relation of blood glucose with liver stiffness in HCV infected patients. A significant positive association of fasting blood glucose with severity of liver fibrosis was observed.

Considering earlier as hepatotropic virus, in the recent past this virus was found to have increased propensity to infect extrahepatic tissues as well. Studies reported increased propensity of HCV virus to dysregulate glucose metabolism. Various mechanisms of glucose dysregulation in the literature have been reported that predispose HCV patients to diabetes, both directly as well as through indirect mechanism. Infection of β-cell of pancreas by HCV effects the insulin signaling pathway, ultimately results in DM13. Besides this direct effect, in some studies, presence of fibrosis, has been shown to be an independent risk factor that contributes to the progression to T2D14. Seventy to eighty percent of HCV cirrhotic have been reported to have glucose intolerance, and 50% of these cirrhotics have developed DM15. The rates of development of diabetes has been reported to be more increased on the background of higher grades of hepatic fibrosis, steatosis, or cirrhosis16. Whereas some literatures like the study done by Hanchanale P et al, reported increased frequency of diabetes even in non-cirrhotic chronic HCV patients and suggested pathogenesis of DM in HCV patients is multifactorial initiated in pre-cirrhotic stage leading to abnormal glucose metabolism and insulin resistance17. The inconsistency in published reports between relation of diabetes with presence of cirrhosis in HCV patients may be because of subtle variations among studies in study design, patient selection as well as difference in modality used for assessment and grading of liver fibrosis.

Like above mentioned studies, numerous other published studies that explored the relation of hepatitis C virus with glycemic status of the patients18,19 used different modality for assessment of liver fibrosis. For example, Saad Y et al, find out the relation of blood glucose and fibrosis in liver. Authors in that study evaluated liver fibrosis in Egyptian diabetic patients with hepatitis C virus20. In other studies, similar relation of glucose with liver fibrosis was reported. The studies conducted by Sabry HS et al, Turner BJ et al, and Chen Yet al, also explored the relation between liver fibrosis with glycemic status of the chronic HCV patients. In these studies, however liver fibrosis is assessed by liver biopsy and APRI and FIB4 respectively21,22,23. These studies also despite of use of varied methodology for the assessment of liver fibrosis unanimously reported the association of liver fibrosis with glycemic status of the patients.

Liver biopsy is the gold standard in the diagnosis and staging of liver fibrosis. But it evaluates only 1/50000 of the liver parenchyma. It is invasive and in rare instances leads to severe complications10. Because of the imperfect nature of liver biopsies, over the last
several years there has been a growing trend to validate non-invasive tools to diagnose and stage liver fibrosis. Laboratory marker like (Alkaline aminotransferase platelet ratio index (APRI)) has been shown to have some value but is inferior to liver biopsy. Alternatively, magnetic resonance has been used for elasticity imaging. Magnetic Resonance Elastography, even though promising, has some disadvantages. Aside from the significant cost, it cannot be performed in a liver with iron overload. It also required longer examination times compared to ultrasound elastography. Ultrasound elastography has been validated and has been shown in many studies to have almost similar sensitivity and specificity to liver biopsies.

Present study was conducted in an attempt to validate the findings of earlier studies. Present study is unique as in this study liver fibrosis is evaluated by non-invasive, shear wave ultra-sonographic technique that measures the liver stiffness in Kpa. Values of liver stiffness in Kpa is categorized and considered equivalent to the various grades of METAVIR classification system. METAVIR scoring system is used to assess the extent of inflammation and fibrosis by histopathological evaluation in a liver biopsy of patients with hepatitis C. The grade indicates the activity or degree of inflammation while the stage represents the amount of fibrosis or scarring. A significant positive correlation of liver stiffness with glycemia in the present study is consistent with the available literatures however it serves as a mean to look this old relation through a new window of non-invasive procedure.

CONCLUSION

Liver stiffness as assessed by elastography has significant positive correlation with glycemia in chronic HCV patients. Thus validated the findings of earlier studies evaluated liver fibrosis by other methodology.

Author’s Contribution: 
Concept & Design of Study: Talat Samreen
Drafting: Sagheer Ahmed, Syed Munawer Alam
Data Analysis: Syeda Asia Perveen
Revisiting Critically: Talat Samreen, Sagheer Ahmed
Final Approval of version: Talat Samreen

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

REFERENCES

Association of Intrahepatic Cholestasis of Pregnancy with Adverse Fetal Outcome

Aisha Aslam¹, Jahanzeb Maqsood², Syed Saif Ur Rehman², Adnan Ghafoor³, Abida Mateen² and Muhammad Wajad Munir²

ABSTRACT

Objective: To determine association of intrahepatic cholestasis of pregnancy with adverse fetal outcome.

Study Design: Cohort Study

Place and Duration of Study: This study was conducted at the Department of Gynecology and Obstetrics of PAEC General Hospital Islamabad from August 2015 to Feb 2016.

Materials and Methods: 110 patients were included in the study during second trimester according to inclusive criteria. Two groups with 55 patients each were made. Group A was assigned to the patients with deranged LFTs while Group B was assigned to the patients with normal LFTs. Patients were followed during third trimester. Adverse outcomes like preterm labor and meconium stained liquor were the parameters observed in both groups and these were compared between groups.

Results: Total 110 patients were included in study. Mean age was 27.89 ± 4.51 years. Out of all 110 patients included in study 27 (24.5%) were primigravida, 33 (30%) had one pregnancy earlier and 50 (45.5%) had 2 or more pregnancies. In group A 14 patients were primigravida, 14 had one pregnancy earlier and 27 and more than two pregnancies. In group B 13 patients were primigravida, 19 had one pregnancy earlier and 23 had two or more pregnancies earlier. In group A mean ALT was 132.75 U/L, AST was 132.04 U/L, ALP was 1049.96 U/L and Bilirubin was 2.34mg/dL. While in Group B, mean ALT was 28.71 U/L, AST was 28.51 U/L, ALP was 622.69 U/L and Bilirubin was 0.931mg/dL. In Group A, 35 patients (63.63 %) had meconium stained liquor while in Group B, only 07 patients (12.72%) had meconium stained liquor. In Group A, 32 patients (58.18 %) had Preterm Labor while in Group B, only 07 patients (12.72%) had Preterm Labor.

Conclusion: ICP is a condition that can affect the fetal outcomes and can cause preterm labor and meconium staining as compared to normal pregnancy. Adverse fetal outcomes are not associated with age and parity.

Key Words: Intrahepatic Cholestasis in pregnancy, Liquor, Liver Function Tests, Meconium, Preterm labor.

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is characterized by intense itching and is associated with deranged liver function tests (raised serum bile acids or/and raised serum transaminases) in prior normal pregnant woman. It starts during the second or third trimester of pregnancy and symptoms get better within 2 to 3 weeks after delivery. Error! Bookmark not defined. Liver function test changes are temporary and their timely interpretation can lead to early treatment and will decrease complications in both mother and fetus.²

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Geographic location and ethnicity effect prevalence of intrahepatic cholestasis of pregnancy with 2% in Pakistan and increases to 10% in South American population. While Europe and United states of America have occurrence of 0.1 -1.5% only.³ Environmental, genetic and hormonal factors play a role in intrahepatic cholestasis of pregnancy. Increased sex hormone production and their altered metabolism in liver leads to bile acid elevation in mother and fetus blood.⁴ Raised bile acids appear to the responsible for severe itching and fetal adverse effects. Most women have benign course but can have increased risk of preterm delivery, meconium staining of amniotic fluid, fetal demise.⁵,⁶,⁷,⁸ According to Geenes et al, there is strong association of intrahepatic cholestasis of pregnancy with a number of complications such as preterm deliveries (25%) as compared to 6.5% in controls and meconium stained liquor in 40.4% as compared to 18.6% to control.⁹ Shobaili et al concluded expectant management to 40 weeks in patients with intrahepatic cholestasis of pregnancy has fetal outcomes comparable to normal pregnancy.¹⁰
Different geographic and ethnic population, timing of delivery and lack of diagnostic criteria of previous studies make their findings variable and cannot be applied to our population. This study will help to establish association of adverse fetal outcomes with intrahepatic cholestasis of pregnancy, so that adverse fetal outcomes can be anticipated before labor and associated fetal complication can be avoided.

**MATERIALS AND METHODS**

This cohort study was conducted at department of Gynecology and Obstetrics of PAEC General Hospital Islamabad from August 2015 to Feb 2016 after approval of ethical committee. Sample size calculations was done with confidence level 95% and P1=40.4% P2=18.6 % and Power of test=80%. Samples were collected through non probability consecutive sampling. 55 patients with singleton pregnancy with deranged LFTs from 24th week of pregnancy were included through non probability consecutive sampling and assigned as group A. Patients with other causes of deranged LFTs like hepatitis A, B, C, E, gallstones, HELLP syndrome and acute fatty liver of pregnancy were excluded from the study. 55 patients with singleton pregnancy with normal LFTs from 24th week of gestation were taken as control and assigned as group B. Informed consent was taken by the patients. Samples were collected from both indoor and outdoor patients.

History was taken and physical examination was done to confirm patient age, gestational age and to rule out history of hypertension, dark colored urine, pale stools and jaundice. Ultrasound Abdomen was performed in radiology department of hospital to rule out any other cause of liver disease. Blood samples were taken to perform the liver function tests, viral serology for hepatitis A, B, C and E. Biweekly follow up in 2nd trimester and weekly follow up in 3rd trimester was done in obstetrics department. Both the groups were compared for fetal outcomes by time of delivery and meconium staining of amniotic fluid.

Data was analyzed on SPSS version 21. Age, parity, Gestational age, Liver Function Tests were Quantitative Variable, Mean SD will be calculated. Preterm delivery, Meconium stained liquor were Qualitative variables. Frequency and percentage will be calculated. Effect modifier like age, gestational age was controlled by stratification, fetal outcome measured post-stratification. Chi square test will be used to compare frequency of fetal outcomes between two groups.

**RESULTS**

Total number of patients included in the study was 110. Group A and B both included 55 patients each. Mean age in Group A was 28.25 ± 4.904 years while in Group B mean age was 27.53±4.104 years as shown in Figure 1.

In group A, 14 patients were prim grvida, 14 had one pregnancy earlier and 27 had more than two pregnancies. In group B, 13 patients were prim grvida, 19 had one pregnancy earlier and 23 had two or more pregnancies earlier as shown in Table 1.

In Group A mean ALT,AST,ALP and bilirubin at time of diagnosis was 132.75 ± 62.25 U/L, 132.04 ± 60.98 U/L, 1049.96 ± 162.44 U/L and 2.34 ± 0.39 mg/dL respectively. In Group B mean ALT,AST,ALP and bilirubin was at the time of diagnosis 28.71 ± 6.42 U/L, 28.51 ± 5.77 U/L, 622.69 ± 84.31 U/L and 0.93 ± 0.078 mg/L respectively as shown in Table 2.

In Group A, mean ALT,AST,ALP and bilirubin at time of delivery was 54.07±27.498 U/L, 62.78±31.309 U/L, 678.02±100.260 U/L and 1.5064±0.251 mg/dL respectively. In Group B mean, ALT,AST,ALP and bilirubin was 38.18±21.852 U/L, 29.58±5.315 U/L, 575.40±124.393 U/L, 0.80±0.085 mg/dL respectively as shown in Table 2.
We found that Preterm labor occurred in Patients having mean ALT of $140 \pm 79.296$ U/L, AST of $139.38 \pm 77.693$ U/L, ALP of $1014.21 \pm 272.007$ U/L and Bilirubin of $2.161 \pm 0.674$ mg/dL. There was statistically significant difference in both groups in terms of ALT, AST, ALP and bilirubin (p Value = 0.00) Preterm labor occurred in patients having mean ALT of $122.24 \pm 74.723$ U/L, AST of $122.52 \pm 73.709$ U/L, ALP of $984.62 \pm 231.918$ U/L and bilirubin of $2.10 \pm 0.64$ mg/dL. There was statistically significant difference in both groups in terms of ALT, AST, ALP and bilirubin (p Value = 0.00) as shown in Table 4.

**DISCUSSION**

Intrahepatic cholestasis of pregnancy like other disorders arising pregnancy such as HELLP, acute fatty liver of pregnancy and hemolysis leads to elevated liver enzymes and serious complication in mother and fetus. Early diagnosis and prompt management can lessen these complications. Error! Bookmark not defined. Error! Bookmark not defined. Error! Bookmark not defined. In our study it was observed that cholestasis during pregnancy can have a detrimental effect on proceeding of pregnancy. Cholestasis can be easily diagnosed by an elevation in LFTs. ALT, AST, Bilirubin and ALP was measured in our study. We have observed that elevated levels of Liver function tests in second trimester influence the fetal outcomes. Meconium stained Liquor and preterm Labor were two of these outcomes observed in our study. Preterm Labor was observed in 58% of the patients with elevated LFTs during second trimester while it was seen in 13% in normal pregnancies. Meconium stained liquor is another serious complication observed in patients with ICP. In our study we observed that Meconium staining was found in 63%. It was further observed that Preterm Labor was associated with meconium staining in both groups. There was statistically significant difference (p value <0.05) in both groups.

A prospective population-based cohort study was carried out over 12 months (June 2010 to May 2011) by Victoria G et al. Cases of severe ICP were identified through the UK Obstetric Surveillance System (UKOSS). In this cohort they have observed meconium staining in patients with ICP at 35 week preterm Labor at 40%. Preterm Labor was observed in 25 % of the cases with ICP. There was positive correlation observed between ICP and complications like preterm delivery and meconium stained liquor. Similar observations were noted in our study.

Age is considered as one of the risk factor for development of ICP. This was identified by Glantz
et al, that age has a correlation with development of ICP and may cause adverse fetal outcome. In our study we couldn’t find any correlation between age and development of ICP. There was no significant difference in both groups in terms of age. (p value >0.05).

Parity is another factor thought to influence development of ICP. Increasing parity is considered to influence adverse fetal outcome in patients having ICP. Al Shobaili et al found some correlation between multiple gestations and adverse fetal outcomes but that was not significant. Our study couldn’t find any correlation among multiparous women or primigravida either in term of development of ICP or adverse fetal outcomes.

CONCLUSION

ICP is a condition that can affect the fetal outcomes and can cause preterm labor and meconium staining as compared to normal pregnancy. Adverse fetal outcomes are not associated with age and parity.

Author’s Contribution:

Concept & Design of Study: Aisha Aslam
Drafting: Jahanzeb Maqsood, Syed Saif Ur Rehman
Data Analysis: Syed Saif Ur Rehman
Revisiting Critically: Adnan Ghafoor, Abida Mateen, Wajid Munir
Final Approval of version: Ayesha Aslam

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

REFERENCES

Assessment of Anxiety Level Among Doctors and Paramedical Staff in a Tertiary Care Hospital, During COVID-19 Pandemic

Muhammad Mahboob Alam\(^1\), Maryam Khokhar\(^2\), Muzzammal Iftikhar\(^4\), Sara Hafeez\(^1\), Noor ul Huda Mahboob\(^5\) and Altarf Pervez Qasim\(^3\)

ABSTRACT

Objective: To assess the level of anxiety among doctors and paramedical staff working in a tertiary care Hospital during COVID-19-Pandemic.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Abwa Hospital & Research Centre attached with Abwa Medical College, Faisalabad for the period of three months i.e. May, 2020 to July, 2020.

Materials and Methods: Total 55 participants including 11 doctors & 44 paramedics serving specifically COVID-19 patients were selected to assess the level of anxiety and its associated factors.

Results: out of total 55 participants, the level of anxiety was higher among medical doctors (mean score =6.91±7.0) as compared to paramedical staff (mean score3.25±4.68) where 31.7% of frontline health workers reported anxiety on BAI. 20 % (n=11) mild symptoms, a single worker only reported moderate anxiety &7.2% reported severe anxiety.

Conclusion: During the pandemic of COVID-19 disease, among health care workers of ABWA hospital, medical doctors reported anxiety problems to a greater extent as compared to paramedical staff although intensity of anxiety was disproportionately higher in paramedical group. Considering this, there is a need of implementing programs of mental health being for health care professionals as an essential component of every epidemic at both national and international level.

Key Words: Anxiety level, Paramedical staff, Medical Doctors, COVID-19, Pandemic

INTRODUCTION

The coronavirus (COVID-19) pandemic has not only emerged as a global medical emergency but is also adversely affecting the public mental health by far it is considered the biggest outbreak of acute respiratory syndrome of the world including Pakistan. Although similar to previous SARS outbreak, little is known about the psychological impact of (COVID-19)

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prone to the stress in shape of physical as well as mental health issues & at times work related stress becomes a common associated factor for suicidal behavior. The perceived risk of infection is warranted: a meta-analysis of the occupational risk from 2009 swine flu pandemic; reports that the odds of healthcare personnel contracting the virus were twice those of comparison groups. This heightened risk for doctors and nurses might be due to their greater exposure to the respiratory secretions of patients. Threat of COVID-19 contagion, especially its impact along frontline paramedics treating patients of Corona Virus, and their perception of self-infection ultimately increases their agonistic behavior. During a panic, Healthcare personnel (HCP) face not only physical challenges but also mental burdens, including psychological distress and fear. Globally, healthcare organizations and governments are striving to protect HCP from COVID-19. Protocols for sterilization, safety, cleaning, and disinfecting in hospitals, isolation centers, and other health center spaces are being communicated and enforced. An important point is to monitor psychological needs of HCP in times of pandemics, especially in relation to their anxiety level and it should also be kept in mind that adapting with a new work environment in quarantined wards also leads to stress among healthcare personnel.

It is imperative to improve the support for healthcare providers during the corona pandemic. Immediate attention is needed to reduce anxiety, workload and family strain in frontline practitioners treating coronavirus patients, and to improve their perceptions of protection.

**MATERIALS AND METHODS**

It is a cross-sectional study in which face to face interviews are carried out with medical and paramedical workers of Abwa hospital, Khurrianwala to assess the presence and severity of anxiety. Along with the demographic information (age, gender, marital status, occupation, number of working hours spent per week), screening for anxiety is carried out with GAD-7 and then the severity of anxiety regarding COVID-19 is assessed with BAI (Beck anxiety inventory). Duration of study was three months i.e. 1st May, 2020 till 31st July, 2020. Participants included were doctors, nurses, dispensers, lab technicians, medical emergency and radiology technicians, ward boys & sanitary workers with a designated duty for the care provision to COVID-19 admitted patients for the last four months in hospital. Samples were collected through Probability (simple random) sampling technique. Ethical approval was granted. After acquiring informed consent from each participant, the interviews carried out, and data collected.

**Statistical Analysis:** GAD-7 total score for the seven items ranges from 0 to 21. Scores of 5,10, and 15 represent cut-points for mild, moderate, and severe anxiety, respectively. Further evaluation is recommended when the score is 10 or greater. Beck Anxiety Inventory (BAI) is a self-reported (four-point scale) of 21 items used to assess the intensity of anxiety during the past week. Score ranged 0 to 63: mild anxiety (8–15), moderate anxiety (16–25) & severe anxiety (26–63). Descriptive single factor correlation and multiple regression analysis are used to explore the associated factors. Chi-square test was used to compare categorical variables whereas; univariate and multivariate logistic regression models were conducted for comparisons of age, gender and marital status.

**RESULTS**

Table No.1: Demographic characteristics of study participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean ± S.D)</td>
<td>28.33±8.18</td>
</tr>
<tr>
<td>Age in Years: 18-25 Years</td>
<td>28(50.9)</td>
</tr>
<tr>
<td>26-35 Years</td>
<td>18(32.7)</td>
</tr>
<tr>
<td>36-45 Years</td>
<td>7(12.7)</td>
</tr>
<tr>
<td>46 Years or above</td>
<td>2(3.6)</td>
</tr>
<tr>
<td>Gender: Male</td>
<td>39(70.9)</td>
</tr>
<tr>
<td>Female</td>
<td>16(29.1)</td>
</tr>
<tr>
<td>Marital Status: Married</td>
<td>19(34.5)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>36(65.5)</td>
</tr>
<tr>
<td>Profession Group: Medical Staff</td>
<td>11(20.0)</td>
</tr>
<tr>
<td>Paramedical Staff</td>
<td>44(80.0)</td>
</tr>
<tr>
<td>Occupation: Doctor</td>
<td>8(14.5)</td>
</tr>
<tr>
<td>Medical Specialist</td>
<td>3(5.5)</td>
</tr>
<tr>
<td>Nurse</td>
<td>12(21.8)</td>
</tr>
<tr>
<td>Midwife</td>
<td>2(3.6)</td>
</tr>
<tr>
<td>Ward boy</td>
<td>8(14.5)</td>
</tr>
<tr>
<td>Dispenser</td>
<td>4(7.3)</td>
</tr>
<tr>
<td>Lab Technician</td>
<td>10(18.2)</td>
</tr>
<tr>
<td>Radio Technologist</td>
<td>3(5.5)</td>
</tr>
<tr>
<td>Surgical Technician</td>
<td>1(1.8)</td>
</tr>
<tr>
<td>Sanitary Worker</td>
<td>4(7.3)</td>
</tr>
<tr>
<td>Working Hours Per Week</td>
<td></td>
</tr>
<tr>
<td>26 hours</td>
<td>1(1.8)</td>
</tr>
<tr>
<td>36 hours</td>
<td>36(65.5)</td>
</tr>
<tr>
<td>48 hours</td>
<td>1(1.8)</td>
</tr>
<tr>
<td>60 hours</td>
<td>1(1.8)</td>
</tr>
<tr>
<td>72 hours</td>
<td>16(29.1)</td>
</tr>
<tr>
<td>Tested for Covid-19: Positive</td>
<td>4(7.3)</td>
</tr>
<tr>
<td>Negative</td>
<td>21(38.2)</td>
</tr>
<tr>
<td>No test</td>
<td>30(54.5)</td>
</tr>
<tr>
<td>Covid-19 Positive Family Member</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2(3.6)</td>
</tr>
<tr>
<td>No</td>
<td>53(96.4)</td>
</tr>
</tbody>
</table>

Descriptive Statistics, Values are expressed as frequency (%).

In this study the total number of participants were 55, out of which 20% (n=11) were medical doctors & 80%
(n=44) belonged to the paramedical profession. 70.1% (n=39) were of male whereas 29.1% (n=16) were of female gender. Mean age was 28.33 ±8.18 years where 50.9% (n=28) aged 18-25 years, 32.7% (n=18) in 26-35 years, 12.7% (n=7) in 36-45 years & 3.6% (n=2) were above 46 years old. Majority of participants, 65.5% (n=36) were unmarried & 34.5% (n=19) were married. Most, 65.5% (n=36), of the health care professionals worked 36 hours a week. Regarding covid-19 testing, 54.5% (n=30) didn't get tested, 21% (n=21) were negative & only 7.1% (n=4) were found positive for disease. Only 3.6% (n=2) had close family members diagnosed with covid 19 disease. There is a significant positive correlation between anxiety and health care profession during covid-19 pandemic. With a GAD-7 score of 6.91 ±7.0, medical doctors were comparatively experiencing higher level of stress as compared to paramedical staff (P-value =0.042). Similar positive scores are found on other anxiety scale too. In addition to, in context of severity on BAI, 7.3% (n=4) of medical doctors reported mild, none for moderate and 3.6% (n=2) for severe level of anxiety which in disproportionately lesser to that of paramedical staff where 7.3% for mild, 3.6% for moderate and 10.9% for severe anxiety.

Table No.2: Comparison of GAD-7 and BAI score between medical and paramedical staff

<table>
<thead>
<tr>
<th>Variables</th>
<th>Medical Staff</th>
<th>Paramedical Staff</th>
<th>p-value</th>
<th>Mean differences (95% Confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAD-7 Score</td>
<td>6.91±7.00</td>
<td>3.25±4.68</td>
<td>0.042</td>
<td>3.66(0.143 to 7.175)</td>
</tr>
<tr>
<td>BAI Score</td>
<td>13.73±15.84</td>
<td>5.95±8.89</td>
<td>0.033</td>
<td>7.77(0.632 to 14.914)</td>
</tr>
</tbody>
</table>

Values are reported as Mean ± SD, Independent sample T-test: p value <0.05

Table No. 3: Assessment of Intensity of Anxiety through Beck Anxiety Inventory scale

<table>
<thead>
<tr>
<th>Groups</th>
<th>Intensity of Anxiety</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimal</td>
<td>Mild</td>
</tr>
<tr>
<td>Medical Staff</td>
<td>5(9.1)</td>
<td>4(7.3)</td>
</tr>
<tr>
<td>Paramedical Staff</td>
<td>34(61.8)</td>
<td>4(7.3)</td>
</tr>
</tbody>
</table>

Values are reported as frequency (%). Chi square Test: *p value <0.05

DISCUSSION

Corona Virus Disease (COVID-19) took the world by storm, emerged as a worldwide health care crisis, resulting in the pandemic of the 21st century. The overwhelming burden of this dreadful disease has resulted in physical as well as psychological pressure on health care workers. The present study identified significantly comparable differences in level of anxiety faced, between medical doctors and paramedical workers. A study conducted on physicians of China during COVID-19 pandemic showed that 12.5% had higher level of anxiety & direct contact to COVID-19 patients in hospital was observed to be an important risk factor associated with higher level of stress. Most of the study participants showed no/minimal anxiety but still a third of Frontline health workers were found having anxiety problems. Findings told that 31.9% (BAI) were suffering from anxiety disorder. Moreover as compared to the general population, frontline health care providers, despite provision of adequate safety measures still have a greater risk of infection as well to spread it to close ones especially family members. Such a threat causes a serious impact on psychological wellbeing where anxiety, PTSD, depression & burnout are commonly felt. A study conducted in Iran by Nemati et al. threw light on association of knowledge about Covid-19 and stress faced during patient handling where mean anxiety score was 6.02 ±2.6 & more than half of the nurses had satisfactory knowledge about disease causation and prevention provided to them with the help of WHO collaboration program and gained by themselves through electronic media. However, 21.8% of paramedical participants experienced anxiety while performing duties in Corona ward. It has been documented recently that financial crisis and increase workload might adversely affect the mental health of doctors where 6-20% of them develop anxiety, depression, somatization disorder and PTSD. Another study conducted in Karachi by Hasan et al. 19 studying the levels of anxiety in 151 Healthcare professionals documented that 45.7% participants had mild anxiety, 14.6% had moderate, and 3.3% had severe symptoms of anxiety, whereas the remaining 36.4% had no anxiety. The early detection of psychosomatic problems needs skilled mental health professionals team as well as prompt strategies of their treatment and prevention in the initial stage of any epidemic & prevalent disease in future so that to render burnout and promote resilience. In this context, conducting awareness campaigns, teaching relaxation techniques, promoting physical fitness exercises along with good nutrition & sleep may serve as a booster of positive mental health.

CONCLUSION

The wellbeing and mental health of HCP during global pandemics is absolutely salient as it could impact on mortality and recovery rates. Immediate attention is needed to reduce anxiety, workload, and family strain in frontline practitioners treating coronavirus patients, and to improve their perceptions of protection. Our
study confirmed great psychosocial impact in healthcare workers during COVID-19 pandemic including effects on their family and personal life hence this demands for a commensurate psychosocial support for healthcare workers at institutional as well as governmental level.

The wellbeing and safety of HCWs will determine the quality of preparedness for the next pandemic or the next wave of the corona pandemic. Collaborative efforts are needed by federal and provincial governments, the health sector, health regulatory bodies, media agents, and the public overall. Improving financial benefits, resources, workplace safety, protective services, and team building with emotional stability during these testing times will have long term benefits for Healthcare professionals in service quality and patient safety standards. 

Author's Contribution:
Concept & Design of Study: Muhammad Mahboob Alam
Drafting: Maryam Khokhar, Muzzammal Iftitkar
Data Analysis: Sara Hafeez, Noor ul Huda Mahboob, Altaf Pervez Qasim
Revisiting Critically: Muhammad Mahboob Alam, Maryam Khokhar
Final Approval of version: Muhammad Mahboob Alam

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

REFERENCES


Comparison of Effectiveness of Topical and Oral Metronidazole for Reducing Postoperative Pain after Hemorrhoidectomy

Sajid Razzaq\textsuperscript{1}, Zardad Khan\textsuperscript{2}, Mohammad Arif Mahmood\textsuperscript{1}, Mohammed Nadeem Khan\textsuperscript{3}, Waheed Iqbal\textsuperscript{4} and Nasir Zareen\textsuperscript{1}

ABSTRACT

Objective: To compare the effectiveness of oral versus topical metronidazole for reducing postoperative pain in patients undergoing Milligan Morgan hemorrhoidectomy.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Surgery, Divisional Headquarter Teaching Hospital Mirpur AJK from July 2019 to June 2020.

Materials and Methods: One hundred and twenty patients of both genders with ages 20 to 60 years undergoing hemorrhoidectomy for 3\textsuperscript{rd} and 4\textsuperscript{th} degree hemorrhoids were enrolled. All the patients were equally divided into two groups, each group contains 60 patients. Group 1 received oral metronidazole postoperatively for 5 days and group 2 received topical metronidazole postoperatively. Postoperative pain was analyzed by VAS on 1\textsuperscript{st}, 3\textsuperscript{rd} and 5\textsuperscript{th} day postoperatively between both groups.

Results: There were 76 (63.33\%) male patients and 44 (36.67\%) were females with mean age 38.7\pm11.42 years. 67 (55.83\%) patients had 4\textsuperscript{th} degree hemorrhoidal disease and 53 (44.16\%) patients had 3\textsuperscript{rd} degree disease. Group 2 (topical) patients had significantly lower postoperative pain at 5\textsuperscript{th} day as compared to group 1 (oral) patients with p value<0.05.

Conclusion: Topical metronidazole is more effective than oral metronidazole in patients undergoing Milligan Morgan hemorrhoidectomy.

Key Words: MilliganpMorgan hemorrhoidectomy, Post-operative pain

INTRODUCTION

Hemorrhoids at 3, 7, and 11 O'clock are symptomatic and prolapsed anal coilings. Among them are secondary haemorrhoids. Patients suffer from fresh rectal bleeding, mucus release, rectal pain irritation, and swelling. Hemorrhoids are four degrees. In the first grade there is no prolapse bleeding per rectum, in the second grade there is spontaneous prolapse, manual haemorrhoids of the third grade and no reduction of the entire prolapse of the fourth grade.\textsuperscript{1,3}

The key indications in clinical practise are third or fourth-grade internal haemorrhoids\textsuperscript{4}; pain, infections, infection, inflammations, haemorrhage, faecal incontinence, unexposed wounds and urinary retention are the major complications in hemorrhoidectomy.\textsuperscript{5,6} Spasma of internal anal sphincter appears as the major indicator of hemorrhoidectomy.\textsuperscript{3} Dolor is the main post-operative problem and it is caused by surgical injury in sensitive anoderm, oedema, spasm, and infection.\textsuperscript{7} Some remedial options such as GTN 0.1\%, topical NSAIDs, calcium channel blockers and metronidazole have been suggested.\textsuperscript{8} Studies show that metronidazole substantially decreases postoperative pain (p<0.004, \textit{p}=0.0011) in all types (topical and oral) and enhances the healing process relative to placebo.\textsuperscript{9,10}

The present study was conducted aimed to compare the efficacy of oral metronidazole versus topical metronidazole for reducing postoperative pain in patients undergoing hemorrhoidectomy.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Surgery, Divisional Headquarter Teaching Hospital Mirpur AK from 1\textsuperscript{st} July 2019 to 30\textsuperscript{th} June 2020. A total of 120 patients of both genders with
ages 20 to 60 years were enrolled in this study. Patient’s detailed demographics including age, sex, and body mass index were recorded. Patients with emergency hemorrhoidectomy, diabetic patients, patients with renal failure and non-compliance patients were excluded. All the patients were received elective Milligan-Morgan hemorrhoidectomy under general anesthesia. Patients were divided into two groups 1 and 2, each group contains 60 patients. Group 1 received oral metronidazole postoperatively for 5-days and group 2 received topical metronidazole postoperatively. Postoperative pain was analyzed by VAS on 1st, 3rd and 5th day postoperatively between both groups. Data was analyzed by SPSS 24.

RESULTS

Seventy-six (63.33%) were male patients and 44 (36.67%) were females with mean age 38.74±11.42 years. Mean BMI of patients was 24.52±2.86 kg/m². 67 (55.83%) patients had 4th degree hemorrhoidal disease and 53 (44.16%) patients had 3rd degree disease (Table 1). At first postoperative day, mean pain score in group 1 was 6.89±1.76 and in group 2 it was 6.42±1.38, no significant difference was observed at first postoperative day. At 3rd postoperative day, mean pain score in group 1 was 3.96±1.28 and in group 2 it was 2.74±1.06, a significant difference was observed between two groups with p value 0.024. At 5th postoperative day, mean score in group 1 was 3.08±0.24 and in group 2 it was 2.14±0.26, a significant difference was observed between both groups with p value 0.01 (Table 2).

Table No.1: Details of enrolled patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>38.74±11.42</td>
<td></td>
</tr>
<tr>
<td>Mean BMI (Kg/m)</td>
<td>24.52±2.86</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>76</td>
<td>63.33</td>
</tr>
<tr>
<td>Female</td>
<td>44</td>
<td>36.67</td>
</tr>
<tr>
<td>Hemorrhoid degree</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd degree</td>
<td>53</td>
<td>44.16</td>
</tr>
<tr>
<td>4th degree</td>
<td>67</td>
<td>55.83</td>
</tr>
</tbody>
</table>

Table No.2: Comparison of postoperative pain score between both groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1st postoperative day</td>
<td>6.89±1.76</td>
<td>6.42±1.38</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>At 3rd postoperative day</td>
<td>3.96±1.28</td>
<td>2.74±1.06</td>
<td>0.024</td>
</tr>
<tr>
<td>At 5th postoperative day</td>
<td>3.08±0.24</td>
<td>2.14±0.26</td>
<td>0.01</td>
</tr>
</tbody>
</table>

DISCUSSION

Post-operative pain control is the most critical problem after hemorrhoidectomy. This pain tends to be multifactorial and depends on individual tolerance, mode of anaesthesia and surgical technique. Besides the spasm of an anal sphincter, the two main causes are after surgical discomfort. Majority of patients were male 76 (63.33) as compared to females 44 (36.67). Results of this study showed similarity to many other previous studies in which population of male patients was high 55% to 70% as compared to females and average age of patients was 40 years. In this study, we found 67 (55.83) patients had 4th degree hemorrhoidal disease and 53 (44.16) patients had 3rd degree disease. A study conducted by Hyder et al reported that 59.67% patients had 3rd degree and 40.32% had 4th degree hemorrhoidal disease. We found that, at first postoperative day, mean pain score in group 1 was 6.89±1.76 and in group 2 it was 6.42±1.38, no significant difference was observed at first postoperative day. The study by Neogi et al indicates that metronidazole (oral and topical) significantly reduces postoperative pain but showed no difference in between oral and topical metronidazole. At 3rd postoperative day, mean pain score in group 1 was 3.96±1.28 and in group 2 it was 2.74±1.06, a significant difference was observed between two groups with p value 0.024. These results showed similarity to previous study, conducted by Ala et al. At 5th postoperative day, mean score in group 1 was 3.08±0.24 and in group 2 it was 2.14±0.26, a significant difference was observed between both groups with p value 0.01. These results were similar to Grekova et al. A study conducted by Elton et al reported topical glyceryl trinitrate for pain after haemorrhoidectomy. We found that group 2 topical metronidazole patients had lower postoperative pain as compared to oral metronidazole patients, showed similarity to other previous studies.

CONCLUSION

Topical metronidazole is more effective than oral metronidazole in patients undergoing Milligan Morgan hemorrhoidectomy.

Author’s Contribution:
Concept & Design of Study: Sajid Razzaq
Drafting: Zardad Khan, Mohammad Arif Mahmood
Data Analysis: Mohammad Nadeem Khan, Waheed Iqbal and Nasir Zareen
Revisiting Critically: Sajid Razzaq
Final Approval of version: Sajid Razzaq

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

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Comparison of Functional Outcome of Proximal Femoral Nail (PFN) and Dynamic Hip Screw (DHS) in Intertrochanteric Fractures of Femur under Spinal Anesthesia

Raja Shoaib Anjum¹, Mubashar Iqbal², Shakeel Asif³, Shahid Adalat Chaudhary⁴ and Mohammad Nadeem Khan⁵

ABSTRACT

Objective: To evaluate and compare the post-operative functional outcome of patients of intertrochanteric fractures of femur undergoing either dynamic hip screw (DHS) or proximal femoral nail (PFN) fixation presenting under spinal anesthesia in tertiary care hospital.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of orthopedic, Unit I and Department of Anesthesia Mohi-ud-Din Teaching Hospital Mirpur AJK from March 2016 to April 2017.

Materials and Methods: One hundred and fifty male and female patients fulfilling inclusion criteria presenting in orthopedic department. Their bio-data was recorded followed by an objective assessment of the intertrochanteric fracture of femur. Seventy-five patients underwent fixation with proximal femoral nail and 75 patients underwent fixation with dynamic hip screw by lottery method. Patients were objectively assessed first operatively and then at 4 weekly intervals for up to 24 weeks for functional outcome in terms of Kyle’s criteria for good to excellent results.

Results: Mean age of patients in dynamic hip screw group and proximal femoral nail group was 61.29±11.94 and 59.10±13.61 years respectively. In Group A, 25(33.34%) patients mode of injury was trauma due to road traffic accident and 50(66.64%) patients mode of injury was fall at home whereas in Group B 28(37.34%) patients had trauma due to road traffic accidents and 47(62.66%) were injured due to fall. Functional outcome was assessed by using Kyle’s criteria. At 8th, 12th, 20th and 24th week good to excellent functional outcome was significantly high in Group B as compared to Group A patients. (8th week: 26.67% vs. 44%, 12th Week: 36% vs. 52%, 20th Week: 85.33% vs. 100%, 24th Week: 92% vs. 98.66%) while at 16th week functional outcome was although high in Group-B patients but it was not statistically significant. (16th Week: 81.34% vs. 89.34%).

Conclusion: Proximal femoral nail is far better implant in terms of post-operative functional outcome as compared to dynamic hip screw for treating intertrochanteric femoral fractures. i.e. (Kyle’s Criteria at 24th Week: DHS: 92% vs. PFN: 98.66%).

Key Words: Functional outcome, Dynamic hip screw, Proximal femoral nail, Spinal anesthesia

Citation of article: Anjum RS, Iqbal M, Asif S, Chaudhary SA, Khan MN. Comparison of Functional Outcome of Proximal Femoral Nail (PFN) and Dynamic Hip Screw (DHS) in Intertrochanteric Fractures of Femur under Spinal Anesthesia. Med Forum 2020;31(10):114-118.

INTRODUCTION

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Hip fractures are extreme and disabled injuries that primarily affect the elderly following a decline, with substantial social and quality of life implications. Risk factors include ageing, female sex, white breed, neurological disability, malnutrition, physical activity decreased, osteoporosis and trauma. The risk factors include: In recent decades, the frequency of intertrochanteric femoral fractures has dramatically increased as the life expectancy has increased. Gulberg et al⁴ estimated that by 2025 the overall hip fractures will be 2.6 million and by 2050 an overall of 4.5 million. In 1990 26% of all hip fractures occurred in Asia, compared to 37% in 2025 and 45% in 2050, 40% in Asia.

Intertrochanteric fractures are generally known as Boyd and Griffin Type-I fractures, which range from larger to lesser trochanters along the crossroads. The fractures of
type II are comminuted. Form III is just distal to or at a lesser trochanter and form IV is trochanter and proximal shaft fractures. Type I and Type II are stable, and type III and Type IV fractures are unstable. A failure to repair fracture with re-displacement or the collapse of parts is the primary complication of unstable intertrochanteric fracture. Dynamic hip screws, dynamic compression screws, and proximal femoral nail are the options for surgery. At the beginning of the 1990s intramedullary devices for the fixation of intertrochanteric fractures were created. These instruments provide many biomechanical and biological advantages compared with the traditional dynamic hip vessel. There are many distinct advantages for the intramedullary devices. The implant itself provides a buffer for the proximal fragment to be lateral translation. Its intramedullary position makes the implant more resistant to binding pressure, since it connects the nail and a lag screw. The intramedullary unit offers a shortened distance from a shorter lever arm between the weight bearing axis and the implant. The bending load is passed into the intramedullary nail of an intramedullary unit, which is resisted by its touch to the medullary duct.

**MATERIALS AND METHODS**

This randomized controlled trial was conducted at Department of orthopedic, Unit I and Department of Anesthesia Mohi-ud-Din Teaching Hospital Mirpur AJK from 1st March 2016 to 30th April 2017. A total of 150 patients were included. They were divided in two each groups; each group comprised 75 patients. Group A treated with dynamic hip screw and group B treated with proximal femoral nail. Radiological diagnosis for both male and female intertrochanteric femoral fractures Type I, II, III, and IV (Boyd & Griffin Classification) in accident or fall intertrochanteric femoral fractures, ASA-I (normal healthy patient) and II (mild, clinically non-functional systemic disease) patients. Hip fracture cases with no prior operation. Written consent of patients notified. The exclusivity requirements were 1) patients who were not eligible for surgery; 2) patients who had compound and/or pathological fractures; 3) who were admitted for reoperation; 4) patients who did not have written consents to surgery; 5). After obtaining ethical approval from the Ethics Committee, the study of research population was carried out according to the ethical guidelines after receiving written informed approval. Information obtained from all patients, including history, general and clinical test results. Besides routine pre-anesthetic examinations, initial hip joint x-rays were performed. Two groups of the 150 patients, 75 each were split. In a sitting or lateral decubitus position in the 25 G quince spinal needle of 0.5% hyperbaric bupivacaine 1.5 to 2mL, both patients had been spinal anesthesia with strict Aseptic controls.

Proximal femoral nailing has been used in patients under group A, and DHS has been used in patients under groups B. Dynamic hip screw or PFN implants were randomly chosen by the surgeon. The cases included in our analysis were dealt with as quickly as possible. Using an X-ray AP goniometer on an unaffected side, the neck wafer angle and the lateral side plate length of the lateral plate were calculated to allow the shaft distal to the fractures to buy a minimum of 8 cortices. All patients were treated using early mobilization, manual veal compression and elastic stuffing methods in our research. Day 1 ankle and veal exercises were promoted and the weight of the second postoperative bearing was adjusted depending on the patient's physical condition. Each drain was taken 24 hours. On the third and 6th day of the operation, the injuries were inspected. On the 11th day, stitches were taken off. One monthly interval to the fracture union was followed up and another one year at a 6 months interval. The data was entered and analyzed through SPSS-20.

**RESULTS**

The mean age was 60.20±12.81 years. Whereas mean age of patients in Group-A (dynamic hip screw) and GroupB (proximal femoral nail) was 61.29±11.94 and 59.10±13.61 years respectively (Table 1). In GroupA, there were 53(70.66%) male and 22(29.34%) female patients. Whereas in GroupB, 47(62.66%) were male and 28(37.34%) were female patients. In GroupA, 25(33.34%) patients mode of injury was trauma (due to road traffic accident) and 50(66.64%) patients mode of injury was fall (at home) whereas in Group-B 28(37.34%) patients had trauma and 47(62.66%) were injured die to fall. In both treatment groups large majority of patients presented with fall as their mode of injury (Table 2). Assessment of fracture shows that there were 47 patients who had Type-I (Group-A=21, Group-B=26), 85 patients had Type-II (Group-A=45, Group-B=41), 13 patients had Type-III (Group-A=6, Group-B=7) and only 4 patients had Type-IV fracture (Group-A=3, Group-B=1). According to this criterion, at 2nd week post-operative none of the patients had fair to excellent outcome in both treatment groups (Table 3). In Group-A 20(26.67%) and in Group-B 33(44%) patients had good to excellent outcome according to Kyle’s criteria at 8th postoperative week. In terms of p-value patients in Group-B had good outcome as compared to Group-A patients as greater number of patients had good to excellent outcome at 8th week post operatively i-e p-value=0.026 (Table 4). In Group-A 61(81.34%) and in Group-B 67(89.34%) patients had fair to excellent outcome according to Kyle’s criteria. In Group-B greater number patients had good outcome as compared to Group-A patients at 16th week post operatively. But this difference of good outcome in terms of Kyle’s criteria was not statistical (Table 5). In
Group A, 69 (92%) and in Group B, 74 (98.66%) patients had excellent to good outcome according to Kyle’s criteria. In Group B greater number patients had better to excellent outcome as compared to Group A patients at 24th week post operatively. But this difference of good outcome in terms of Kyle’s criteria was statistically significant i.e. p-value=0.050 (Table 6).

Table No.1: Descriptive statistics for age of patients (n=150)

<table>
<thead>
<tr>
<th>Age</th>
<th>Group A (40-90 years)</th>
<th>Group B (40-80 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>61.29±11.94</td>
<td>59.10±13.61</td>
</tr>
</tbody>
</table>

Table 2: Fracture classification (Boyd and Griffin type) of patients

<table>
<thead>
<tr>
<th>Fracture classification</th>
<th>Group A</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>21</td>
<td>26</td>
</tr>
<tr>
<td>II</td>
<td>45</td>
<td>41</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3: Objective assessment of patients in treatment groups at 2nd week

<table>
<thead>
<tr>
<th>Kyle’s Criteria (Good to Excellent)</th>
<th>Group A</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Yes</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>75</td>
<td>100.0</td>
<td>75</td>
</tr>
</tbody>
</table>

Chi square=22.57 P-value=0.026

Table 4: Objective assessment of patients in treatment groups at 8th week

<table>
<thead>
<tr>
<th>Kyle’s Criteria (Good to Excellent)</th>
<th>Group A</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Yes</td>
<td>20</td>
<td>26.67</td>
</tr>
<tr>
<td>No</td>
<td>55</td>
<td>73.33</td>
</tr>
</tbody>
</table>

Chi square=22.57 P-value=0.026

Table 5: Objective assessment of patients in treatment groups at 16th week

<table>
<thead>
<tr>
<th>Kyle’s Criteria (Good to Excellent)</th>
<th>Group A</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Yes</td>
<td>61</td>
<td>81.34</td>
</tr>
<tr>
<td>No</td>
<td>14</td>
<td>18.66</td>
</tr>
</tbody>
</table>

Chi square= 1.918 P-value = 0.166

Table 6: Objective assessment of patients in treatment groups at 24th week

<table>
<thead>
<tr>
<th>Kyle’s Criteria (Good to Excellent)</th>
<th>Group A</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Yes</td>
<td>69</td>
<td>92.0</td>
</tr>
<tr>
<td>No</td>
<td>6</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Chi-Square= 3.476 P-value= 0.050

DISCUSSION

Intertrochanteric fractures are most commonly seen in the elderly population more so in patients with osteoporotic bones. The elderly people also have the risk of medical conditions like diabetes mellitus and ischemic heart disease. Non-operative treatment for fractures in previous clinical practice showed. Complications such as pneumonia, bedsores, and venous thrombus, and the mortality rate was up to 15%-20%. In recent years, with the development of technology and better pre- operative care, the intertrochanteric fractures are seldomly treated non operatively. There are two methods for surgical fixation, one is extra medullary which is DHS and other is intramedullary which is PFN. 10-13 Reportedly there are cases of delirium 44% adjuvant disorders 22% panic attacks 17% depression 11% and psychosis 6% in post-operative cases. Other risk factors are older age, longer time of surgery, infections, blood transfusion and deranged serum electrolytes. 14 Dynamic hip screw is extra medullary fixation system and was first used in clinical practice in 1967; it was considered a major treatment for intertrochanteric fractures. 15-18 The side plate of the DHS can slide within the screw and cause compression on the fracture end. The discrepancies in DHS are that a large operative incision, exposure is large, and more bleeding. The biggest shortcoming is that DHS lacks effective internal support and poor anti-torsional strength, especially for unstable intertrochanteric fractures; the femur calcar loses holding power and the armor plate must take on more power, which causes many complications, such as femoral head cut out, breaking the plate, or displacement of fractures. Many clinical studies show that DHS should be used for stable fracture patterns and is not the ideal method for treating unstable intertrochanteric fractures. 19-21

Proximal femoral nail is a new generation of intramedullary internal fixation systems. The screw blade replaced two screws to increase pressure and counter rotation action. 26-28 Compared to DHS, PFNA has its advantages; firstly, the bearing axis of PFN is closer to the hip joint, and the arm of force is significantly shorter. Thus, it can directly pass load to the femoral shaft, causing compression and improve the stability of the construct. Secondly, PFN is a minimally invasive system that does not cause opening of fracture hematoma and soft tissue sleeve and thus protects the biological environment around the fracture. Relative to DHS, PFN is an intramedullary device with a helical blade rather than with a screw; this allows a better purchase in the femoral head to limit cut-outs due to various deviation and rotation. In terms of reoperation, present results show that PFN had evidence of superiority to DHS. PFN represented the core of bone operation and minimally invasive surgery, and was
favored for fracture recovery. PFN was designed to minimize the risk of these implant-related complications, and preliminary results suggested that this goal might have been achieved. Additionally, PFNA has other advantages, such as easy operation, short exposure time, and it does not involve reaming, thereby avoiding the occurrence of internal blood loss and maintaining low operative risk. Thirdly, the design of the screw blade locked technique is suitable for elderly patients with osteoporosis. Additionally, implantation of the screw blade is not necessary to ream the marrow in patients, which avoids bone loss. Postoperative follow-up revealed that there were fewer complications in the PFNA group than in the DHS group. Fourthly, the design of the gamma nail is hollow, and a small incision is needed to place a guide pin into the marrow cavity. Moreover, the gamma nail was designed as an eversion angle at 6 degrees, which allows it to insert conveniently at the top of the greater trochanter of the femur. The end-point locked hole is locked dynamically or statically. Finally, the extended sharp end and socket design of the gamma nail allows it to be inserted conveniently during surgery and avoids gathering forces in one position so as to reduce the incidence of broken nails and re-fracture with pointed nails.

Historically, general anesthesia has been the gold standard for major hip surgery; however, total hip arthroplasty is now commonly being performed under spinal anesthesia. Recent data shows that the comparable benefits of neuraxial anesthesia with general anesthesia, such as less blood loss and decreased transfusion requirements, lower rates of thromboembolic events, and reduced rates of surgical site infection in hip fracture patients treated with spinal anesthesia in recovery phase includes better postoperative pain control, less bleeding, early mobilization, and fewer chances of deep vein thrombosis.

CONCLUSION

Both dynamic hip screw and proximal femoral nail remained the implant of choice for the stable intertrochanteric fractures. In the more unstable types of fracture, the PFN has distinct advantages over DHS and should be the preferred implant for fixation since it had better overall functional outcome, less operative time and less blood loss. The mobilization time (i.e. weight bearing time) was significantly less in PFN compared to DHS. PFN should be preferred in cases of severe osteoporosis as it has got inherent stability and being intramedullary there is no question of screw cutout which is a very common complication in osteoporotic fractures treated with DHS. By observing our outcomes we prefer PFN as the best choice implant for Intertrochanteric fractures especially in unstable type as it is superior in terms of stability, blood loss, duration of surgery, post-operative functional recovery and early union.

Author's Contribution:
Concept & Design of Study: Raja Shoaib Anjum
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Revisiting Critically: Raja Shoaib Anjum, Mubashar Iqbal
Final Approval of version: Raja Shoaib Anjum

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

REFERENCES

Effective Use of Transversus Abdominis Plane Block for Postoperative Analgesia after Open Appendectomies in Children

Mubashar Iqbal¹, Zulfiqar Ahmed², Shahid Adalat Chaudhary³, Mohammad Nadeem Khan³ and Zardad Khan⁴

ABSTRACT

Objective: To evaluate the use of transversus abdominis plane block for effective postoperative analgesia in children after open appendectomies.

Study Design: Single blind randomized control trial study.

Place and Duration of Study: This study was conducted at the Department of Anesthesia and Pediatric Surgery Mohi-ud-Din Teaching Hospital Mirpur AJK from May 2018 to June 2019.

Materials and Methods: Forty children of both sexes, aged 6-14 years undergoing open appendectomy by the McBurney method were enrolled in the study. These children were divided into two groups; Group A received ultrasound guided transversus abdominis plane block with bupivacaine0.25%, 0.25 mL/kg (maximum 20 mL) and Group B (control group) were operated by same method without transversus abdominis plane block.

Results: There was significant decrease in pain intensity in TAP block group as compared to control group (at 6hrs &8hrs ±2 vs. 3.9±2.3 % 5.28±0.60 vs. 2.36±0.83 respectively with p value <0.001). Apart from the comfort of the children and parenteral satisfaction, hospital stay was reduced in group receiving TAP block (3 vs. 4 days, P = 0.045).

Conclusion: The transversus abdominis plane block should be used as part of multimodal analgesia in pediatric surgical patients, which is minimally invasive procedure with promising result that may improve the quality of life along with enhanced recovery.

Key Words: Transversus abdominis plane, Postoperative analgesia, Appendectomy

INTRODUCTION

Acute appendicitis (AP) is the world's most prevalent abdominal surgery.¹ Appendectomies with a number that goes up to 8 per cent over the entire lifespan constitute the main share of all surgeries undertaken on children as well as adults. One of the most significant issues in today's medical practice is management in acute pain after the procedure.² Opioids are widely used to control pain in after operative patients; however, their use has multiple side effects and opiate often slows postoperative recovery.³⁴ Although the block length in various studies is variable, analgesia efficacy was recorded up to 36 hours after the TAP block was mounted.⁵ The duration of the block is variable and effective analgesia have been reported up to 36 hours after a single injection.⁶ The monitoring of the patient during procedures includes the monitoring of blood pressure, ECG and pulse oximetry.⁷ Seyed hejazi et al⁸ showed that caudal block by bupivacaine and adrenaline in preterm infants is more effective and safe than spinal anesthesia and reduced the need for analgesics after surgery.⁹ In a study by Carney et al. in 2010 in children with the appendectomy, infiltration of local anesthesia by TAP block up to 48 hours after was effective in comparison to the placebo for pain control surgery.⁹ In this study, we aimed at evaluating the efficacy of TAP block in post-operative pain in patients with appendectomies.

MATERIALS AND METHODS

This single blind randomized control trial was conducted at Department of Anesthesia and Pediatric Surgery.
Surgery Mohi-ud-Din Teaching Hospital Mirpur AJK from 1st May 2018 to 30th June 2019. Perforated appendices, children allergic to local anesthesia and heart defects and physical deterioration were included. Forty patients (20 in each group) were reported in the sample size. 40 children diagnosed and prepared for appendectomy aged 6 to 14 years were randomly divided into two classes with written informed parental consent. The two classes were exposed to general appendectomy anesthesia. Pre-operative intravascular access has been developed. Monitoring of ECG, pulse oxymeter and NIBP in the operation theatre. General anesthesia with Nalfuphine 0.1 mg / kg accompanied by Propofol, Induction and Intubation 01-1.5 mg / kg of suxamethonium was performed. The suitably large cuffed tracheal tube was intubated for all patients. Anesthesia with isoflurane was sustained 1.2–1.4 percent with a combination of oxygen / air or oxygen / N2O along with atracurium 0.3-0.4 mg / kg. All patients received a Grid-Iron appendectomy, were detected by a Tania-coli presence, and removed with a finger or swab by cecum after opening the abdomen. The appendix has historically been regulated with forceps applied to babcock or lane in a manner that encircled and did not harm the appendix. The meso-Annex’s base was clamped, separated and connected into one hemostat. The appendix was crushed near its border with caecum in a hangover, removed and reconstituted only distally into the crushed section. Group A was formed by scrubbing with pydine solution after inducing a block anesthesia field. After preparing the sample, the transducer was located in the supine position between the costal border and the iliac crest. Three distinct layers have been established, external oblique, internal oblique and transversal abdominal and peritoneal. The 23 G spinal needle with in-line approach leads between internal oblique and transversal abdominal muscle in potential space. The solution distribution has been described as an elliptical two-layer separation. The Petit Triangle injected arbitrarily with Bupivacaine 0.25 per cent, 0.25 mL/kg (maximum 20 mL). Voltarol ® Suppository 12.5 mg or 25 mg is administered as part of multimodal therapy after surgery in all patients depending on age and weight. In the recovery and in the paediatric ward at 0th, 2nd, 8th, 16th and 24th hours, after appendectomy using the McBurney approach the grade of postoperative (Visual Analog Scale = VAS) pain score has been registered. The pain levels were 1 to 10, 1 showing no pain and 10 meaning maximum pain. If the pain level was 4 or higher, children had an analgesic treatment. The acetaminophen Rescue Analgesia was 10 mg/kg intravenous. Statistically important was called a P value < 0.05.

RESULTS

Patients did not statistically difference in both groups in terms of age, sex, baseline pulse and body mass. The operative time was comparable in both groups. The procedure time was about 10 minutes which corresponds to the average time difference between both groups. Length of hospitalization in TAP block group was shorter comparing to the other group [3 vs. 4 days, P = 0.045] (Table 1).

There was significant reduction in pain intensity in TAP block group as compared to control group at 2hrs, 6hrs &8hrs Mean Visual Analogue Scale (4±1.5 vs. 1.82±0.8, 56±2 vs. 3.9±2.3 and 5.28±0.60 vs. 2.36±0.83 respectively) with p value <0.001 (Table 2).

| Table No.1: Patient characteristics, surgical and anaesthesiological factors |
|------------------------|------------------------|------------------------|------------------------|
| Variable               | Control group          | TAP group              | P value                |
| Age (years)            | 10 (7–13)              | 8.8 (6.5–12.5)         | 0.34                   |
| Sex (male/ female)     | 13/7                   | 12/8                   | 0.13                   |
| Body mass (kg)         | 33 (26–50)             | 28.5 (20.5–42)         | 0.63                   |
| Hospitalization time (days) | 4 (3–6)            | 3 (3–5)                | 0.045                  |
| Baseline pulse         | 91.29±9.65             | 90.10±9.01             | 0.37                   |

| Table No.2: Pain severity based on VAS scores during the 24 hours after surgery |
|------------------------|------------------------|------------------------|------------------------|
| Time of check          | Control group          | TAP group              | P value                |
| 2 hours after surgery  | 4±1.51.8               | 2±0.85                 | <0.001                 |
| 4 hours after surgery  | 4.7±2.2                | 3.3±2.1                | 0.01                   |
| 6 hours after surgery  | 6±2                    | 3.9±2.3                | <0.001                 |
| 8 hours after surgery  | 5.28±0.60              | 2.36±0.83              | <0.001                 |
| 12 hours after surgery | 4.9±2                  | 3.3±3                  | 0.01                   |
| 16 hours after surgery | 3.25±1.71              | 2.65±1.42              | 0.236                  |
| 24 hours after surgery | 2.60±1.33              | 2.10±1.03              | 0.296                  |

DISCUSSION

Acute appendicitis remains the most common surgery with a 7 percent incidence over the span of one life. A timely diagnosis and an early operation are important for successful treatment of acute appendicitis. Acute appendicitis is also not readily detected clinical and negative laparotomy rates between 20% and 25% are not exceptional.
An operating specialist who treats appendicitis on a clinical basis is at risk of a rise in the incidence of negative appendicitis or a rise in drilling and sequelae. A medical problem is acute abdominal pain in infants. Although several cases of acute pain in the abdomen are mild, some patients need prompt diagnosis and care to avoid disease.

Transversus abdominis plane block is a regional block used during abdominal surgery for postoperative pain relief. There is a peripheral nerve of spinal roots T6-L1 in the anterolateral abdominal wall. The object of a TAP block is to examine those sensory nerves by adding between the inner Oblique and the transversal abdominal muscles 20-40 ml of the local anesthetics to the neurological plane. Rafi identified the TAP block for the first time in 2001.

The first post-caesarean block experiments in TAP were published in 2008, thanks to a variety of anatomical and clinical tests, by McDonnell et al. New horizons have emerged for successful postoperative analgesia with the advent of the transversal abdominal block. The TAP block was intended to decrease pain by interrupting the conduction from the wound to the abdominal wall of somatic adverse events. In the possible space between the oblique and transverse muscles of the abdomen in local anesthetic drugs, T7–12 intercostal T7-12, ilioinguinal, and iliohypogastric nerve, as well as lateral branches of the L1-3 dorsal rami, are effectively blocked. Abdominal blocks of the abdominal wall.

Our analysis decreased pain rates in the postoperative period at 2 hours, 6 hours and 8 o'clock. When the pain score was over four on a VAS-level rescues analgesic, pain was compared between the group TAP and the control group without intervention. In the TAP block with bupivacaine (0.25 percent 0.25 mL/kg maximum 20 ml) with p-value < 0.001 the favourable results are clearly seen.

The literature review indicates that TAP decreases postoperative analgesia opioid requirement, measured by Tan et al. in a two blind, controlled study. "40 women had a C-section. None of them had general anesthesia. Half of the TAP was given, and no local analgesia was given to other half. In the TAP community, the intake of morphine and patient satisfaction are lower. However, there has been no improvement in visible discomfort, vomiting nausea or antiemetic treatment.

Transversus abdominis plane blocks can become technically simpler and safer by expanding the use of ultrasound technology. As an alternative medical aid to analgesia during abdominal procedures, there has been an growing interest in the TAP blocks. Different abdomen-chirurgical procedures such as caesarean sectors, hysterectomy, cholecystectomy, colectomy, appendectomy and hernia have received the evidence in the past decade to support the efficacy of TAP blocks.

In our research, we used a quick and safe lateral TAP approach. We injected 0.25% of Bupivacaine between the cross-sectional abdominal plane with ultrasound guidance. That effectively provided lower abdominal analgesia (T10-L1) between the midline and the mid-clavicular line, corresponding to the region of interest in the pain following appendectomy.

CONCLUSION

The use of TAP block as part of multimodal analgesia in pediatric surgical patients, particularly in developing countries with less availability of modern and short acting narcotic agents and fewer up-to-date post-anesthesia care units. TAP block is minimally invasive procedure with promising result that may improve the quality of life along with enhanced recovery.

Author's Contribution:

Concept & Design of Study: Mubashar Iqbal
Drafting: Zulfiqar Ahmed, Shahid Adalat Chaubdary
Data Analysis: Mohammad Nadeem Khan, Zardad Khan
Revisiting Critically: Mubashar Iqbal, Zulfiqar Ahmed
Final Approval of version: Mubashar Iqbal

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

REFERENCES


Comparison of C-Reactive Protein, Neutrophil Count and Computed Tomography Severity Index in Predicting Outcome in Acute Pancreatitis

Mumtaz Ahmad Khan¹, Namrah Mahmood¹ and Saïra Mahmood²

ABSTRACT

Objective: To compare the severity and outcome of acute pancreatitis by comparing the CLI and computed tomography, the serum C-reactive protein and neutrophil levels.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Department of General Surgery, Pakistan Institute of Medical Sciences Islamabad from June 2016 to June 2020.

Materials and Methods: A total of 354 patients were enrolled. All patients > 18 years, with confirmed diagnosis of AP were eligible to take part in the study. Patients with symptoms for more than 3 months at the time of data collection were excluded from the study. Complete clinical history and examination were performed on all patients. An improved abdominal computed tomography test was carried out intravenously for pancreas status assessment and computed tomography severity index (CTSI) measurement in these patients. Both patients were also tested on a neurological basis in addition to CTSI, neutrophil-lymphocyte ratio (NLR) and C-reactive protein (CRP). The length of hospital stay, ICU admission and hospital mortality have been measured for the seriousness of acute pancreatitis.

Results: The mean age of 54.5±12.4 years. The most frequent etiology of acute pancreatitis was gallstone, 195 (55.1%) followed by infection in 79 (22.32%) and hyperlipidemia in 50 (14.12%) of the patients. The majority of the patients (84;53.8%) with a CTSI score between 7-10 were hospitalized for more than two weeks. Hospital mortality within 72 hours was most frequent in patients who scored higher on CTSI. Out of the 25 patients who expired, 8 (32%) had moderate acute pancreatitis while 15 (60%) had severe acute pancreatitis. Neutrophil to leukocyte ratio and C-reactive protein were both more frequently elevated in patients who scored more frequently elevated than in cases. Half of the patients scored highly on CTSI. Both patients were also tested on a neurological basis in addition to CTSI, neutrophil-lymphocyte ratio (NLR) and C-reactive protein (CRP). The length of hospital stay, ICU admission and hospital mortality have been measured for the seriousness of acute pancreatitis.

Conclusion: Computed tomography severity index and C-reactive protein were better predictors of patient severity and outcome while neutrophil-lymphocyte ratio did not seem to differ with the severity of the disease.

Key Words: C-reactive protein, computed tomography severity index, neutrophil, neutrophil-lymphocyte ratio.

Citation of article: Khan MA, Mahmood N, Mahmood S. Comparison of C-Reactive Protein, Neutrophil Count and Computed Tomography Severity Index in Predicting Outcome in Acute Pancreatitis. Med Forum 2020;31(10):123-126.

INTRODUCTION

Acute pancreatitis is usually characterized as self-limiting disease with very minute systemic effects and is usually non-lethal. Nevertheless, in a small percentage of patients, complications develop including progression into a systemic inflammatory response syndrome (SIRS) and multiple organ failure. The mortality rate of acute pancreatitis can be up to fifty percent as per some studies.

In case of severe presentation of the disease, if the patient is recognized at the initial stage then the prognosis and mortality rate could be improved by timely intervention and close monitoring. The mortality and severity of AP is linked with old age, obesity, consumption of tobacco and alcohol, serum, urea and creatinine levels and inflammatory response markers like cytokines, chemokines and others. For detecting and predicting acute pancreatitis severity and prognosis, measures of multifactorial clinical and laboratory measurement scales (such as Ranson score, BISAP (Security Index) score, acute physiology, and Chronic Health Assessment (APACHE II) are used for the existence of systemic inflammatory response syndrome (SIRS) Score, harmless acute pancreatitis score (HAPS).

Currently, the AP updated computed tomographical severity (MCTSI) prognostic radiological scoring system, computed tomography extra-pankreatic inflammation (EPIC) and the renal rhythmic sign are in use. APACHE II (score 8) is considered to be the gold standard for all the above listed techniques. It is

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Printed: October, 2020
however, a highly complex and time-consuming technique and therefore in any scenario not a viable option.

Procalcitonin (> 1.8 ng / mL) and C-reactive protein (CRP) – 150 mg / l) provide serum biomarker of some pregnancy-managed AP factors. It was proposed that these two variables be used to predict the seriousness of the disease. After 48 hours of admission, serum procalcitonin and CRP are evaluated. Some inflammators, such as interleukins (IL) 6, 8, and 10, are also used as an early indicator of acute pancreatitis for assessing the extent of organ dysfunction in AP patients.

The recent targets are the platelet-to-lymphocyte link and the peripheral blood count of CD4+ T cells for the assessment and forecasting of inflammation in AP patients’ neutrophil-lymphocyte ratio (NLR). The precise determination of the degree of inflammatory reactions in an AP patient is an excellent guide for predicting or not intensive treatment complications or phases of the disease. However, there is insufficient and contentious comparative evidence on the medical and radiological scoring systems for the collection of results for AP. In order to predict the severity and outcome of acute pancreatitis, the current trial aimed at comparing the clinical-computer gravity index (CTSI), serum CRP level, and neutrophil levels.

MATERIALS AND METHODS

A prospective observational was conducted at the general surgery department, Pakistan Institute of Medical Sciences, Islamabad between June 2016 to June 2020 for a duration of five years. All patients >18 years of age with verified AP diagnosis were included. At the time of data collection, patients with symptoms longer than 3 months were removed. Both participants were given with informed written or verbal consent. The criteria were used to diagnose AP abdominal pain trait, higher serum or lipase amylas than a typical level of three and AP's standard studies on contrast-enhanced computed tomography (CT), MRI, or ultrasonography (US). A total of 354 patients were included with confirmed AP diagnosis. Both patients have had full clinical records and tests. There have been recorded etiologies like gallstones, alcohol, medications etc. Everyone was watched and monitored until they were released or died. Blood samples were obtained within 1 hour of admission for haematological and biochemical results. NLR was described as the absolute neutrophil count quotient to the absolute lymphocyte count. An improved abdominal CT test was carried out intravenously for pancreas status assessment and CTSI measurement in these patients. The spectrum of pancreatic inflammation, necrotizing and the presence or lack of fluid collections were determined for the CTSI. On entry, the score for Ranson and BISAP were determined. Both patients were also tested on a neurological basis in addition to CTSI, lymphocyte neutrophil ratio (NLR) and C-reactive protein (CRP).

The length of hospital stay, ICU admission and hospital mortality measured the seriousness of acute pancreatitis. The data was analyzed through SPSS-26.

RESULTS

A total of 354 patients were presented with acute pancreatitis during the study period. The mean age plus standard deviation was 54.5 (12.4) years. Most frequent etiologies of acute pancreatitis in our setting were gallstone, 195 (55.1%) followed by infection in 79 (22.32%) and hyperlipidemia in approximately one-fourth of the patients. Mean Body mass index (BMI) of patients was 22.8±5.4 kg/m². Upon assessing the comorbidities, it was found that one-half the population had hypertension, followed by diabetes mellitus type 2 and chronic liver disease in 12.7% patients (Table 1).

<table>
<thead>
<tr>
<th>Table No.1: Patients characteristics and clinical profile (n=354)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable</strong></td>
</tr>
<tr>
<td>Mean age (years)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Etiologies of AP</strong></td>
</tr>
<tr>
<td>Gallbladder</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Obscured causes</td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Chronic liver disease</td>
</tr>
<tr>
<td><strong>Scoring systems</strong></td>
</tr>
<tr>
<td>Ranson</td>
</tr>
<tr>
<td>CT Severity Index</td>
</tr>
<tr>
<td>Bedside index of severity in acute pancreatitis score</td>
</tr>
<tr>
<td>White blood cells in mm³</td>
</tr>
<tr>
<td>Neutrophil to lymphocyte ratio</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
</tr>
<tr>
<td>Mean Hospital stay (days)</td>
</tr>
<tr>
<td>ICU admission</td>
</tr>
<tr>
<td>Hospital Mortality</td>
</tr>
</tbody>
</table>

Two hundred and ninety-eight (84.18%) patients were treated conservatively, 57 (16.10%) patients underwent surgical intervention in the form of laparotomy, washout and drain placement. One hundred and forty-nine (42.09%) patients with severe acute pancreatitis were admitted to ICU for intensive support. 25/354 (7%) patients expired within 48 to 72 hours of presenting to the emergency department secondary to sepsis and co-morbidities. The mean hospital stay
(standard deviation) was found to be 10.5±3.6 days. 156 (44.07%) patients were hospitalized for more than two weeks while the remaining 198 (55.93%) had a hospital stay of <2 weeks. The majority of the patients 84 (53.8%) with a CTSI score between 7-10 (severe) were hospitalized for more than two weeks. Hospital mortality within 72 hours was most frequent in patients who scored higher on CTSI. Out of the 25 patients who expired, 8 (32%) had moderate acute pancreatitis while 15 (60%) had severe acute pancreatitis. Neutrophil to leukocyte ratio and C-reactive protein were both more frequently elevated in patients with severe acute pancreatitis as assessed by hospital stay, ICU admission, and hospital mortality (Table 2).

Table 2: Association of CTSI, CRP, and NLR with the severity of acute pancreatitis

<table>
<thead>
<tr>
<th>Modalities</th>
<th>Hospital stay of &gt; 2 weeks (n = 156)</th>
<th>ICU admission (n = 149)</th>
<th>Mortality (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTSI score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>27 (17.3%)</td>
<td>24 (16.1%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>45 (28.8%)</td>
<td>40 (26.8%)</td>
<td>8 (32%)</td>
</tr>
<tr>
<td>Severe</td>
<td>84 (53.8%)</td>
<td>85 (57%)</td>
<td>15 (60%)</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate elevation (1.0 to 10.0)</td>
<td>22 (14.1%)</td>
<td>19 (12.7%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Marked elevation (10.0-50.0)</td>
<td>42 (26.9%)</td>
<td>51 (34.2%)</td>
<td>7 (28%)</td>
</tr>
<tr>
<td>Severe elevation (&gt;50.0)</td>
<td>91 (58.3%)</td>
<td>79 (53%)</td>
<td>17 (68%)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

This study was conducted to compare clinical values of CTSI (CT severity Index), neutrophil count and serum CRP to predict the outcome of acute pancreatitis. In our results, we found out that the majority of the patients were treated conservatively and the minority had undergone surgical procedures. 42.09% of the patients who were suffering from severe acute pancreatitis were transferred to the intensive care unit however, only 7% of the patients passed away in 48 to 72 hours. Majority of patients who had a severe CTSI score were hospitalized for more than 2 weeks and had a higher hospital mortality rate.

A study was conducted in 2015 in Rawalpindi, Pakistan, during the duration of nine months to find out the prevalence of patients having necrotising pancreatitis while also suffering from acute pancreatitis and serum CRP above 150mg/l. It was concluded that CRP is the gold standard marker to find out the gravity of pancreatitis. Patients who had a serum CRP level of less than 150 mg/l were less likely to progress into necrosis however those with serum CRP level of more than 150 mg/l were more likely to progress to acute necrotising pancreatitis. CRP was also concluded to be easily available and posed no economic burden.

Our results differed from a study done in 2018 by comparing different scoring systems such as CTSI, Ranson’s and BISAP to find out the response of patients with pancreatitis. The study was done on 106 who were diagnosed with acute pancreatitis. The BISAP score was found to be an effective tool to foresee the prognosis of pancreatitis and also to find the patients who will be needed ICUs as a complication of acute pancreatitis. These numbers of patients could actually benefit from early life saving procedures such as resuscitation when needed.

Another study was conducted in 2005 in Karachi to find out if CT scan had an effect in management and prognosis of patients with pancreatitis. In this study, it was found out that among the 40 patients with pancreatitis, there was no relationship between necrosis level and moderate pancreatitis. However, CTSI was found to have a correlation with complications and the level of damage in the pancreas. CT was also found to be useful with ultrasound for a few procedures involving drainage.

Another study was conducted in Iran in 2019 to examine if the ratio of neutrophils, C-reactive protein (CRP) and procalcitonin (PCT) had an effect on management and diagnosis of severe acute pancreatitis. This study was conducted on patients with severe acute pancreatitis and mild acute pancreatitis. It was found out that procalcitonin, C-reactive protein and ratio of neutrophils were greater in patients with severe acute pancreatitis and not in mild acute pancreatitis. This proved that greater levels of procalcitonin, C-reactive protein and neutrophil ratio lead to greater chances of severe acute pneumonia.

In 2018, a study was done comparing the ratio between neutrophil and lymphocyte (NLR) and platelet and lymphocyte (PLR) and their effect on acute pancreatitis. It was concluded that NLR and PLR work well with other systems of finding out the severity of acute pancreatitis but only for those with gallstone. In diseases such as alcoholic acute pancreatitis, PLR and NLR did not work well with other systems that were being used to find out the severity of acute pancreatitis. Although in previous studies, it was found out that PLR was a more efficient system than NLR to find out survival rate in patients this study concluded that both were equally efficient.

In 2020, a study was done differentiating NLR, CRP, clinical values and scoring methods involving radiology to find out the death and severity level of patients suffering from acute pancreatitis. Some others have focused on NLR as being the primary system to find out the severity and prognosis of certain diseases. A high NLR has been known to be associated with multi organ failure and SIRS but in this study the BISAP score...
system has also been proved to be effective in predicting the prognosis of patients with acute pancreatitis. However, there proved to be some limitations in our study. A greater sample size could have ensured different probabilities in our data. An interview based questionnaire could have allowed more insight into the patients. The correlation between CRP, neutrophil count and CTSI was not fully studied, more information is required in this area.

CONCLUSION

Computed tomography severity index and C-reactive protein were better predictors of patient severity and outcome while neutrophil-lymphocyte ratio did not seem to differ with the severity of the disease.

Author’s Contribution:

Concept & Design of Study: Mumtaz Ahmad Khan
Drafting: Namrah Mahmood
Data Analysis: Saira Mahmood
Revisiting Critically: Mumtaz Ahmad Khan, Namrah Mahmood
Final Approval of version: Mumtaz Ahmad Khan

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

REFERENCES

Frequency of Early Complication in Mesh Repair of Paraumbilical Hernia

Naheed Akhtar¹, Ahmad Mehmood², Raja Ijaz¹, Umer Ijaz¹, Farzana Sabir¹ and Ziyad Afzal Kiani¹

ABSTRACT

Objective: The objective of this study was to determine the frequency of early complications in mesh repair of paraumbilical hernia.

Study Design: Descriptive case series study.

Place and Duration of Study: This study was conducted at the Combined Military Hospital, Muzaffarabad from January 2019 to December 2019.

Materials and Methods: This study involved 170 patients of both genders aged between 20-50 years undergoing mesh repair of paraumbilical hernia. These patients were followed in the post-operative period to look for early complications; wound infection, seroma and hematoma formation. A written informed consent was taken from every patient. Statistical analysis has been done by SPSS 20.0. Mean±SD has been calculated for age and BMI while frequency and percentage has been calculated for gender, wound infection, seroma and hematoma formation. Data has been stratified for age, gender and BMI to address effect modifiers. Post-stratification chi-square test has been applied taking p-value ≤0.05 as statistically significant.

Results: The age of the patients ranged from 20 years to 50 years with a mean of 42.1±6.9 years. Majority (n=147, 86.5%) of the patients were aged between 36-50 years. There were 34 (20.0%) male and 136 (80.0%) female patients with a male to female ratio of 1:4. BMI of these patients ranged from 24.0 Kg/m² to 34.8 Kg/m² with a mean of 30.3±2.8 Kg/m². Among the various complications, wound infection was the most frequent and was observed in 15 (8.8%) patients followed by seroma (n=12, 7.1%) and hematoma (n=6, 3.5%) formation. When stratified, there was no significant difference in the frequency of wound infection, seroma and hematoma formation across various subgroups based on patient’s age, gender and BMI.

Conclusion: Wound infection and seroma formation were observed in a substantial proportion of patients undergoing mesh repair of paraumbilical hernia which warrant meticulous surgical dissection and appropriate antibiotic prophylaxis in such patients to decrease the likelihood of these complications as well as watchful follow-up to timely identify and treat these complications when they occur.

Key Words: Paraumbilical Hernia, Mesh Repair, Complications


INTRODUCTION

Hernia is a presentation of a viscous or part of a viscous through the walls of the cavity in which it normally resides. Umbilical hernia is relatively common in adults, and account for 3%-8.5% of abdominal hernias, third in incidence after inguinal (70%-75%) and femoral (5%-17%) hernias. Conditions that lead to increased intra-abdominal pressure such as obesity, Ascites, multiple pregnancies, and large abdominal tumors, contribute to the development of umbilical hernias. Complications such as irreducibility, obstruction, strangulation, skin ulceration, and visual rupture are more common in paraumbilical hernias than in other abdominal hernias. Potential complications of umbilical hernia repair include seroma, hematoma, wound infection, bowel injury, paralytic ileus, and hernia recurrence. Out of these complications infection needs to be cared for most. Therefore, every measure should be taken to reduce the incidence of infection after mesh repair.

A nationwide prospective study of umbilical and epigastric hernias demonstrated that complications requiring readmission included hematoma (46% of cases), seroma (19%), and pain readmission rate was (5%) and infection rate was (19%). In another randomized control trial complication like wound infection was in cases (11.11%) in GROUP A and in 2 cases (6.2%) in GROUP B, which were treated conservatively. Hematoma and seroma was higher in GROUP A (5.5%-2.7%) and lower in GROUP B (0.00%-3.1%).
My rationale is to highlight main early complications, as less no of studies are available in our area; it will help us in early diagnosis and prompt treatment. With such approach we can prevent the wound infection which causes recurrence and bad scarring of the wound. Based on prevalence of complications, one can adopt measures which can reduce these morbidities among our population.

**MATERIALS AND METHODS**

It’s a descriptive case series. This research was conducted at Department of Surgery, Combined Military Hospital Muzaffarabad. Total 170 patients were selected by Non-Probability, Consecutive Sampling. Patients of age 20 to 50 years were included in study (because patients having age >50 are associated with different comorbidities). Patients admitted through emergency were excluded as they usually present with obstructed or strangulated hernia. Patients with co-morbid condition like diabetes were also excluded. Patients were selected through outpatient department (OPD) after taking informed written consent. Personal bio data was taken on predesigned proforma. Hernia was examined for any sign of inflammation or infection. After admission patient were tested for routine investigations. All surgery was done by consultant surgeons having enough experience in open mesh, repair of paraumbilical hernia. In this procedure hernia sac was removed. Mesh was placed beneath the hernia site. The mesh was attached using sutures sewn into the stronger tissue surrounding the hernia. Polypropylene mesh and sutures were used. The mesh was extended 3 to 4 cm beyond the edges of the hernia. The umbilicus was fixed back to the muscle. All patients after recovery were kept under close observation for three days for screening of complications like seroma and hematoma, and follow up was done on 7th post-operative day after discharge for surgical wound infection. Seroma and hematoma develops within 3 days and wound infection occurs at 5th to 7th post-operative day, according to operational definitions. Statistical analysis has been done by SPSS 20.0. Mean±SD has been calculated for age and BMI while frequency and percentage has been calculated for gender, wound infection, seroma and hematoma formation. Data has been stratified for age, gender and BMI to address effect modifiers. Post-stratification chi-square test has been applied taking p-value ≤0.05 as statistically significant.

**RESULTS**

The age of the patients ranged from 20 years to 50 years with a mean of 42.1±6.9 years. Majority (n=147, 86.5%) of the patients were aged between 36-50 years. There were 34 (20.0%) male and 136 (80.0%) female patients with a male to female ratio of 1:4. BMI of these patients ranged from 24.0 Kg/m² to 34.8 Kg/m² with a mean of 30.3±2.8 Kg/m² as shown in Table 8.1. Among the various complications, wound infection was the most frequent and was observed in 15 (8.8%) patients followed by seroma (n=12, 7.1%) and hematoma (n=6, 3.5%) formation as shown in Table 8.2.

When stratified, there was no significant difference in the frequency of wound infection, seroma and hematoma formation across various subgroups based on patient’s age, gender and BMI. Of the total 170 patients, 23 were in age group 20-25yrs, among these only 2% got wound infection and 137 patients were in age group 36-50yrs, among these 137 patients, 13(8.8%) got infection. Which shows no significant effect of age on wound infection?6 patients having BMI between 25-30 kg/m², and out of these 6 pt no one got wound infection, 71 patients having BMI between 25-30 kg/m² and out of these 6(8.5%) got infection, 93 patients had BMI between 30-35 kg/m² out of which 9(9.7%) got wound infection.

Regarding seroma, 1(4.3%) pt in age group 20-35yrs got post-operative seroma and 11(7.5%) pts in age group 36-50yrs got seroma. 2(5.9%) males and 10(7.9%) females got seroma. On basis of BMI, no pt of BMI between 20-25 kg/m² got seroma, whereas 3(4.2%) and 9(9.7%) of patient with BMI 25-30 kg/m² and 30-35 kg/m² respectively got seroma.

Regarding hematoma, 1(4.3%) pt in age group 20-35yrs got post-operative seroma and 5(3.4%) pts in age group 36-50yrs got seroma. 1(2.9%) males and 5(3.7%) females got hematoma. On basis of BMI, no pt of BMI between 20-25 kg/m² got hematoma, whereas 2(2.9%) and 4(4.3%) of patient with BMI 25-30 kg/m² and 30-35 kg/m² respectively got hematoma.

**Table No.1: Baseline Characteristics of Study Participants**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Participants n=170</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.1±6.9</td>
</tr>
<tr>
<td>• 20-35 years</td>
<td>23 (13.5%)</td>
</tr>
<tr>
<td>• 36-50 years</td>
<td>147 (86.5%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>34 (20.0%)</td>
</tr>
<tr>
<td>• Female</td>
<td>136 (80.0%)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
</tr>
<tr>
<td>• 20-25 Kg/m²</td>
<td>6 (3.5%)</td>
</tr>
<tr>
<td>• 25-30 Kg/m²</td>
<td>71 (41.8%)</td>
</tr>
<tr>
<td>• 30-35 Kg/m²</td>
<td>93 (54.7%)</td>
</tr>
</tbody>
</table>

**Table No.2: Frequency of Various Complications**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Frequency (n)</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Infection</td>
<td>15</td>
<td>8.8</td>
</tr>
<tr>
<td>Seroma</td>
<td>12</td>
<td>7.1</td>
</tr>
<tr>
<td>Hematoma</td>
<td>6</td>
<td>3.5</td>
</tr>
</tbody>
</table>
DISCUSSION

Hernia formation is a multifactorial process involving endogenous factors including age, gender, anatomic variations, inheritance and exogenous factors such as smoking, comorbidity, and surgical factors. Paraumbilical hernia is relatively common in adults, and account for 3%-8.5% of abdominal hernias \(^1\). Paraumbilical hernia repair is often culmination of a complex decision-making process by the surgeon. Defect size, location, patient comorbidities, the presence of contamination, acuity of the patient’s presentation, necessity for an ostomy, and history of prior repairs with or without a prosthetic all weigh into the ultimate repair approach. Disappointingly, high recurrence rates of up to 54-5% have been reported with suture repair \(^3\). The use of mesh has proven to be beneficial in hernia repair, and mesh repair has therefore become the gold standard repair associated with low recurrence rates of up to 1% of large umbilical hernias \(^3\). However, there are studies which claim increased risk of complications particularly infection, hematoma and seroma formation with the use of mesh \(^7\). The existing evidence however contained conflicting results while there was limited local such published material which necessitated the present study as knowing the magnitude of these complications would enable better intra-operative and post-operative management thus improving the patient outcome.

The objective of this study was to determine the frequency of early complications in mesh repair of paraumbilical hernia. In the present study, the mean age of the patients was 42.1±6.9 years. A similar mean age of 41.2±9.2 years has been reported by Kiani et al. (2014) among patients presenting with paraumbilical hernia at Holy Family hospital, Rawalpindi \(^11\), Malik et al. (2009) reported similar mean age of 41.0±19.1 years among such patients presenting at Liaquat University of Medical and Health Sciences, Jamshoro \(^5\) while Aziz et al. reported it to be 40.0±9.6 years at Nishtar Hospital Multan \(^12\). A similar mean age of 41±9.1 years has been reported by Sarhan et al. (2016) among Egyptian such patients \(^13\).

We observed that there were 34 (20.0%) male and 136 (80.0%) female patients with a male to female ratio of 1:4. A similar female predominance among such patients has been reported by Aziz et al. at Nishtar Hospital Multan \(^12\) and Tunio et al. at Gambat Institute of Medical Sciences, Gambat \(^10\) with male to female ratio of 1:4. Kiani et al. reported similar female predominance with male to female ratio of 1:3.4 at Holy Family Hospital, Rawalpindi \(^11\).

In the present study, the BMI of patients ranged from 24.0 Kg/m\(^2\) to 34.8 Kg/m\(^2\) with a mean of 30.3±2.8 Kg/m\(^2\). Our observation is in line with that of Berger et al. (2014) and Wormer et al. (2013) who reported similar mean BMI of 30.5±0.3 Kg/m\(^2\) and 30.2±5.5 Kg/m\(^2\) respectively in American such patients \(^15,16\). Kaufmann et al. (2018) reported it to be 28±4 Kg/m\(^2\) in Netherlands \(^17\).

Among the various complications, wound infection was the most frequent and was observed in 15 (8.8%) patients. A comparable frequency of wound infection has been reported by Khan et al. who reported that 12.5% of patients undergoing mesh repair of paraumbilical hernia acquired wound infection \(^18\). Habib et al. in 2017 (7.5%) and Abdel-Baki et al. in 2007 (9.5%) also reported comparable frequency of wound infection following mesh repair of paraumbilical hernia \(^19,20\).

In the present study, seroma formation was observed in 7.1% patients. Afzal et al. in another local study, observed similar frequency of seroma formation after mesh repair of paraumbilical hernia and reported that 6.3% of patients developed seroma in the early post-operative period. Sarhan et al. in 2016 (6.0%) and Arroyo et al. in 2001 (6.0%) reported similar frequency of seroma formation after mesh repair of paraumbilical hernia \(^11,21\).

We observed that 3.5% of patients undergoing mesh repair of paraumbilical hernia developed hematoma in the early post-operative period. Our observation is in line with that of Aziz et al. who reported similar frequency of 4.0% for post-operative hematoma formation among such patients at Nishtar Hospital, Multan \(^12\). Tunio et al. reported similar frequency of 4.3% at Gambat Institute of Medical Sciences, Gambat \(^10\) while Malik et al. reported it to be 3.0% at Liaquat University of Medical and Health Sciences, Jamshoro \(^5\). Habib et al. reported similar frequency of 3.8% in Egyptian such patients \(^19\).

The present study has identified wound infection and seroma formation as potential frequent complications of mesh repair of paraumbilical hernia. It is therefore advisable that meticulous dissection should be adopted during the surgery and dead space should be appropriately obliterated to decrease the likelihood of seroma formation. The patient should receive appropriate antibiotic prophylaxis to decrease the risk of wound infection. The surgeon should also be vigilant in the post-operative period to timely identify these complications once they occur as timely identification and management can improve the patient outcome.

A very strong limitation to the present study was that we didn’t consider the various methods of mesh repair like onlay, inlay or sublay techniques to see if there was any difference in the frequency of these complications among various placements of abdominal mesh. This could have further helped in the appropriate management planning of these patients. Such a study is highly recommended in future research.
CONCLUSION

Wound infection and seroma formation were observed in a substantial proportion of patients undergoing mesh repair of paraumbilical hernia which warrant meticulous surgical dissection and appropriate antibiotic prophylaxis in such patients to decrease the likelihood of these complications as well as watchful follow-up to timely identify and treat these complications when they occur.

Author’s Contribution:
Concept & Design of Study: Naheed Akhtar
Drafting: Ahmad Mehmood, Raja Ijaz
Data Analysis: Umer Ijaz, Farzana Sabir, Ziyad Afzal Kiani
Revisiting Critically: Naheed Akhtar, Ahmad Mehmood
Final Approval of version: Naheed Akhtar

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

REFERENCES

Comparative Study Between Insertions of Postoperative Drain Versus No Drain After Total Thyroidectomy

Raja Ijaz¹, Naheed Akhtar¹, Sehrish Khizar², Naheem Butt³, Umer Ijaz¹ and Nabeel Imran¹

ABSTRACT

Objective: To compare total thyroidectomy with insertion of post-operative drain versus no drain in terms of level of post-operative pain, duration of hospital stays and post-operative hematoma, seroma and wound infection.

Study Design: Randomized controlled clinical trial study.

Place and Duration of Study: This study was conducted at the Department of General Surgery, SKBZ/CMH, Muzaffarabad for 02 years from June 2018 to June 2020.

Materials and Methods: After taking permission from hospital ethical committee, a total of 62 patients were included, who were undergoing total thyroidectomy for benign multinodular goiter admitted in Department of Surgery, SKBZ/CMH, Muzaffarabad.

Results: Mean age of patients was 39.90 ± 14.13 years. Male patients were 54.8% while females were 45.2%. The score of pain and duration of hospital stay was statistically high in the drain group in comparison to the no drain group. After T-test and Chi-square test, there was no significant association found in both groups in terms of hospital stay or Post-operative pain regarding effect modifiers like age or gender.

Conclusion: In post-operated cases of thyroid surgery where drains were not placed, were associated with short duration of hospital stay and less post-operative pain. So the results of this study do not support the regular insertion of drain after thyroid surgery.

Key Words: Postoperative thyroid complications, Total Thyroidectomy, Post thyroidectomy drain.

INTRODUCTION

Among all the operations of general surgery, thyroidectomy is a commonly performed operations. Thyroid is a highly vascular gland, having multiple thin walled vessels. This is the reason that thyroidectomy is associated with preoperative and postoperative bleeding complications. Postoperative hemorrhage in a closed space leads to compression of the air way causing respiratory depression and then leading to fatal complications. To detect the early occurrence of postoperative bleeding many surgeons prefer to insert a drain in the operative area.

On the other hand, there are arguments that postoperative bleeding is a rare complication of thyroidectomy.¹ Although postoperative bleeding can lead to fatal complications in thyroid surgery but it is reported in only 0.3–1 % of thyroid surgeries. Drains are placed to indicate early bleeding complication in postoperative period of thyroid surgery but it is a fact that many times these drains are blocked with clotted blood and give a false perception of no postoperative bleeding. Site of exit of a drain is usually around the collar bone of the patient, which is a highly cosmetically sensitive area, and this wound of drain leaves an ugly scar in this area. Also drains are associates with patient’s anxiety and sometimes are also financial burden for the patient.² In recent years, the number of all the malignancies are increasing worldwide and thyroid carcinomas are about 1.7% of all the malignancies. Due to this rise of thyroid malignancies, thyroidectomies are also increasing.³

With the development of surgical techniques, overall occurrence of postoperative complications is reduced in cases of thyroidectomies but still there are cases which are getting postoperative complications, including haemorrhage (0.3–6.5%), haematoma formation (1–1.2%), recurrent laryngeal nerve injuries (0.5–4.4%)⁴ and hypocalcaemia (3.1–11%)⁵. According to many surgeons insertion of a drain in postoperative cases of thyroidectomy reduces dead space which helps in
prevention of seroma formation and also helps in early detection of bleeding complication. Many patients undergoing thyroidectomy have bleeding disorders, in these cases drains are very beneficial. But insertion of postoperative drains have bad impact on patients and causes scar formation, high infection rate and longer duration of hospital stay. As thyroidectomy is a common surgical procedure and multiple studies were carried out to detect both the necessity as well as the complications of postoperative drain placement, but despite all this there is still no structured formation of guidelines or recommendations; so, weather to place a drain or not postoperatively depends upon the surgeon’s personal experience and choice.

MATERIALS AND METHODS

A total of 62 patients undergoing surgery for benign multinodular goiter admitted in CMH, Muzaffarabad, were selected for the study. Permission from hospital ethical review committee was taken over. Written informed consent was taken from all the patients. Patients were divided into 2 equal groups randomly by lottery method. Each group having 31 patients. All the patients were diagnosed by detailed history, thorough clinical examination, ultrasound neck, FNAC of thyroid and laboratory investigations including thyroid function tests. Patients diagnosed as being multinodular goiter and with normal thyroid function tests (euthyroid) were included in the study.

In Group A patients, Redivac suction drain of size 14 F was placed after total thyroidectomy beneath the deep cervical fascia. Drain output was measured after every 6 hours and drain was removed when the output was not increasing in a 6-hour period. While in group B patients, drain was not placed and the wound was closed by continuous subcuticular sutures. All the patients were followed postoperatively for severity of pain, duration of hospital stay and other post-operative complications like hematoma formation, seroma formation and wound infection. Patients were taught VAS (visual analog score) for pain and a record of pain was made on 1st postoperative day and then on 7th postoperative day. Hospital stay and postoperative complications were recorded. Post-operatively patients were followed on 1st, 7th and 14th postoperative days for development of hematoma formation, seroma formation and wound infection. Data in both the groups were recorded on a predesigned proforma. All patients were given due respect and their comfort was considered during the study.

Data was analyzed by SPSS version 20. Mean and SD were calculated for quantitative variables including age, pain as per VAS and hospital stay. Frequency and percentage were computed for qualitative variables like gender and postoperative complications including hematoma formation, seroma formation and wound infection. Data was stratified for age and gender. Post-stratification independent sample t-test was used to compare mean postoperative pain and hospital stay between the two groups. Chi-square test will be used to analyze postoperative complications between the two groups. P-value ≤0.05 was taken as significant.

RESULTS

Minimum age was 15 years and maximum was 60 years with mean and standard deviation of 39.90 ± 14.13 years. The minimum postoperative pain was 3 and maximum was 6 with mean and standard deviation of postoperative pain was 4.5 ± 1.13. Minimum duration of hospital stay was 1 day, and maximum duration was 4 days with mean and standard deviation of 2.53 ± 0.99 days.

Males were 34/62 (54.8%) while females were 28/62 (45.2%). Hematoma formation was present in 2/62 (3.2%) patients while it was absent in 60/62 (96.8%) patients. Seroma formation was present in 6/62 (9.7%) patients while it was absent in 56/62 (90.3%) patients. Wound infection was present in 2/62 (3.2%) patients while it was absent in 60/62 (96.8%) patients.

Independent T-test was applied after stratification of age, it was found that in both groups of age (< 40 years and ≥ 40 years) p-values were 0.208 and 0.103 respectively. Therefore, no significant association was found in both groups and hospital stay regarding the age of patients. By the stratification of age, it was found that in both groups of age (< 40 years and ≥ 40 years) the mean Post-operative pain was not significant in both groups. Independent T-test was applied, and it was found that there were no significant differences in groups and hospital stay, post-operative pain regarding male and female patients.

<table>
<thead>
<tr>
<th>Table No.1: Descriptive statistics</th>
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<tr>
<td>Minimum</td>
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<tr>
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<td>Postoperative Pain</td>
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<tr>
<th>Table No.2: Hematoma formation</th>
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<tbody>
<tr>
<td>Hematoma formation</td>
</tr>
<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
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<tr>
<th>Table No.3: Seroma formation</th>
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<tbody>
<tr>
<td>Seroma Formation</td>
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<tr>
<td>Present</td>
</tr>
<tr>
<td>Absent</td>
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<tr>
<td>Total</td>
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</tbody>
</table>

Chi-square test was applied to see effect in the both groups of age (< 40 years and ≥ 40 years) and there was no significant association in both groups and hematoma.
formation. There was no significant association in both groups (insertion with drain and without drain) between hematoma formation and gender. Chi-square Test was applied to see the effect in both groups of age (< 40 years and > 40 years) and there was no significant association found in both groups (With drain or without drain) and Seroma formation according to the age of patients. There was no significant association between both groups (p-value greater than 0.05). When Chi-square Test was applied to see effect in the both groups of gender, no significant association was between both groups and Seroma formation.

<table>
<thead>
<tr>
<th>Table No:4: Wound infection</th>
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<tbody>
<tr>
<td>Wound infection</td>
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<td>------------------</td>
</tr>
<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
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<tr>
<td>Total</td>
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</table>

**DISCUSSION**

The objectives of the present study were to compare total thyroidectomy with insertion of post-operative drain versus no drain in terms of severity of post-operative pain, duration of hospital stay and frequency of post-operative complications. In this regard, the present survey was conducted from the patients visiting at department of General Surgery, CMH Muzaffarabad. A sample of 62 patients was selected by using non-probability consecutive sampling technique.

From 62 patients, the minimum age was 15 years and maximum was 60 years with mean and standard deviation of 39.90 ± 14.13 years. The minimum postoperative pain was 3 and maximum were 6 with mean and standard deviation of 4.5 ± 11.3. The minimum duration of hospital stay was 1 day, and maximum was 4 days with mean and standard deviation of 2.53 ± 0.99 days.

Males were 34/62 (54.8%) while females were 28/62 (45.2%). Hematoma formation was present in 2/62 (3.2%) patients while it was absent in 60/62 (96.8%) patients. Seroma formation was present in 6/62 (9.7%) patients while it was absent in 56/62 (90.3%) patients. Wound infection was present in 2/62 (3.2%) patients while it was absent in 60/62 (96.8%) patients.

Independent T-test was applied after stratification of age, it was found that in both groups of age (< 40 years and > 40 years) p-values were 0.208 and 0.103 respectively. Therefore, no significant association was found in both groups and hospital stay regarding the age of patients. By the stratification of age, it was found that in both groups of age (< 40 years and > 40 years), the mean Post-operative pain was not significant in both groups (i.e. insertion with drain and without drain). Independent T-test was applied, and it was found that there were no significant differences in both groups and hospital stay regarding male and female patients.

In a previous study postoperative pain score of 24 hours had revealed finding of a significant higher pain score in the group that had placement of a drain. The minimum hospital stay in drain group was 4 days and in case of no drain 1 day. In patients where drain was inserted had more frequency of postoperative infection than as compared to the patients in which no drain was inserted (pooled OR = 2.94, 95% CI 1.27−6.85, P = 0.012). In case of the hospital stay, it was prolonged in patients where drain was inserted in comparison to the patients having no drain (pooled difference in mean = 1.16, 95% CI 0.72−1.59, P < 0.001). As a result of this meta-analysis there was no statistically significant differences between the groups in terms of seroma or hematoma formation, hypoparathyroidism, injury to recurrent laryngeal nerve and duration of hospital stay.

Tian J et al conducted a meta-analysis in which 14 studies comprising if 1927 patients were included. This meta-analysis was conducted to find out the frequency of postoperative complications of thyroidectomy such as sroma or hematoma formation, wound site infections, hypoparathyroidism, injury to recurrent laryngeal nerve and duration of hospital stay. The results of that meta-analysis showed that the patients in which drain was inserted, had more frequency of postoperative infection than as compared to the patients in which no drain was inserted (pooled OR = 2.94, 95% CI 1.27−6.85, P = 0.012). As a result of this meta-analysis there was no statistically significant differences between the groups in terms of seroma or hematoma formation, hypoparathyroidism, injury to recurrent laryngeal nerve. It was concluded from the study that there is no significant advantage of postoperative drain insertion in thyroidectomies. But on the other hand, this Study also concluded that frequency of infection and duration of hospital stay was higher in patients where drain was inserted.
insert drain after thyroidectomy to prevent seroma or hematoma collection in the operative field. Bleeding complication after thyroidectomy leading to hematoma formation is not constant and ranges between 0.3–2.5%. The duration of hospital stay was found lesser in the patients without a drain and these findings were also reported by other studies. Short hospital stay is also economical for our patients as majority of them are poor patients having minimum resources, belong to far-flung areas and they can’t take long leave from work. In short, in all cases of thyroidectomy, drains are not always required. Along with prolonged hospital stay, drains are a source of infection as well as discomfort for the patient. Post-thyroidectomy bleeding chances are more with recurrent goiter, Graves’ disease, retrosternal goiter and in patients taking anticoagulants. When thyroid surgeries are performed by meticulous surgeons then the rate of major postoperative complications is very low. As bleeding is a common complication among all the complications of thyroidectomy, thus, surgeons generally place drains after thyroid operations to detect bleeding early. On the other hand, the insertion of drains itself causes high rate of infection and prolonged hospital stay. Postoperative bleeding mostly occurs in the first 6 hours of the thyroid surgery, leading to the hematoma formation and respiratory distress, so patients should be kept under close observation during this period and can be discharged on the next day. This practice reduces duration of hospital stay as well as reduction in financial burden.

**CONCLUSION**

Total thyroidectomy, without insertion of post-operative drain is better than with drain in terms of post-operative pain, hospital stays and cost effectiveness. There is no need of inserting a drain in patients who don’t have any risk factor. In case a large hematoma is formed, it can be aspirated by a needle. Finally, the insertion of a drain predisposes a patient to infections as well as increase patient discomfort, prolongs the hospital stay and increases financial burden on patient.

**Author’s Contribution:**

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<th>Concept &amp; Design of Study:</th>
<th>Raja Ijaz</th>
</tr>
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<tr>
<td>Drafting:</td>
<td>Naheed Akhtar, Sehrish Khizar</td>
</tr>
<tr>
<td>Data Analysis:</td>
<td>Naheem Butt, Umer Ijaz, Nabeel Imran</td>
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<tr>
<td>Revisiting Critically:</td>
<td>Raja Ijaz, Naheed Akhtar</td>
</tr>
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<td>Final Approval of version:</td>
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

**REFERENCES**

One Year Experience of Poisoning Patients in a Medical Ward of a Tertiary Care Hospital
Syed Hashim Raza, Ali Imran, Wajih ur Rehman, Ashfaq Ahmad and Qazi Masroor Ali

ABSTRACT

Objective: To determine the etiological and demographic pattern of poisoning among admitted patients in a tertiary care hospital of southern Punjab.

Study Design: Retrospective Observational study

Place and Duration of Study: This study was conducted at the department of Medicine (Medical unit 1), Bahawal Victoria Hospital (BVH), Bahawalpur from January, 2019 to December, 2019.

Materials and Methods: All cases of acute poisoning admitted in Medical unit 1, through Accident & Emergency (A&D) department of BVH, Bahawalpur from January, 2019 to December, 2019 were included in the study. The etiological and demographic details were documented by using a specifically designed proforma in the light of their medical record files.

Results: Out of 342 patients of acute poisoning enrolled in the study, 251 (73.4%) were females and 91 (26.6%) were males. The overall mean age was 23.58 years. Most cases of acute poisoning presented among 21-30 year of age group (44.4%) followed by 13-20 years of age group (41.8%). Majority of subjects were married (62%). The most common agent used for poisoning was paraphenylene diamine (PPD / Kala patthar) (49.4%) followed by organophosphorus (OP) compounds (40%). The reason of poisoning in majority of cases (96%) was suicidal attempt. Overall mortality among poisoning patients was 19.3%. PPD poisoning emerged the major contributor of mortality in 87.9% of cases.

Conclusion: The majority of poisoning cases in our setup occurs in females of younger age group for suicidal attempt carrying substantial mortality. PPD (Kala Patthar) being the commonest and most lethal poison in such cases.

Key Words: Poisoning, paraphenylene diamine, organophosphorus compounds, suicidal attempt, mortality

INTRODUCTION

Poisoning is known as the potential related to chemical substance in doing adverse to the body.1 Changes in lifestyle and social behaviors have impacted increase in poisoning cases in the recent decades.2 Poisoning is also considered a frequent cause of medical emergency and admissions. As per World Health Organization, more than 3 million cases of poisoning are reported annually, out of which, a quarter million die. It is also seen that 99% of the deaths are reported in developing countries.3 Available data on suicide suggests that in Pakistan about 8 per 100,000 commit an act of deliberate self-poisoning per year.4 Knowledge about the pattern of poisoning among different regions is thought to be helpful in timely diagnosis and management of frequently occurring cases in the region along with initiating appropriate strategies of prevention. Not much is known about trends of acute poisoning in our region among adult population. This study was done to know the pattern as well as outcome of acute poisoning among adults admitted in a medical ward of a tertiary care hospital, Bahawal Victoria Hospital, Bahawalpur.

MATERIALS AND METHODS

This was a retrospective observational study, conducted in Medical Unit-1 of Bahawal Victoria Hospital (BVH), Bahawalpur from Jan., 2019 to Dec., 2019. Approval from institutional Ethical and Research committee was taken for this study. All adult (≥13 year old) patients admitted in Medical Unit-1 during the aforementioned period through emergency department of BVH, Bahawalpur with history of acute poisoning due to various agents were included in the study. Cases with pre-existing renal or cardiac disease, food poisoning, insect/snake bites, poisoning due to some unknown agent and patients
having doubtful history of poisoning were excluded from the study.
A retrospective analysis of all the cases regarding age, sex, marital status, reason of poisoning, type of poisoning agent and mortality were documented in a specifically designed proforma with the help of hospital medical record files of the patients. Data was presented in terms of frequencies and percentages. SPSS version 20.0 was used for data analysis.

RESULTS
A total of 5344 patients were admitted in Medical Unit-1 during the study period. Out of these, 342 patients of acute poisoning (6.4% of total admissions) fulfilling the selection criteria were enrolled in the study. Among these 342 patients, 91 (26.6%) were males and 251 (73.4%) females, with overall male to female ratio of 1:2.75. There was wide variation of age ranging from a minimum of 13 to 65 years, with mean age of 23.58 years. The majority of patients (86.25%) were less than 30 years of age.
Regarding the marital status, two hundred and twelve (62%) were married and 130 (38%) were unmarried. The reason for acute poisoning was mainly suicidal in 328 cases (96%), followed by accidental 13 cases (3.8%) and homicidal one case (0.2%).
In the present study, the commonest poisoning agent was paraphenylene diamine (169 cases, 49.4%) followed by organophosphorus compounds (137 cases, 40%), acid ingestion (20 cases, 5.8%), wheat pill (09 cases, 2.6%), bleach (04 cases, 1.2%), rodent killer (02 cases, 0.6%) and cloth dye (01 case, 0.3%).

Eight hundred and seventy-nine deaths were documented in the ward during the study period, out of which 66 deaths were contributed by acute poisoning cases representing 7.5% of the total all cause mortality of the ward. On the other hand, mortality among acute poisoning cases in our study was 19.3% (66 out of 342 cases). Paraphenylene diamine (PPD) was major contributor to mortality in 87.9% of cases (58 out of 66 deaths), followed by organophosphorus compounds in 09% (06 out of 66 deaths), acid ingestion in 1.5% (01 out of 66 deaths) and wheat pill in 1.5% (01 out of 66 deaths).

DISCUSSION
Trends of poisoning vary greatly among different populations. Management of cases with acute poisoning may significantly improve if we know the patterns and causes of poisoning among different set of populations. In our study the acute poisoning cases accounted 6.4% of the total admissions of the ward, which is a substantial figure to highlight the burden of poisoning cases in our set up. Paudyal BP has also reported 4% of total medical admissions were contributed by acute poisoning cases in his study. Frequency of poisoning reported of medical emergency departments is noted from 0.2 to 1% of total emergency department visits around the world. Developing countries report the major bulk of poisoning, representing a 13 fold increased incidence in comparison to developed countries.9
Regarding gender comparison, we noticed significantly high proportion of females being victim of acute poisoning (male to female ratio of 1:2.75). The fact that females are more vulnerable to poisoning is also observed in Nepal, India, Turkey, Iran and

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**Table No.1: Characteristics of Patients (n=342)**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of Patients (%)</th>
</tr>
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<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>91 (26.6%)</td>
</tr>
<tr>
<td>Female</td>
<td>251 (73.4%)</td>
</tr>
<tr>
<td><strong>Age (Years)</strong></td>
<td></td>
</tr>
<tr>
<td>13-20</td>
<td>143 (41.8%)</td>
</tr>
<tr>
<td>21-30</td>
<td>152 (44.8%)</td>
</tr>
<tr>
<td>31-40</td>
<td>37 (10.8%)</td>
</tr>
<tr>
<td>41-50</td>
<td>7 (2.0%)</td>
</tr>
<tr>
<td>51-60</td>
<td>2 (0.6%)</td>
</tr>
<tr>
<td>61-70</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>212 (62.0%)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>130 (38.0%)</td>
</tr>
<tr>
<td><strong>Reason of Poisoning</strong></td>
<td></td>
</tr>
<tr>
<td>Suicidal</td>
<td>328 (95.9%)</td>
</tr>
<tr>
<td>Accidental</td>
<td>13 (3.8%)</td>
</tr>
<tr>
<td>Homicidal</td>
<td>1 (0.3%)</td>
</tr>
</tbody>
</table>

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**Figure No.1: Frequency of Poisoning Agents Among Patients (n=342)**

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**Figure No.2: Mortality Among Poisoning Agents (n=66)**

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**Figure No.3: Mortality Among Poisoning Agents (n=66)**
Acute poisoning cases contributed 7.5% of the total all cause mortality of the ward in our study, which is a significant figure to note in the background of potentially preventable problem. The overall mortality among poisoning patients in this study was about 19%. A higher mortality among poisoning patients were observed in similar studies conducted at Sargodha (27%) and Peshawar (23%). Mortality in our study is due to a large number of PPD victims which contributed about 88% of the total mortality. The better outcome of poisoning cases may be due to different nature of poisoning agents and availability of better health care facilities to deal such cases in those regions. Current study shows PPD as a newly emerging domestic poison in this region. Keeping in view the rising trend of this poison, it is mandatory to launch public awareness campaign regarding toxic effects of hair dye through electronic and print media. The sale of kala pather should be legally banned by the concerned authorities to save precious lives.

CONCLUSION

Acute poisoning cases contributes appreciably in total ward admissions. The all-cause mortality of the ward is also significantly contributed by these cases. The majority of poisoning cases in this study were seen in females of younger age group for intentional self-harm. Paraphenylene diamine is the most commonly used agent for acute poisoning in this series. A significantly high mortality is noted among the poisoning cases with major contribution from paraphenylene diamine (kala pather) ingestion.

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

Author's Contribution:
Concept & Design of Study: Syed Hashim Raza
Drafting: Ali Imran, Wajih ur Rehman
Data Analysis: Ashfaq Ahmad, Qazi Masroor Ali
Revisiting Critically: Syed Hashim Raza, Ali Imran
Final Approval of version: Syed Hashim Raza

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


Frequency of Different Types of Ocular Trauma

Maria Khan, Abdul Hameed Siddiqui, Afshan Mateen and Asmat ullah Khan

ABSTRACT

Objective: To determine the frequency of different causes of ocular injuries in patients presenting at Liaquat National Hospital, Karachi.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Liaquat National Hospital, Karachi from November 2016 to March 2018.

Materials and Methods: Total 684 patients of acute ocular trauma were included. History of ocular trauma was taken. The refractive errors if existing before and usage glasses were inquired. Descriptive statistics were calculated. Stratification was done and post stratification, chi square test was applied, taken P value ≤0.05 as significant.

Results: There were 489 male and 198 female patients. Mean duration was 146.92±738.24 hour. Mostly cases had either right or left eye trauma. 86.2% patients had mechanical trauma, 9.3% had chemical trauma, 1.9% had photic trauma, and 2.06% had thermal trauma. Mechanical trauma was significantly associated with age groups, eye involved, and socio economic status. Results showed significant association of chemical trauma with age group and eye involved. There was also significant association of photic trauma with gender, age groups, and education. Study found significant association of thermal trauma with eye involved and socio economic status.

Conclusion: Majority of the trauma was of mechanical type presenting in young adult males in unilateral eyes.

Key Words: Ocular Trauma, Mechanical, Chemical, Photic, Thermal

INTRODUCTION

In Pakistan, 6.78% of all hospital admissions comprise of ocular emergencies,(1) that makes them the third most common ophthalmic indication for hospitalization,(2) approximately 1.6 million people go blind from eye injuries, 2.3 million with bilateral visual impairment and 19 million with unilateral visual loss worldwide, making ocular trauma the commonest cause of unilateral blindness.(3) Male gender is an important risk factor in ocular trauma.(4,5) Majority of these injuries are preventable by patient education and use of protective wear alone.(6)

Ocular trauma can have mechanical (83.5%), chemical (7.6%), photic (2.3%) and thermal (2.2%) causes. (5) Ocular trauma can be caused by various agents. Due to lifestyle modifications, these trends shifted overtime. Road traffic accidents have been a major cause during early 80’s. Sports and leisure activities related injuries replaced them later in the decade.

Department of Ophthalmology, Liaquat National Hospital, Karachi.

However, with the start of this millennium, terror attacks and counter terrorism war, presented unique challenges. Largest number of attacks occurred in South Asia and the near east, which also has the highest number of causalities.7 Blast injuries have resulted in significant 9% cases of ocular trauma.8 Pakistan is in itself in the middle of various military operations. Aim of this study was to find out frequency of different causes of ocular injuries in our population. As literature search shows very limited data available locally in this regard. Result of this study will help us estimate the correct magnitude of different causes of ocular trauma in current scenario, which will in turn be helpful in modification of management of ocular emergencies in a better way.

MATERIALS AND METHODS

This study was conducted at the Department of Ophthalmology, Liaquat National Hospital, Karachi from 1st November 2016 to 22nd March 2018

Sample size: 684 patients were included in the study. WHO software was used for sample size calculation considering p=2.2%, d+1.1% and 95% confidence level.

Sampling Technique: Non-probability, Consecutive sampling

Study Design: Descriptive Cross Sectional study

Inclusion criteria: Patients of age group (pediatric age group 2-12 years and adult age group 12-50 years) and

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gender of acute ocular trauma presenting to eye emergency or OPD.

**Exclusion criteria:** All those patients who have injuries involving lids and surrounding orbital structures or those who have received treatment (medical or surgical) for their trauma somewhere else. Or those who have a co-existing ocular disease potentially affecting visual acuity.

**Data Collection Procedure:** After taken approval from hospital ethical committee, 684 patients fulfilled the selection criteria were included from OPD of Department of Ophthalmology, Liaquat National Hospital, Karachi. Informed consent was taken from each patient or parents of underage children. Demographic information (name, age, sex, contact, education and socioeconomic status) was obtained. A detailed history of ocular trauma was taken regarding settings, agent, type and time of injury. The refractive errors if existing before and usage glasses were inquired. All the information was noted on Performa.

**Data Analysis Procedure:** All data hence collected was entered and analyzed by SPSS software version 20. Mean and standard deviations were calculated for age, duration of trauma, frequency and percentages were calculated for gender, education level, socioeconomic status and cause of ocular trauma. effect modifiers like eye involved, age, gender, education level and socioeconomic status was controlled through stratification, post stratification, chi square test will be applied by taking $p \leq 0.05$ as significant.

**RESULTS**

Data was entered and analyzed by Statistical Package for the Social Sciences Software (SPSS, version 20). Mean and standard deviation were calculated for quantitative data. Frequency and percentages were presented for qualitative data. Stratification was done and post stratification chi square test was applied to control effect modifiers. $P$-value $\leq 0.05$ is considered as significant.

A total of 687 patients presented to the Liaquat National Hospital, Department of Ophthalmology with the trauma injury over a period of 6 months were evaluated. Out of all study subjects, 489 were male and 198 were female.

The overall mean age of all the study subjects was 23.93±14.33 years. The age was further stratified in two groups such as pediatrics and adults. 29% (200 patients) were in pediatrics group and 31% (487 patients) were adults.

The overall mean duration was 146.92±3.24 hour. Among total study subjects, mostly cases had either right 43.5% (299 patients) or left eye 41% (282 patients) trauma. Only 15.4% (106 patients) presented with bilateral ocular trauma. According to the education status of trauma patients, 43.5% (299 patients) majority were illiterate while only 4.5% (31 patients) were post graduate. 41% (282 patients) had primary qualification, 15.4% (106 patients) were matric and 18.2% were intermediate whereas 30.6% (210 patients) were graduate.

Patients who enrolled in our study had different socio economic status. There were 42.5% patients (292 patients) belong to the low socio economic status (<20,000Rs/Month). 29% earned 20,000-40,000Rs/Month and 28.5% (196 patients) belonged to >40,000Rs/Month class of monthly income.

There are different trauma injuries among total study subjects, 86.2% had mechanical trauma, 9.3% had chemical trauma, 1.9% had photic trauma, and 2.06% had thermal trauma.

Stratification with respect to age, gender, eye involved, education status and socio economic status was done to observe effect of these modifiers on eye trauma injuries. $P$-value $\leq 0.05$ was considered as significant.

The results showed that there was significant association of mechanical trauma with age groups ($p=0.019$), eye involved ($p=0.001$) and socio economic status ($p=0.007$) while no significant association was found with gender ($p=0.693$), and education ($p=0.067$).

Out of 592 patients of mechanical trauma, 71.5% (423 patients) were males and 28.5% (169 patients) females. Similarly, 69.26% (410 patients) were adults while 30.74% (182 patients) belonged to pediatric group. Only 9.2% (n=55) eyes had bilateral mechanical trauma whereas 46.28% (n=274) of the eyes were right and 44.43% (n=263) were left. With regards to education status, 30.40% (n=180) were graduates and in majority while 37.11% (n=22) were postgraduate. 14.7% (n=87) were illiterate, 15.37% (n=91) primary, 16.89% (n=100) were matric and 18.91% (n=112) were intermediate.

According to socioeconomic groups, 42.23% (250 patients) earned <20,000Rs/Month, 30.91% (183 patients) earned 20,000-40,000Rs/Month and 26.86% (159 patients) had > 40,000Rs/Month income.

We found significant association of chemical trauma with age group ($p=0.027$) and eye involved ($p=0.001$) while insignificant association was found with gender ($p=0.187$), education ($p=0.415$) and socio economic status ($p=0.231$). Out of 64 patients of chemical trauma, 64.06% (41 patients) were males and 35.94% (23 patients) females. Similarly, 82.81% (53 patients) were adults while 17.19% (11 patients) belonged to pediatric group. 50% (n=32) eyes had bilateral chemical trauma whereas 31.25% (n=20) of the eyes were right and 18.75% (n=12) were left. With regards to education status, 32.81% (n=21) were graduates and in majority while both postgraduate and primary were 7.8% (n=5). 17.19% (n=11) were illiterate, 14.06% (n=9) were matric and 20.31% (n=13) were intermediate.

According to socioeconomic groups, 39.06% (25 patients) earned <20,000Rs/Month, 23.44% (15
patients) earned 20,000-40,000Rs/Month and 37.5% (24 patients) had > 40,000Rs/Month income. There was significant association of photic trauma with gender (p=0.014), age groups (p=0.014), and education (p=0.028) while no significant association was found with eye involved (p=0.115) and socio economic status (p=0.408). All 14 patients of photic trauma were adult males. Bilateral and right eye both presented with 35.71% (n=5) and 28.56% (n=4) were left. With regards to education status, 42.86% (n=6) were illiterate and in majority while 14.29% (n=2) were primary, graduate or postgraduate. 7.14% (n=1) were matric and intermediate. According to socioeconomic groups, 57.14% (8 patients) earned <20,000Rs/Month, 14.29% (2 patients) earned 20,000-40,000Rs/Month and 28.57% (4 patients) had > 40,000Rs/Month income. We found significant association of thermal trauma with eye involved (p<0.001) and socio economic status (p=0.029) while no significant association was found with gender (p=0.788), age group (p=0.452), and education (p=0.423). There were 19 patients of thermal trauma, out of which 68.42% (13 patients) were males and 31.58% (6 patients) were females. Similarly, 63.15% (12 patients) were adults while 36.84% (7 patients) belonged to pediatric group. 73.68% (n=14) eyes had bilateral thermal trauma whereas 10.58% (n=2) of involved eyes were right and 15.79% (n=3) were left. With regards to education status, 36.84% (n=7) were graduates and in majority while 5.26% (n=1) were intermediate. Both illiterate and postgraduate were 10.53% (n=2). 15.79% (n=3) were primary and 21.05% (n=4) were matric. According to socioeconomic groups, 47.39% (9 patients) belonged to each <20,000Rs/Month and classes > 40,000Rs/Month income. 5.26% (1 patient) earned 20,000-40,000Rs/Month.

**DISCUSSION**

In Pakistan, 6.78% of all hospital admissions comprise of ocular emergencies. (1) that makes them the third most common ophthalmic indication for hospitalization. (2) approximately 1.6 million people go blind from eye injuries, 2.3 million with bilateral visual impairment and 19 million with unilateral visual loss worldwide, making ocular trauma the commonest cause of unilateral blindness. (3) Majority of these injuries are preventable by patient education and use of protective wear alone. (6)

There were no recent studies on ocular trauma in our region i.e. Pakistan. Last study was published in 2007 where Khan et al. reported 1.9% patients suffering from trauma to both eyes. Almost 80% patients were male and 69% patients were below 30 years of age. Delayed presentation was more common and 63.61% patients presented after one week. (1) Although, our study shows similar trends like less incidence (15.4%) in bilateral eyes, more common in males (71.7%). Time of presentation was also around 146.92hours (around 6 days). difference in percentages over the years may be due to more privileged settings (Karachi vs peshawar) and increased education and awareness. Studies from around the world, have also reported increased association of ocular trauma with male gender (4, 5, 9, 10, 11)

Liggett et al conducted a study of 510 patients, of which 427 (83.7%) were male and 462 (90.6%) were literate. Adults, children and elderly comprised 403 (79%), 90 (17.6%) and 17 (3.3%) of the study population.12

According to Liggett12 and Glynn13, less educated and less wealthy persons are prone to partake in risk taking activities and thus to be injured. In a door to door survey in rural Nepal, Khatry reported 50.9% literate males and 31.2% of literate females, among all ocular injury patients.14 In their study from a south India community, Nirmalan et al reported lower odds ratios for literates for eye trauma. (15) However, studies from an urban slum population in Delhi, India did not corroborate the reported decreased risk of ocular trauma in literates. (16) This is in consistency with our findings of increase incidence of ocular trauma in lower socioeconomic population group. Also most people seeking treatment had higher education level i.e. graduate level.

Most of the above mentioned studies didn’t take into account the causative agents. Ocular trauma was classified into mechanical (83.5%), chemical (7.6%), photic (2.3%) and thermal (2.2%) causes by Jafari et al. (5) Our population showed nearly similar patterns of mechanical (86.2%), chemical (9.3%), photic (1.9%) and thermal (2.0%).

Weak points of this study were that we did not use any international classification system. Also visual assessment at the time of presentation and visual prognosis were not recorded.

Aim of this study was to find out patterns of different causes of ocular injuries in our population. As literature search shows very limited data available locally in this regard. Result of this study will help us estimate the correct magnitude of different causes of ocular trauma in current scenario, which will in turn be helpful in modification of management of ocular emergencies in a better way.

**CONCLUSION**

We have compared the patterns of various types of ocular trauma, presenting to our setting. Majority of the trauma was of mechanical type presenting in young adult males in unilateral eyes. Trauma was more prevalent in lower socioeconomic status. However, educated people came for treatment more frequently. Regardless of the type of trauma, age group and involvement of laterality of eye is significant.
Author’s Contribution:
Concept & Design of Study: Maria Khan
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Revisiting Critically: Maria Khan, Abdul Hameed Siddiqui
Final Approval of version: Maria Khan

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

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Ocular Manifestations in Thyroid Disorders in Karachi

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ABSTRACT

Objective: To analyze the ocular findings in thyroid disorders presented in Karachi.

Study Design: A Cross-sectional study

Place and Duration of Study: This study was conducted at the outpatients departments of two tertiary care hospitals of Karachi, Liaquat National Hospital and Dow University of Health Sciences Ojha Campus, Karachi in the department of Endocrinology and Ophthalmology from June, 2018 to June, 2019.

Materials and Methods: Inclusion criteria of thyroid disorder patients were: age between 12-60 years, known hypothyroidism or hyperthyroidism, finding of thyroid abnormalities and visible goiter or exophthalmos. The exclusion criteria were, known diabetic or hypertensive, on iodine containing drugs, pulsatile exophthalmos, poly glandular autoimmune diseases and lens/corneal/retinal abnormalities. One hundred and eleven patients were selected according to the inclusion criteria. After consent recent detailed history, clinical examination and ophthalmic examinations were done. Required laboratory and radiological investigations were done and analyzed. The data were entered in SPSS version 20 for descriptive and other relevant statistical analysis. Each patient was examined with slit lamp for anterior segment, snellen chart for measurement of visual acuity, ophthalmoscope for fundoscopy, Goldmann Applanation Tonometer for intraocular pressure measurement, Torch for examination of pupil and extraocular movements and Hertel exophthalmometer to measure amount of exophthalmos. CT and (Hertel) MRI in selected cases were done.

Results: The mean age of involvement was 39+/- 15 years and there was female preponderance 2.6:1. Out of 111 patients 70% were hyperthyroid and 30% were fixed with the diagnosis of hypothyroidism. Almost 20% had bilateral proptosis while unilateral exophthalmos was 5.5%. Goiter was visible among 28%. Around 20% had family history of thyroid disorders and habitual usage of iodized salt was 17%. Addiction to smoking was 26%. The main ocular sign in hypothyroidism was ocular pressure and increased myopia and while xerosis of eyes and loss of hairs in eyebrows were main ocular presentation among hypothyroidism. The most elicited sign in hyperthyroidism was lid lagging and eye protrusion while congested eye lids, dry eyes and week ocular movements were main signs among hypothyroidism. Marcus Gunn pupil and papilledema were present in 2 patients. Optic neuropathy was present in one patient. The latter signs were red flag signs of oculopathies in hyperthyroidism.

Conclusion: Eyes are good representative of thyroid disorders if examined according to the standard protocol. Hyperthyroidism has sine qua non ocular markers while in hypothyroidism the slow basal metabolic rate represents in eyes as xerosis and loss of eyebrows.

Key Words: Ocular manifestations, thyroid eye diseases


INTRODUCTION

Thyroid disorders are one of the diseases which have specific peripheral stig mata or target organ involvement.1 Thyroid dysfunction has specific changes in whole eye including adjacent structures that is thyroid orbitopathy.2 It is said that if these ocular signs are present in euthyroid status, the patients in future ultimately develop the clinical features of thyrotoxicosis with biochemical evidence.3 This is an interesting fact that hypo and hyper function of thyroid gland, both can involve the specific changes in eye4 Incidence of thyroid eye disease (TED) in hyperthyroidism is 77% and less frequently in euthyroid 20% and 3% among hypothyroidism in most of the studies conducted around the world.5 In Pakistan the ocular manifestations associated with thyroid disorders varies between 27%-46% in different
TED is one of the mysterious disease in which pathogenesis is arguable since many decades. Exact pathology is yet not known however different theories are suggested. The most important pathogenesis effect detected is increased TSH, T₃, T₄ and increment of receptors in the orbit. Other factor postulated is release of long acting thyroid stimulating hormone and exophthalmos producing substance. Another view widely accepted is the production of antibodies against different constituents of orbit especially intra ocular muscles. Histopathology in cadavers had shown excessive deposition of mucopolysaccharides inside the orbit.

MATERIALS AND METHODS

This is an observational cross-sectional study conducted at Liaquat National Hospital and Dow University of Health Sciences Ojha Campus, Karachi in the department of Endocrinology and Ophthalmology from June 30th, 2018 to June 30th, 2019. The study was approved by Institutional and Ethical Review Committees of both institutions. Verbal consent was taken from each patient included and recorded. Inclusion criteria were, (a) known patient of thyroid disorders for at least 6 months, (b) known or detected unilateral or bilateral exophthalmos, (c) goiter clinically visible or palpable, (d) biochemical evidence of thyroid hyper or hypo function, (e) age between 12-60 years to exclude genetic disorders and degenerative impact on eyes. Exclusion criteria were, (a) known case of diabetes and hypertension, (b) those who took iodinated compounds for more than 6 months, (c) polyglandular autoimmune diseases, (d) those who had bilateral cataracts and retinal/corneal abnormalities, (d) pulsatile exophthalmos. The patients were selected from the Outpatient Departments and indoors of the hospitals fulfilling the inclusion criteria. The detailed history and clinical examination were done by the consultants and full ophthalmological reviews were done by the ophthalmologists for ocular findings. The investigations were also analyzed by the consultants including thyroid function tests, thyroid scan, and MRIs of the orbits where indicated. Autoimmune profile was also obtained in the indicated patients. All the informations were recorded in patients profile and then entered in SPSS, version 20 for data analysis. Chi square statistical test is applied where indicated and p value of <0.05 was taken as statistically significant.

RESULTS

One hundred and eleven patients were enrolled in the study as per inclusion criteria. Their ages range between 12-60 years and the mean age was 39±15 years. The proportion of females was 78/111 that becomes 70.2% and females to males ratio was 2.3:1. Overall as per thyroid function tests, 78/111 or 70.2% had hyperthyroidism and 33/111(29.7%) had hypothyroidism. Twenty two patients, 22/111 or 20% had bilateral proptosis while 6/111(5.4%) had unilateral exophthalmos. Thirty one patients 31/111 or 27.9% had clinical goiter and 23/111 that is 20.7% had positive family history of thyroid disorders. Forty one patients 41/111 belonged to rural areas of Sindh. Habitual use of iodized salt were present in 19/111 patients that is 17.1% and all belonged to urban areas. Twenty nine patients or 26.1% (24 males and 5 females) were addicted to cigarette smoking or huqqa. Sixty eight patients that is 68/111 or 61.2% were already on anti-thyroid drugs/thyroxine.

<table>
<thead>
<tr>
<th>S. No</th>
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<tr>
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<tr>
<td>8</td>
<td>Ocular pressure (pain)</td>
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</table>
DISCUSSION

It is known from ancient times that swelling of eyes is related to thyroid glands.\(^{15}\) Inspite of the disputed pathogenesis of ocular manifestations related to thyroid disorders specific eye changes are seen in both hyper and hypothyroidism.\(^{16}\) Overall, females are more involved than males in this research article supported by many researchers.\(^{17}\) The female preponderance is most probably due to the sensitivity to estrogen, pregnancy and lactation.\(^{18}\) In this study the prevalence of hyperthyroidism is more than hypothyroidism which is against the study done by Knuden and co-workers.\(^{19}\) In year 2000 in Denmark and surrounding temperate zones were hypothyroidism more seen. Probably in our areas sufficient iodine in water and food cause Weil-Cheikoff effect which cause enhancement for hyperactivity of gland, twenty five percent in our study showed exophthalmos among them almost 5% was unilateral. As compared to American and European countries where proptosis is more than 42-45% among overall hyperthyroid patients but this figure is lower because of genetic, racial and environmental factors.\(^{20}\) In our study the family history was present in 20.7% while study done by Medgalchi and his co-workers found the higher association that is > 60.5% in the areas near Turkey border.\(^{21}\) This difference is probably due to higher rate of consanguineous marriages and iodine content in water and soil. Indigenous usage of iodine salts in diet and food, very low/high in iodine content has positive and negative influence on thyroid eye diseases. In our study the habitual use of iodized salt was 17.1% supporting the study done by Rati and Uberti in 2004.\(^{22}\) Smoking has linear relationship found in this study supported by work done by Kim and co-researchers in 2019.\(^{23}\) The major ocular symptoms in hyperthyroid in this study was xerosis of eyes with puffiness and gazing stance, increase in myopic error and ocular pressure while in hypothyroidism, dryness of eyes with grittiness, puffy eyelids and reduced visual acuity. These observations are supported by Perroz and coworkers in 2009\(^{24}\).
The main etiology of hyperthyroidism in this study was Graves’ disease, thyrotoxicosis, toxic multinodular goiter and toxic solitary nodular goiters among the majority of cases while the cause of hypothyroidism in this study was Hashimoto’s thyroiditis (autoimmune) and nutritional and sub-clinical hypothyroidism. There was one case of secondary hypothyroidism and two were detected as secondary hyperthyroidism. These facts are supported by many studies done in the last 4 decades especially elaborated in a study done by Kurian and colleagues in 2008. 24. The major signs in ophthalmology of hyperthyroidism were reduction of visual acuity plus increased myopia, congested conjunctiva, fullness of eyes, infrequent blinking, limited upward gaze, vongraffe sign, relative afferent pupillary defect (RAPD) and papilledema while 4 cases of optic neuropathy were detected. These signs are supported by the study done by Satli and Gunduz in 2017. 25. The major ocular signs in hypothyroidism in this study were xerosis of eyes, loss of hairs of eyelashes and lateral one third of eyebrows and only one patient who had primary hyperthyroidism demonstrated proptosis. These observations are supported by the study done by Mahto in 1972. 26.

CONCLUSION
Thyroid disorders either manifest as hyper or hypothyroidism has specific ocular changes. In majority of cases in hyperthyroidism, decrease in visual acuity, conjunctival injection, proptosis, lid lagging, gazing stance and weakness of extra ocular muscles are major manifestations. On the other hand, in hypothyroidism, xerosis of eyes and loss of hair of eye lashes and brows are common presentations. Blindness can occur due to optic neuropathy in severe untreated cases. The impact of genetics, smoking and indigenous use of iodized salts on thyroid functions and associated ocular changes are also highlighted.

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Data Analysis: Abdul Hameed Siddique, S. Ali Haider
Revisiting Critically: Abdul Hameed Siddique, S. Ali Haider
Final Approval of version: Abdul Hameed Siddique

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

REFERENCES
Acute Kidney Injury: Causes, Laboratory Findings and Impact of Conservative Management on its Outcome

Syed Sajid Hussain Shah¹, Mohammad Ali Raza¹, Shahzad Najeeb¹, Bibi Alia³, Khyal Muhammad¹ and Ejaz Hussain²

ABSTRACT

Objective: To know the major causes, changes in laboratory findings and impact of conservative treatment on outcome in patients with AKI.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the High Dependency Unit (HDU) of Paediatric B Ward, Ayub Teaching Hospital, Abbottabad from January, 2018 to December, 2019.

Materials and Methods: Young children of both gender and age between 1 month to 2 year diagnosed with AKI were included while patients with other and chronic co-morbid were excluded. A predesigned proforma was used to extract the data regarding demographics, investigations, diagnosis, and outcome. Data was analyzed using SPSS v.20.0.

Results: In total of 50 patients the means age of the sample was recorded as 6.82 ± 5.95 years, in which 29 (58%) were males and 21 (42%) were females. The serum creatinine of had a mean value of 2.06 ± 1.23 mg/dl, while blood urea recorded a mean of 137.75 ± 62.80 mg/dl. Majority 45 (90%) of patients were admitted with diagnosis of septicemia leading to AKI. In total, 30(60%) patients got discharged, 18(36%) patients expired and 2(4%) patients were referred to other centers.

Conclusion: Septicemia is leading cause of AKI in young children and high mortality was recorded for conservative management.

Key Words: children, acute kidney injury, septicemia, outcome


INTRODUCTION

Acute kidney injury (AKI) is defined as “the abrupt loss of kidney function, leading to a decrease in glomerular filtration rate (GFR), and impaired control of acid-base, electrolyte and fluid balance.”¹ It is associated with high mortality and morbidity and one of the common issues in children who are admitted to intensive care unit and high dependency unit.² The children with AKI are prone for chronic kidney injury (CKD) in long term. Studies have shown that significant number of paediatric patients are at risk for CKD in coming few years after episode of AKI.³

Though there are different criteria used for predicting AKI in children yet the RIFLE (Risk, Injury, Failure, Loss, End Stage Renal Disease) criteria was the first consensus approach for identification and management of AKI.⁴ Serum Creatinine is also used for assessment of AKI but it is insensitive marker rather it is late marker of acute kidney in jury. The level of serum creatinine rises when already there is loss of 25-50% renal function.⁵ There are advance AKI markers like cystatin C, neutrophil gelatinase-associated lipocalin, interleukin 18, kidney injury molecule 1, neutrophilelastase-2 and liver-type fatty acid-binding protein.⁶ But these advance markers are not available in most of the tertiary care hospitals in third world countries. The exact incidence of AKI is not known in children, yet different studies have reported different incidence rate. One study form Africa showed the incidence of AKI in children 12.7 / 1000 admissions, Severe AKI was present in 64.7% and mortality rate of 26.5%.⁷ Another study from Nigeria showing the incidence of AKI 17.4 cases / 1000 children in one of teaching hospital.⁸ The incidence of AKI in Pakistan in not know as no such study has been done. Literature search has shown the incidence of AKI 5% in children who were hospitalized. While children who were admitted to paediatric intensive care unit (PICU) and neonatal intensive care unit were having incidences of 30% each.⁹
Most of the data in children with AKI and its management are from west. Though there are studies from our part of world yet most studies have limitations. Children who are admitted to high dependency unit (HDU) and PICU are at risk for developing AKI. None of studies done in Pakistan has shown the causes of AKI and outcome of conservative management. The objective of this study is to know the major causes, changes in laboratory findings and impact of conservative treatment on outcome in patients with AKI.

MATERIALS AND METHODS

This study was conducted in HDU of Paediatric B ward, Ayub Teaching Hospital, Abbottabad. This was retrospective study and data was retrieved from the patient records after approval of institutional review board. The data was recorded from January, 2018 till December, 2019 i.e. over two years. It was cross sectional study. Sample size was calculated by open epi sample size calculator taking incidence of AKI 5%, confidence limit 5% and confidence level 95%. Calculated sample size was 73 patients. But as our hospital is not referral center for paediatric nephrology services, so the estimated sample size was 50 patients. Retrieved from data young children of either sex from age of 1 month to 2 years were selected. Admitted patients who remain in HDU with diagnosis of acute kidney injury and preceding cause and who were given dopamine infusion in renal dose i.e. 3-5 microgram/kg/min were included in the study. Children known case of renal anomalies, chronic kidney disease, syndromic features and post-operative surgery were excluded. Due to non-existence of paediatric subspecialties including paediatric nephrology and infrastructure, peritoneal dialysis was not done in any of the patient. Patients with acute kidney injury and underlying pathology, age, sex, weight, urea, creatinine, diagnosis and outcome in hospital were recorded on predesigned proforma. Any patient in whom serum creatinine 1 mg/dl or more were taken as acute kidney injury and outcome recorded in form of discharge, expire, referred and left against medical advice. Data was analyzed by SPSS 20 and Chi square test applied.

RESULTS

There were total of 50 patients included in the study, 29 (58%) were male and 21 (42%) were females. Age of patients ranged from 1 month to 24 months with mean age of 6.82 ± 5.95 years. Out of 50 patients, 45 (90%) patients were 12 months or less in age while only 5 (10%) patients were more than one year of age. Weight of patients ranged from 1.8 kg to 12 kg with mean weight of 5.68 ± 2.69 kg.

The serum creatinine of patients ranged from 1.08 mg/dl to 7.60 mg/dl with mean value of 2.06 ± 1.23 mg/dl. Blood urea ranged from 70 mg/dl to 416 mg/dl with mean of 137.75 ± 62.80 mg/dl. Ultrasound of renal tract could not be done during the hospital stay in 36 (72%) patients due to critical condition. In 14 patients where ultrasound was done, one (2%) patient had normal study, 3 (6%) patients had urinary tract anomaly and 10 (20%) patients had renal parenchymal disease and increase echogenicity. During the stay urine detail report could not be done in 35 (70%) patients. In remaining 15 (30%) patients, 11 (22%) patients had microscopic hematuria. Majority 45 (90%) of patients were admitted with diagnosis of septicemia leading to AKI. Other diagnosis included 2 (4%) patients with pyogenic meningitis, 2 (4%) patients with acute gastroenteritis and severe dehydration, one (2%) patient with diabetic ketoacidosis. Out of 50 patients, 30 (60%) patients got discharged, 18 (36%) patients expired and 2 (4%) patients were referred to other centers. Males had more expiry as compare to females as shown in table 1. Patients with age one year and less also had more expiries as compare to over one year children as shown in table 2.

DISCUSSION

AKI is one of the common complications in children admitted to paediatric intensive care unit and HDU. Though AKI was considered to be self limiting after recovery from the hospital yet literature has shown that it is associated with chronic sequelae. Studies have shown that paediatric patients with AKI had more visits to doctor and have increase chance of hospitalization after discharge form hospital. Devarajan P in mini review recommended to use the early non invasive biomarkers for diagnosis of AKI in children but in our set up availability of these biomarkers is limited. Muhle-Goll C et al did one pilot study and concluded that Nuclear magnetic resonance spectroscopy in children with AKI has got high diagnostic accuracy. But this in not available in our part of the world and we have to rely on clinical findings for diagnosis. In this study the patients with AKI had increased serum
creatinine. Though serum creatinine is insensitive biomarker yet it indicates serious renal damage. This study has been done to know the major causes, changes in laboratory findings and impact of conservative treatment on outcome in patients with AKI. Quenot JP et al\textsuperscript{14} in one of editorial reported the incidence of AKI in children 45 to 70% with sepsis, while is our study the patients in whom AKI develop, sepsis was in 90% of patients. It is too high in our study population. Bekele BA et al\textsuperscript{15} in one of study included children aged 4 months to 15 years where as in our study patients were aged from 1 month to 2 years. In their study females were 54.3% while in our study females were 42%. Sepsis along with diarrhea and pneumonia constitute for 20% of cases with AKI while in our study sepsis and diarrhea accounted for 94% of AKI.

Kari JA et al\textsuperscript{16} did study in paediatric intensive care units of three tertiary care hospitals in Kingdom of Saudi Arabia. In their study it was concluded that patients with AKI complicated 1/3rd of intensive care patients and has six time mortality as compare to children with normal renal function. In our study the mortality associated with AKI was 36%. Rasheed S et al\textsuperscript{17} did study in Nishtar Hospital Multan and Bahawal Victoria Hospital, Bahawalpur and included children aged 1 to 10 years. In their study 75.7% patients recovered and 3.8% expired, while in our study children less than 2 years were included and 36% patients expired. Expiry in our study population is too much high as compare to Rasheed S et al study. Rustagi RS et al\textsuperscript{18} did one study in paediatric intensive care unit of one developing country and included 53 children with AKI. Severe dehydration, central nervous system illness and acute lower tract infections were the underlying causes of AKI. The children with AKI had 4.5 times more mortality rate as compare to children who were not having AKI and admitted in intensive care unit. In our study the under lying disease was sepsis in 90% of patients and two patient had meningitis and two patients with severe dehydration and 36% patients expired. Gupta S et al\textsuperscript{19} in their study included children with AKI based on pRIFLE criteria. In their study majority (56%) of patients were females while in our study majority (58%) were males. The major cause leading to AKI in their study was septicemia and multi-organ dysfunction syndrome which accounted for 59.39% while in our study sepsis accounted for 90% causes of AKI. In their study mortality in children with AKI was 46.03% while in our study it was 36%.

Adedoyin OT et al\textsuperscript{20} did one study in Nigeria and included children aged 4 to 17 years and in their study sepsis was cause of AKI injury in 28% of patients while in our study the patients were young and sepsis was cause of AKI in 90% of patients. Macedo E et al\textsuperscript{21} in their study which was part of “The Global Snapshot, conducted by the ISN ‘0 by 25’ AKI initiative” evaluated paediatric patients with AKI who were hospitalized. Paediatric patients with AKI in upper middle income countries and low and low middle income countries are 11 fold higher adjusted risk of death as compare to patients in high income countries. Baalaaji M et al\textsuperscript{22} studied AKI in children with DKA. In their study 71.8% patients recovered with fluid management. In our study there was one child with DKA having AKI who recovered.

In one of the editorial by Ranawaka R et al\textsuperscript{23}, it was concluded that use of dopamine for management AKI in not beneficial and long term follow up of children should be done to for complete recovery and to detect and monitor for recurrence and progression to CKD. In our study dopamine was used for management but mortality was also 36%. Andreoli SP\textsuperscript{24} in one of editorial review concluded that intervention in form of dopamine in renal dose does not affect the AKI course. In fact, prognosis of patient depends on underlying pathology and these patients can develop chronic kidney disease in coming years after initial presentation.

Westrope C et al\textsuperscript{25} did one audit to assess the efficacy of continuous renal replacement therapy (CRRT) in children with acute kidney injury in UK and Ireland. There is no facility of renal replacement therapy in our setup. Mortality in infants was around 38.5% while in our study mortality was 36% which is almost equal. Deep A et al\textsuperscript{26} in their study also concluded that paediatric AKI patients need supportive care and mostly drugs interventions are not effective. Renal replacement therapy was recommended as main supportive therapy including peritoneal dialysis, CRRT and hemodialysis. Due to logistic issues peritoneal dialysis was not available in our setup, so only conservative management was done in children with AKI but the mortality was too high i.e. 36%. Goldstein SL\textsuperscript{27} in one of editorial recommended using the renal replacement therapy modalities in management of paediatric AKI. There are limitations in this study. The data has been corrected retrospectively. Dopamine was given in the patients but underlying pathology was also important as blood culture was not sent in any of the patient due to non-availability in hospital.

**CONCLUSION**

This study concluded that younger males have higher incidence of AKI and sepsis was found to be the major cause of AKI. The study also recorded a high mortality with conservative management.

**Author’s Contribution:**

**Concept & Design of Study:** Syed Sajid Hussain Shah

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

REFERENCES


A Study on Patient Satisfaction Involving the role of Assigned Counselor for Cataract Surgery

Ali Afzal Bodla, Muhammad Awais Ashraf, Asim Mehmood and Ghulam Abbas

ABSTRACT

Objective: To quantify the satisfaction fostered after counseling and association of outcomes in alleviation of pre-operative and post-operative anxiety, discomfort and risk apprehension whilst increasing the overall satisfaction among the cataract patients.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Bodla Eye Care, Multan and Multan Medical and Dental College, Multan from January 2019 to July 2019.

Materials and Methods: The study includes seventy patients from South Punjab with Pre-operative cataract. Out of these patients thirty-five were provided with the counseling services in addition to their routine treatment and were allocated as intervention group. The other thirty-five respondents were offered the routine clinical treatment but no counseling and were designated as control group.

Results: Prior and after the surgery, patients from intervention group employed convalescent sequel in terms of anxiety (P<.01) and their current satisfaction with experience (P<.01) together with the cooperativeness, which was found substantial in the intervention group, depicting the p <.01. On the contrary, patients in the intervention group had insignificant results in discomfort, risk apprehension and sleep quality in comparison to the respondents of the control group.

Conclusion: This causal study indicated to us that recruitment of an assigned counselor could significantly enhance patient’s satisfaction and reduce patients’ pre-operative anxiety, discomfort and risk apprehension levels. It emphasizes the relevance of patient education and counseling in a cataract surgery setting. This could help to improve overall patient satisfaction by meeting his informational needs.

Key Words: Anxiety, Counseling, Phacoemulsification, Satisfaction.

INTRODUCTION

In this retrospective study, we assessed the various effects of counseling for the treatment of patients from South Punjab with pre-operative cataract alongside anxiety. In the developed world, the cataract surgery has unfolded as a widespread surgical intervention whereas in the developing world, cataract is still the widespread root of blindness. In the developing world patients usually prefer conventional cataract surgery, which costs less than phacoemulsification with IOL implantation.

Every Surgery is a startling event even when it’s hardly considerable. Several interventions are however practiced to alleviate perioperative torment and to vanquish adverse effects from the patients. However, these intercessions have borne no fruit and still have restrictive effectiveness for the treatment of patients with pre-operative cataract. Alternative treatment is still needed for patients with pre-operative cataract to prevent and to treat their anxiety and fear before the surgery. Counseling is a potential intriguing candidate to treat such condition. Perhaps it is well documented that lack of preparation for surgery, postoperative symptomology, and negative thoughts and beliefs are significantly associated with psychiatric comorbidity.

Thus, the purpose of the pre surgical counseling period is to pacify surgical anxiety and psychological pedagogy for surgical interventions, to confer rational apprehension of the suggested surgery and prognosis, to make the patients informed of surgical procedure and postsurgical complications, and to direct the patient on operation theater environment. Presently, very little research has been implied upon the perioperative nervousness before a cataract surgery, whilst literature has described that patients with preoperative cataract (PC) are often wretched with anxiety and fear.
lack of awareness in patients and their high threshold of tolerance have led to an inadequate emphasis on counseling before cataract surgery. People with lesser knowledge and families with low socioeconomic groups are also unmindful. Studies also reported that providing preoperative information has positive effects and reduces postoperative stress, pain, and anxiety in surgical patients.10

MATERIALS AND METHODS

This is a retrospective study that was performed in the affiliated hospital of Multan Medical and Dental College, Multan from January 2019 to July 2019. A signed Informed consent was also provided to the respondent patients. The study includes seventy patients from South Punjab with Pre-operative cataract. Out of these patients thirty-five were provided with the counseling services in addition to their routine treatment and were allocated as intervention group. The other thirty-five respondents were offered the routine clinical treatment but no counseling and were designated as control group. All of the results were analyzed prior and former to the surgery on SPSS version 20.

Patients were included presuming they were at waiting list of cataract surgery, aged eighteen years or more, no prior history of cataract surgery (including fellow eye), and with an educational ability to listen and write Urdu. The patients were taken from middle class socio-economic status. Nevertheless, patients were excluded in the event that they suffered from any severe disease such cancer, any psychiatric or neurologic conditions such as dementia; in addition, respondents having adequate information about procedure and its characteristics were excluded.

A consistent meticulous treatment i.e. phacoemulsification (Alcon, Infinity) was given to all the respondents included in the research. Besides this the intervention group also underwent regular counseling. The patients were given information about the structure of the eye as well as adjacent structures, and the advantages of intraocular lens implants (IOLs) over conventional aphakic corrections; prognosis for vision was also reviewed by the ophthalmologist. In this way, while assuring the patient of the need for surgery or treatment, they were not quite inaccurate in assessing the prognosis for visual recovery. Additionally, patients were told to make psychological preparations to relieve anxiety. Such counseling sessions were done at the time of first consultation as well as before surgery.

The patient satisfaction was measured preoperatively on a structured questionnaire that had the questions on anxiety scales.11 It included (1) anxiety before surgery (2) level of discomfort (3) risk apprehension, and (4) current level of satisfaction (CSE). These parameters were estimated individually in the structured questionnaire. Hence the credibility and authenticity of questionnaire have been established.

Post-operative evaluation included the same questionnaire with additional questions about sleep quality, cooperation during procedure, and visual functions, whereby visual function was estimated for the impairment caused due to the surgery.12 It was authenticated as well. An additional scale was employed to estimate the cooperativeness of patients during surgery, with 1 score indicating total uncooperativeness to score 7 indicating total cooperativeness. This scale was also authenticated by the previous study.13 Additionally, sleep quality was measured before the surgery. Anxiety scales, visual function as well as sleep quality were measured, at baseline, 1 week prior and former the surgery. However, cooperativeness whilst the surgery period was measured after the surgery.

RESULTS

Over a time period of 6 months, 77 patients (n=35 control and n=35 intervention) were recruited in this study. Out of which 7 were lost up in the follow ups. The mean age of patients in the intervention group was 70.6 (10.5) and the mean age of control group was 71.3 (11.1). There were 20 (57.1%) males in intervention group and 18 (51.4%) in the control group, whereas there were 15 (42.9%) females patients in intervention group and 17 (48.6%) in the control group. The comparison of characteristics of all included patients was analyzed and no significant differences had been reported between the two groups. Before implicating any kind of intervention on the patients, the analysis of both groups gave us the statistics having an almost equal level of risk, anxiety, CSE (current satisfaction with experience) and discomfort.

Before and after the surgery, patients in the intervention group employed convalescent development in anxiety (P<.01) (table 1 and table 2), alongside current satisfaction with experience (P<.01) (table 1 and table 2) , both measured by a structured questionnaire, as well as the coop cooperativeness among the two groups was found greater in the intervention group 6.0(4.4, 7.0) in comparison to the control group 4.5 (2.8, 5.9), depicting a difference of 1.5 (0.9, 2.1) and the p <.01 (table 3). On the contrary, patients in the intervention group had insignificant results in discomfort (before, P=.51, after, P=.16), and risk (before, P=.47, after, P=.28,) and sleep quality (before, P=.32, and after, P=.20,) before and after the surgery and in comparison to control group as well (table 1 and table 2). The changes in visual functions before and after the surgery were significant (p=0.02) however no significant difference was reported concerning the visual outcomes when comparing the two groups (p=0.3).
DISCUSSION

Currently, no specific study has been done in south Punjab pointing towards the effects of pre-operative cataract counseling using standardized anxiety scores. Thus, to our best knowledge, this retrospective study is the first of its kind in determining the effects of counseling on pre-operative cataract patients of south Punjab. We hereby report that providing counseling to patients before the cataract surgery not only relieves their anxiety but also enhances their cooperation and satisfaction during surgery.

The high rate of success achieved by modern cataract surgery has created a situation in which patient expectations are very high; in most cases, such expectations are fulfilled. Yet we have seen highest levels of anxiety pre-operatively in the patients. This finding is in accordance to study done by Foggitt. Other studies focusing on patient education showed rather low levels of knowledge with respect to cataract, and misperceptions in cataract patients who needed surgery, in addition to limited information retention. Various other studies have reported the effects of counseling as well as patient education before any elective surgery inclusive of cataract surgery. Morrell and some others in their study had demonstrated the effects of patient education as well as exposure towards the therapeutic goals of cataract surgery. The result of that study is congruent to our study. Foreshadowing the positive effects of counseling prior to a cataract surgery, in order to administer the patient satisfaction and expectations another study employed a videotaping method in a day stay cataract surgery; these results also demonstrated the patient satisfaction and reduction in anxiety.

The results of our study are somehow similar to the previous studies. According to our study the patients in the intervention group were found less anxious more cooperative and satisfied at the end as compared to the control group. Besides the patients in the intervention group were corresponding better during surgery. No difference was however shown in terms of sleep, visual functions, the risks and discomfort levels between the two groups.

This retrospective study has various constraints as well strengths. This study is a pristine study of its kind being administered in south Punjab and it provides potential evidence for the clinical practice. As far as the limitations are concerned the patients were given both the counseling as well as the treatment for pre-operative cataract rather than the counseling alone, however, the treatment among the patients was regular and constant. The results of this study might have been altered due to smaller sample size and the study is a nonrandomized controlled trial, with higher risks of selection bias. Hence, all of these limitations should be avoided in future study.

CONCLUSION

This study has demonstrated the effects of counseling on pre-operative cataract patients and it is therefore found that counseling enhances their satisfaction and alleviates anxiety in patients and increases their cooperativeness during the surgery. Nevertheless, supplemental studies are needed to reiterate the results of this study.

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Revisiting Critically: Ali Afzal Bodla, Muhammad Awais Ashraf
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Glycation Induced 3D Structural Changes of Human Serum Albumin in Diabetes Mellitus
Sajjad Ghani¹, Fariha Niaz², Saira Mushtaq¹ and Attiya Anwar³

ABSTRACT

Objective: The present study was planned to find out the structural changes of proteins due to glycation in diabetic and non-diabetic patients.

Study Design: Experimental Study.

Place and Duration of Study: This study was conducted at the Civil Hospital Faisalabad and Bioinformatics Lab GC University Faisalabad from January 2018 to June 2019.

Materials and Methods: A total 60 subjects, 30 without diabetes and 30 with diabetes were selected. From each subject 0.5 ml was drawn from antecubital vein using plastic disposable syringe. Serum was separated after centrifugation of clotted blood. Serum glucose, total proteins and albumin was immediately analyzed and a part of serum was stored in storage cup for future analysis of glycated albumin. In silico prediction models was used to predict change in glycated proteins, for this purpose different bioinformatics tools were used in present research work. These tools helped to construct three dimensional (3D) models of proteins before glycation and after glycation as well as their stability after glycation.

Results: The study revealed that structural and functional features of glycated HSA, isolated from diabetic patients were significantly different from the HSA isolated from non-diabetic subjects. These findings suggest that active sites of HSA may not be available under extensive glycation, leading to the impairment of its important functions. Results amino acid residue at 114 position was glycated, the normal functioning of human serum albumin was stopped. Ramachandran plot was constructed for glycated and non-glycated human serum albumin, hence showed UN functionality of protein with red color. Thus, glycated HSA may be involved in the pathogenesis of diabetes and its complications.

Conclusion: The overall glycation rate, the thermodynamics of this process, and the modification rate in certain regions were considered in such studies. The role of glycation conditions in the types of modifications formed was also examined.

Key Words: Glycation, Human Serum Albumin, Diabetes, amino acid

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INTRODUCTION

Glycation is a non-enzymatic unconstrained procedure in proteins which has astounding effect on its physical and utilitarian angles. The procedure of glycation has important impact on structures and elements of proteins. Three-dimensional auxiliary difference in HSA is so unfaltering and stable that it replaces HbA1C as infection marker for diabetes⁴.

Alongside auxiliary changes the cancer prevention agent movement of albumin additionally diminished with non-enzymatic Glycation⁵. Also, advance discoveries demonstrated that after NEG of albumin may promt hindrance of dynamic site and engaged with diabetic intricacies like interminable kidney infection⁶.

Albumin is one of the major and biggest plasma proteins. The typical grouping of albumin in plasma contributes 35-50g/l which empowers it most plenteous plasma protein having various physiological capacities. Human albumin additionally adds to half sound people plasma proteins.⁷ The protein has three areas I,II,III that further subdivided into two subdomains, A and B that empowers it to into practical conformational structure nearness of 17 disulphide extensions makes it impervious to the adjustment in the pH and other modifying condition. The typical physiological capacity of albumin is to keep up osmotic weight in the plasma: this interesting property emerges because of its low sub-atomic weight contrasted with other plasma proteins⁸.

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The structure of albumin alters with enzymatic and non-enzymatic Glycation (5). The glycation of albumin has huge impact on albumin activity and cell capacities (6). These auxiliary and useful changes because of Glycation in vivo has been found in vitro in commercial Bovine Serum Albumin (BSA). Bovine serum albumin has proof to indicate 76% arrangement homology to human serum albumin (HSA) and the two has comparable ellipsoidal shape having three spaces I, II, III connected together through helical expansions. Because of glycation, the albumin structure is changed and it diminished the medication liking of albumin (5). Non-enzymic glycosylation begins with the buildup of a free amino gathering of an amino acid or protein and the carbonyl gathering of a diminishing sugar in its open chain structure bringing about the development of a temperamental adduct, named an aldime or Schiff base which, quickly experiences cyclisation to the relating \( n \)-substituted aldosylamine (Aglycosylamine). The Schiff base quickly and balance is come to in matter of hours. The consistent state level of Schiff base mirrors the encompassing glucose focus (over a predefined timeframe). The procedure of glycation has vital impact on structures and elements of proteins. The investigation of proteins has consistently been a significant piece of therapeutic research and sub-atomic analysis. Proteins coursing in human blood are promptly available and can break down legitimately to deliver symptomatic data 

Our findings suggest, the glycation level ranged between 0.024 mole/mole of protein to 0.30 mole/mole of protein in normal individuals. The value of glycation level in diabetes patients ranged from 0.032 mole/mole to 1.96 mole/mole of protein.

RESULTS

The change in albumin structure after diabetes was predicted by glycation of normal albumin and albumin of diabetic patients in the form of carbonyl group. The comparison of both models has no structural changes but due to glycation three-dimension protein is inactive. In the structures below first is three-dimension structure of human serum albumin and it is completely functional but after glycation the green lines showed the glycation of protein and in this form, it is not able to perform its normal functions. Below the pictures explained single amino acid glycation consequences. When amino acid residue at 114 position was glycated the normal functioning of human serum albumin is stopped. When the Ramachandran plot was constructed for normal human serum albumin all amino acids fall in allowed region and protein is fully functional. When the Ramachandran plot was constructed for glycated human serum albumin all amino acids fall in allowed region but the protein is un functional. This is due to glycation, all amino acids lost their functionality. Their red color showed dead proteins.


DISCUSSION

Glycation-induced changes in the structure and function of proteins are of particular interest since numerous studies in vivo have reported the strong involvement of glycated albumin in the development and progression of chronic diabetes complications\textsuperscript{5,11}. Various beneficial functions linked to Albumin, including regulating oncotic pressure, the transport and binding capacities of metabolites and therapeutic agents\textsuperscript{12}. The most striking property of HSA is its antioxidant activity, which has been shown to be impaired due to glycation\textsuperscript{13}. The change in albumin structure after diabetes was predicted by glycation of normal albumin and albumin of diabetic patients in the form of carbonyl group. The comparison of both models showed that due to glycation three-dimensional protein is inactive. Our results can be compared with the work of Monacelli who found that the structure of albumin modifies with enzymatic and non-enzymatic glycation\textsuperscript{5}. The glycation of albumin has significant effect on albumin action and cell functions\textsuperscript{6}. These structural and functional changes due to glycation in vivo has been found in vitro in commercial bovine serum albumin (BSA). Due to glycation, the albumin structure is changed and it reduced the drug affinity of albumin\textsuperscript{14}. Our results showed lost functionality of protein in (Fig 1, 2) where green lines displayed glycation.

CONCLUSION

The glycation of HSA has been an issue of interest for several decades and especially in the past ten years. Part of this interest relates to the clinical use of glycated HSA as a biomarker for the control of blood sugar over short to medium periods. There is also increasing interest in the effects of glycation on the structure of HSA. A variety of methods have been used to examine the number, location, and type of modifications that can occur with glycated HSA. Many possible modification sites for both early-stage glycation products and AGEs have been identified on this protein, but a smaller subset of these sites appear to be involved in most of these reactions. Some information about the similarities or differences between in vivo and in vitro glycated HSA has been obtained from such work. The overall glycation rate, the thermodynamics of this process, and the modification rate in certain regions were considered in such studies. The role of glycation conditions in the types of modifications formed was also examined.

Author’s Contribution:
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Revisiting Critically: Sajjad Ghani, Fariha Niaz
Final Approval of version: Sajjad Ghani

\[ \text{Fig 1, 2} \]
Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

The Influence of Plasma Protein Glycation in Diabetes Mellitus Type 2 and its Complications
Zarrin Khaliq¹, Sajjad Ghani², Fariha Niaz³ and Sidra Mushtaq⁴

ABSTRACT

Objective: The present project was planned to study effect of Glycation in diabetic complications.

Study Design: Correlational and experimental study

Place and Duration of Study: This study was conducted at the DHQ Faisalabad and Allied hospital Faisalabad from March 2018 to April 2019.

Materials and Methods: A total 100 patients were taken. They were grouped in 5, each having 20 patients. These groups were according to the complications, normal and normal diabetics. Blood samples of diabetic patients with and without complication were collected from D.H.Q and Allied Hospital Faisalabad. The information included age, sex, and duration, family history of diabetics, treatment status and diabetic control in relation to complications. (Neuropathy, nephropathy, foot ulcer, retinopathy) were taken by using a self-designed Performa. Specific techniques of spectrophotometer and software were used to analyze all the collected samples. The biochemical parameters were protein estimation, glucose estimation, determination of level of Glycation, determination of protein marker by SDS_PAGE analysis.

Results: We have found levels of glucose, protein and Glycation for both normal and diabetic patients. Correlational analysis between glucose, and Glycation level showed positive outcomes for normal subjects and r=0.242 for glycated. Analysis between protein and Glycation level for normal individuals was r=0.4977. After SDS-PAGE Analysis of diabetic patient's blood with complications and without complications and normal revealed a difference of migrating bands with molecular weights between 20 and 30. One faster migrating band was missing in diabetic patients with Ischemic heart disease and two bands were of less intensity in with neuropathy and foot ulcer of age 64 years. While the diabetic patients without complications and normal showed no missing band. So, our results show that some protein is missing in diabetic complications.

Conclusion: Our results suggest that increased level of Glycation participate in long term complications.

Key Words: Diabetic complications, Glycation, plasma protein, glucose

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INTRODUCTION

Diabetes mellitus is a syndrome characterized via persistent hyperglycemia this is because of relative insulin deficiency, or resistance or both.

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It impacts extra than 30 million humans international. Diabetes is generally irreversible and, even though sufferers will have a reasonably everyday lifestyle, its overdue complications results in reduces existence expectancy and extensive uptake of heath resources. Macro-vascular disorder results in an increased incidence of coronary artery disease, peripheral vascular disease and stroke.¹ Micro-vascular damage reason diabetic retinopathy and nephropathy and contributes to diabetic neuropathy. Diseases result in lessens life expectancy and considerable uptake of health resources². Almost 366 million people worldwide have diabetes and till 2030 it will affect 522 million people worldwide (Guariguata et al. 2011). WHO ranked Pakistan at 7th on diabetes prevalence list. Recent view on the occurrence has shown that about more than 4.7 million people suffering from diabetes.³ The continual hyperglycemia of diabetes is related to long time damage; disorder and failure of numerous organs, in particular the eyes, kidney, nerves, coronary heart and blood vessels, numerous pathogenic methods are concerned in the improvement of diabetes. These
variety from autoimmune destruction of β cells of the pancreas with consequent insulin deficiency to abnormalities the bring about resistance to insulin movement.

Diabetes can commonly be recognized on the idea of fasting or random blood glucose size. The GTT should be reserved for border line cases simplest. The main aim of diabetes management is to achieve the normal glycemic state long follow-up studied have shown good glucose control may prevent or delay the manifestation of complication, despite the long duration of the disease.

Erythrocytes are freely permeable to glucose. In cell, glucose attaches to the free ends of amino acids of hemoglobin molecules and this process called non-enzymatic glycation, caused glycosylated hemoglobin to be formed directly proportional to the blood glucose concentration. As the average erythrocyte life span is about 120 days, glycosylated hemoglobin levels give information on the mean average blood glucose level over the past 2 to 3 months. Glycosylation of serum proteins, mainly albumin, has also been used in diabetes monitoring. The half-life of albumin is 2 to 3 weeks and degree of albumin glycosylation hence provides an index of glycemia over a shorter period of time glycosylation of hemoglobin. One of the most widely used measurements of glycosylated serum proteins is fructosamine assay. The method of glycation has noteworthy impact on structures and functions of proteins. The analysis of proteins has always been a critical part of medical research and molecular prognosis. Proteins circulating in human blood are easily accessible and may examine at once to produce diagnostic data on disorder repute in sufferers. Molecular weight determination of plasma from normal subjects in assessment from diabetic patients may additionally monitor huge and biologically essential difference in those proteins.

The main objective of the research was to increase a relationship between the blood glucose stage and plasma proteins glycation and protein awareness with diabetic complications like neuropathy, nephropathy, foot ulcer, and retinopathy.

MATERIALS AND METHODS

The main objective of the project was to develop a relationship between the blood glucose level and plasma proteins glycation and protein concentration with diabetic complications like neuropathy, nephropathy, foot ulcer, and retinopathy. To check the protein profile SDS_PAGE analysis was done. A total 100 patients were taken. They were grouped in 5, each having 20 patients. These groups were according to the complications, normal and normal diabetics. Blood samples of diabetic patients who were clinically diagnosed by physician were collected from D.H.Q. hospital Faisalabad and Allied Hospital Faisalabad.

Blood of diabetics without complications and non-diabetics were also collected from above mentioned hospitals. 5 ml of blood sample from each of 100 patients were collected by using sterilize disposable syringes by venopuncture. The blood is transferred into tubes containing the anticoagulant like EDTA or heparin. These samples containing anticoagulants mixed gently by tapping then centrifuge at 3000 rpm. Plasma frictions were collected by using micro pipette, and then these samples were collected into autoclaved Eppendorf tubes and stored at -20 degree centigrade. In this study we included socioeconomic and biochemical parameters. Basic informations of patients were collected by using a typical Performa containing all the information and history of patients. These informations included age, sex, and duration, family history of diabetics, treatment status and diabetic control in relation to complications. (Neuropathy, nephropathy, foot ulcer, and retinopathy).

Specific techniques of spectrophotometer and software were used to analyze all the collected samples. The biochemical parameters were protein estimation, glucose estimation, determination of level of Glycation, determination of protein marker by SDS_PAGE analysis.

RESULTS

SDS-Page Analysis of plasma of diabetic patients with complications showed bands of less intensity in neuropathy, foot ulcer and retinopathy and a missing band in nephropathy.

In normal subjects, the glycation level ranged between 0.024 mole/mole of protein to 0.30 mole / mole of protein.

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In normal subjects, the glycation level ranged between 0.024 mole/mole of protein to 0.30 mole / mole of protein.
mg/dl to 283 mg/dl as in normal but their glucose level will be monitored during disease. These changes in glucose levels clearly indicates that glycation in diabetic patients increases the blood glucose level. The protein concentration in normal ranged from 6g/100 ml to 14g/100 ml. Protein concentration in diabetics was 5g/100 ml to 14g/100 ml. Correlation between glycation level and glucose in normal subjects showed a positive correlation (r= 0.4199), as shown in figure 3. Using the standard curve and the r intercept the dilutions for the obtained glucose samples were prepared in order to perform SDS-PAGE.

Figure No.2: Correlation between Glycation level and protein for normal

Figure No.3: correlation between glycation and glucose in diabetic patients

Considering the correlation between glycation level and proteins in normal subjects showed a positive correlation (r= 0.4977), as shown in figure. Using the standard curve and the r intercept the dilutions for the obtained protein samples were prepared in order to perform SDS-PAGE for the determination of molecular weight. Correlation between diabetes and glucose in diabetic patients also showed a positive result (r= 0.242). The standard curve was plotted by calculating the RF values of each standard protein against the log 10 of its molecular weight (Figure). The molecular weight of the unknown polypeptide or protein was determined by finding its RF value on the standard curve and reading the log10 molecular weight from the ordinate. The anti-log of this number was the molecular weight of the protein. Low (6,500 to 66,000) and High molecular weight protein markers (25000-127000 Daltons) from Sigma Chemicals and from life Technologies were used in this study.

Figure No.4: Analysis

After SDS-PAGE Analysis of diabetic patient's blood with complications and without complications and normal revealed a difference of migrating bands with molecular weights between 20 and 30. One faster migrating band was missing in diabetic patients with Ischemic heart disease and two bands were of less intensity in with neuropathy and foot ulcer of age 64 years. While the diabetic patients without complications and normal showed no missing band. So, our results show that some protein is missing in diabetic complications.

Lane 1: Protein marker; Lane 2: Diabetic with nephropathy
Lane 3: diabetic with neuropathy; Lane4: Normal
Lane 5: Diabetic ischemic heart disease
Lane 6: Diabetic with foot ulcer;
Lane 7: Neuropathy with foot ulcer
DISCUSSION

The present study was designed to study non-enzymatic glycation which is one of the primary modification factors that contribute to various alterations of intrinsic protein structure and functions. Blood is a complex mixture of different biological molecules including proteins. The analysis of proteins has always been an important part of medical research and molecular diagnosis. Proteins circulating in human blood are readily accessible and can analyze directly to produce diagnostic information on disease status in patients. So blood sample was taken from diabetic and non-diabetic patients. To study the status of glycation in controlled and diabetic patients was the first objective of the study. For it level of glycation was measured for further proceedings, result showed glycation level ranged from 0.047 mole/mole of protein to 0.448 mole/mole of protein. The value of glycation level in diabetes patients ranged from 0.032 mole/mole to 1.96 mole/mole of protein. The results can be compared with who checked the glycation level from 0.2 mole/mole to 1.13 mole/mole of protein. Our results can be compared with who reported the increase level of glycosylated proteins in diabetics as compared to normal subjects. Glucose level in normal range from 83 mg/dl to 140 mg/dl. Our results can be compared with who reported glucose range from 45mg to 130 mg/dl in normal. Results can be compared with who reported that protein level of diabetic patients was mostly like normal healthy persons. Our results are not compared to who reported that malnutrition caused low proteins level as 3.5 g/100ml. Correlation between glycation level and glucose in normal subjects showed a positive correlation ($r=0.4977^*$). Correlation between glycation level and glucose in patients of diabetes showed a positive correlation ($r=0.242^*$). After SDS-PAGE Analysis of diabetic patient's blood with complications and without complications and normal revealed a difference of migrating bands with molecular weights between 20 and 30. One faster migrating band was missing in diabetic patients with Ischemic heart disease and two bands were of less intensity in with neuropathy and foot ulcer of age 64 years. While the diabetic patients without complications and normal showed no missing band. So, our results show that some protein is missing in diabetic complications. Our results can be compared with who observed the fast migrating bands of molecular weights between 20 and 40kDa in normal subjects but not in diabetic patients. This difference of range of molecular weights may be due to age difference. Increase mol.wts of human proteins for diabetic subjects is also revealed through the work of. The difference in molecular weights of protein among diabetic and non-diabetic is due to complications.

CONCLUSION

Diabetes mellitus is a disease caused by either insulin deficiency or nonfunctioning of hormone insulin. The insulin deficiency results in prolonged exposure to hyperglycemia which is primary factor for diabetic complication. Therefore, present project was planned to analyze relationship between protein concentration and Glycation and diabetic complications. Hence our results suggest that increased level of Glycation participate in long term complications.

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ABSTRACT

Frequency and Causes of Medico-Legal Cases

Objective: To determine the frequency and causes of medico-legal cases reported at three major hospitals of Karachi City.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the three major tertiary care hospitals of Karachi, Abbasi Shaheed Hospital, Jinnah Postgraduate Medical Centre and Civil Hospital, from January 2007 to December 2018.

Materials and Methods: Total of 306,406 medico-legal cases in twelve years retrospective study period received at three major hospitals of Karachi were overseen. The data was collected with the permission of concerned authorities. Assault, Intoxication, Accident and Sexual Assault medico-legal cases were included in the study. A detailed examination was conducted in each case to determine the different causes of injury. Medico-legal deaths were excluded in the present study. The results were collected from the respective hospitals on a prepared structured Performa and were statistically analyzed using SPSS version 15.

Results: Out of all, in our study, among medico-legal cases reported (306,406), assault cases were the predominant 190,029 (62.01%), followed by Intoxication 60,233 (19.65%), accident 47,543 (15.51%) and sexual assault cases, 8,601 (2.8%) respectively. Among the outnumber assault medico-legal cases, the commonest one caused by hard and blunt object 135,086 and amongst accident cases were of road traffic accident 30,896. In sexual assault cases, rape cases were about 5,505 and in Intoxication cases, 54,270 Poisoning were at highest.

Conclusion: Hard and blunt injuries remained most common type of injury. Rape and poisoning cases are also recognized as most differentiating part of study. Enactment of the laws is the need of present period which can curtail accident cases and other medico-legal cases.

Key Words: Medico-legal, Assault, Injury, Karachi.

INTRODUCTION

WHO defines Injury as those caused by acute exposure to physical agents such as mechanical injury, heat, electricity, chemical or ionizing radiation interacting with the body in amount and rate that exceed the threshold of human tolerance. It is important to clarify injuries for proper dispersal of justice in any system. The detailed and distinct record of injuries and other pointful particulars of the injured noted during the medico-legal examination form the footing of medico-legal diagnosis and epidemiological observations in the criminal justice system.

In all government hospital a medico-legal officer or a casualty medical officer may be asked to examine an injured person. The details of examination must be entered in an accident register, which would be confidential record and if required by a court of law should be produced in the court. A case in general is said to be labelled “medico-legal” when the attending doctor by takes history and doing examination of the patient comes to know that it is required by law enforcing agencies to make inquiry and affix the responsibility for the case. Medical officers or medico-legal officers are to be trained for how to write a “certificate” or “report”, so that all the competent facts to consummate the opinion are mentioned properly and with possible scientific deviation and limitation without giving undue weight age to the observed facts. The role of forensic expert is to help in the administering of justness. The qualities needed in forensic expert are qualification, training and experience to identify the problem with professional knowledge, detect accurately and decode the results properly to form a scientific conclusion and to furnish speculation on his findings. Results of study of frequency and types of medico-legal injuries showed that males are more likely to be involved in such cases compared to females.

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involved in outdoor work therefore they are involved in such mishaps or violation. Manner of injury is detected mainly on circumstantial evidence but to some extent the question can be solved by the medico-legal officer by examination of an injured person. One of the comportment of injury is assault which is due to any gesture or application of force causing harm to another person. In assault cases, apart from detail of injuries sometimes portrayal of pattern of tears in apparel is a valuable clue to ascertain the weapon of an offence. Examination of apparel is very valuable clue to ascertain the weapon of an offence.

Accidents as the manner of injury account for in majority of cases, these injuries occur due to unplanned, uncontrolled event which has led to or could have led to injury to people. Attempted suicide, which is failing act of person to tail the life and self-inflicted injuries for the purpose of falsely stigmatize the other persons are also other manners of injury.

Trauma is one of the most frequently encountered medical emergencies and second leading cause of death and disability. In Karachi, violence shares significantly to trauma cases, but RTA still contributes to most of the cases reported. Burn injuries, a unique form of trauma which is sometimes available, is categorized among the most severe injuries an individual can experience.

MATERIALS AND METHODS

The 12 years study was conducted from January 2007 to December 2018. Total of 306,406 medico-legal cases in this retrospective study period at three major hospitals of Karachi were overseen. The data was collected with the permission of authorities. Assault, Intoxication, Accident and Sexual Assault medico-legal cases were included in the study. A detailed examination was conducted in each case to determine the different causes of injury. Medico-legal deaths were excluded in the present study. The results were collected from the respective hospitals on a prepared structured Performa and were statistically analyzed using SPSS version 15.

RESULTS

Out of all medico-legal cases, assault (62.01%) was the predominant followed by intoxication (19.65%), accident (15.51%) and sexual assault (2.80%) cases. Total of assault 190,029 cases, 135,086 by hard and blunt object followed by firearm 33,641, sharp object 9,414, explosive 3,795, maltreatment 926 and human bite 321 respectively. Number of brought dead cases recorded was 6,846.

| Table No. 1: Total No. Of Medico-Legal cases (2007-2018) |
|-----------|---------|---------|
| Medico-Legal cases | Frequency | Percentage |
| Assault | 190,029 | 62.01 |
| Intoxication | 60,233 | 19.65 |
| Accident | 47,543 | 15.51 |
| Sexual assault | 8,601 | 2.80 |
| Total cases | 306,406 | 100 |

| Table No. 2: Year wise Pattern of Assault cases in the study period (2007-2018) |
|-------------|---------|---------|---------|---------|--------|---------|--------|
| Year | Hard & Blunt | Firearm | Sharp Edge | Explosive | Maltreatment | Human bite | Brought dead | Total |
| 2007 | 12,241 | 2,891 | 890 | 344 | 142 | 60 | 542 | 17,110 |
| 2008 | 11,855 | 3,330 | 1,106 | 147 | 139 | 63 | 458 | 17,098 |
| 2009 | 11,770 | 3,388 | 1,075 | 266 | 164 | 44 | 541 | 17,248 |
| 2010 | 11,900 | 3,103 | 1,029 | 420 | 142 | 58 | 502 | 17,154 |
| 2011 | 11,394 | 3,719 | 729 | 342 | 105 | 9 | 722 | 17,020 |
| 2012 | 9,911 | 4,070 | 694 | 349 | 85 | 41 | 885 | 16,035 |
| 2013 | 10,355 | 4,367 | 583 | 952 | 41 | 21 | 1,304 | 17,623 |
| 2014 | 10,895 | 3,133 | 766 | 578 | 38 | 4 | 874 | 16,288 |
| 2015 | 12,253 | 2,398 | 735 | 204 | 20 | 3 | 486 | 16,099 |
| 2016 | 3,170 | 411 | 191 | 101 | 7 | 2 | 113 | 3,995 |
| 2017 | 13,620 | 1,566 | 769 | 27 | 29 | 7 | 219 | 16,237 |
| 2018 | 15,722 | 1,265 | 847 | 65 | 14 | 9 | 200 | 18,122 |
| Total | 135,086 | 33,641 | 9,414 | 3,795 | 926 | 321 | 6,846 | 190,029 |
Among the accident cases, most frequent was Road traffic accident cases 30,896, followed by 7,713 burn cases, 1,837 fall cases, 234 train accident cases, 206 factory cases and brought dead cases were 6,657. (Table 3, Graph 3). Total number of sexual assault cases 8,601, out of which 5,505 rape, sodomy 1,318 and under this heading 1,778 age estimation cases reported. (Table 4, Graph 4)

Amidst the 60,233 intoxication cases, 54,270 are of general poisoning followed by 4,724 of alcohol poisoning and 1,239 of drug poisoning. (Table/Graph 5)

### Table No.3: Year wise Pattern of Accident cases in the study period (2007-2018)

<table>
<thead>
<tr>
<th>Year</th>
<th>Road traffic</th>
<th>Burns</th>
<th>Fall</th>
<th>Railway</th>
<th>Factory</th>
<th>Brought Dead</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>2,981</td>
<td>582</td>
<td>252</td>
<td>21</td>
<td>25</td>
<td>469</td>
<td>4,330</td>
</tr>
<tr>
<td>2008</td>
<td>3,052</td>
<td>702</td>
<td>208</td>
<td>23</td>
<td>22</td>
<td>469</td>
<td>4,476</td>
</tr>
<tr>
<td>2009</td>
<td>3,052</td>
<td>807</td>
<td>136</td>
<td>26</td>
<td>34</td>
<td>550</td>
<td>4,605</td>
</tr>
<tr>
<td>2010</td>
<td>3,095</td>
<td>789</td>
<td>140</td>
<td>25</td>
<td>23</td>
<td>427</td>
<td>4,499</td>
</tr>
<tr>
<td>2011</td>
<td>2,360</td>
<td>720</td>
<td>149</td>
<td>10</td>
<td>13</td>
<td>352</td>
<td>3,604</td>
</tr>
<tr>
<td>2012</td>
<td>2,649</td>
<td>794</td>
<td>228</td>
<td>23</td>
<td>18</td>
<td>558</td>
<td>4,270</td>
</tr>
<tr>
<td>2013</td>
<td>2401</td>
<td>667</td>
<td>102</td>
<td>22</td>
<td>5</td>
<td>649</td>
<td>3,846</td>
</tr>
<tr>
<td>2014</td>
<td>2,282</td>
<td>631</td>
<td>97</td>
<td>27</td>
<td>2</td>
<td>625</td>
<td>3,664</td>
</tr>
<tr>
<td>2015</td>
<td>2,709</td>
<td>604</td>
<td>153</td>
<td>13</td>
<td>8</td>
<td>824</td>
<td>4,311</td>
</tr>
<tr>
<td>2016</td>
<td>793</td>
<td>483</td>
<td>0</td>
<td>4</td>
<td>39</td>
<td>271</td>
<td>1,590</td>
</tr>
<tr>
<td>2017</td>
<td>2,694</td>
<td>506</td>
<td>189</td>
<td>18</td>
<td>5</td>
<td>651</td>
<td>4,063</td>
</tr>
<tr>
<td>2018</td>
<td>2,828</td>
<td>428</td>
<td>183</td>
<td>22</td>
<td>12</td>
<td>812</td>
<td>4,285</td>
</tr>
<tr>
<td>Total</td>
<td>30,896</td>
<td>7,713</td>
<td>1,837</td>
<td>234</td>
<td>206</td>
<td>6,657</td>
<td>47,543</td>
</tr>
</tbody>
</table>

### Table No.4: Year wise Pattern of Sexual Assault cases in the study period (2007-2018)

<table>
<thead>
<tr>
<th>Year</th>
<th>Active Poison</th>
<th>Passive Poison</th>
<th>Active Sodomy</th>
<th>Passive Sodomy</th>
<th>Male Age Determination</th>
<th>Female Age Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>122</td>
<td>222</td>
<td>45</td>
<td>57</td>
<td>70</td>
<td>83</td>
</tr>
<tr>
<td>2008</td>
<td>157</td>
<td>267</td>
<td>54</td>
<td>70</td>
<td>124</td>
<td>82</td>
</tr>
<tr>
<td>2009</td>
<td>90</td>
<td>239</td>
<td>33</td>
<td>54</td>
<td>55</td>
<td>70</td>
</tr>
<tr>
<td>2010</td>
<td>121</td>
<td>266</td>
<td>33</td>
<td>51</td>
<td>52</td>
<td>75</td>
</tr>
<tr>
<td>2011</td>
<td>145</td>
<td>278</td>
<td>43</td>
<td>57</td>
<td>72</td>
<td>69</td>
</tr>
<tr>
<td>2012</td>
<td>149</td>
<td>294</td>
<td>53</td>
<td>44</td>
<td>64</td>
<td>65</td>
</tr>
<tr>
<td>2013</td>
<td>177</td>
<td>325</td>
<td>34</td>
<td>45</td>
<td>61</td>
<td>81</td>
</tr>
<tr>
<td>2014</td>
<td>201</td>
<td>324</td>
<td>30</td>
<td>59</td>
<td>117</td>
<td>63</td>
</tr>
<tr>
<td>2015</td>
<td>204</td>
<td>342</td>
<td>85</td>
<td>61</td>
<td>122</td>
<td>70</td>
</tr>
<tr>
<td>2016</td>
<td>89</td>
<td>190</td>
<td>16</td>
<td>24</td>
<td>73</td>
<td>69</td>
</tr>
<tr>
<td>2017</td>
<td>254</td>
<td>331</td>
<td>37</td>
<td>72</td>
<td>39</td>
<td>77</td>
</tr>
<tr>
<td>2018</td>
<td>307</td>
<td>411</td>
<td>115</td>
<td>146</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>Total</td>
<td>5,505</td>
<td>1,318</td>
<td>1,778</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table No.5: Year wise Pattern of Intoxication cases in the study period (2007-2018)

<table>
<thead>
<tr>
<th>Year</th>
<th>Poison</th>
<th>Alcohol</th>
<th>Drugs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>2,607</td>
<td>515</td>
<td>223</td>
<td>3,345</td>
</tr>
<tr>
<td>2008</td>
<td>2,844</td>
<td>575</td>
<td>179</td>
<td>3,598</td>
</tr>
<tr>
<td>2009</td>
<td>2,917</td>
<td>512</td>
<td>21</td>
<td>3,450</td>
</tr>
<tr>
<td>2010</td>
<td>3,119</td>
<td>609</td>
<td>214</td>
<td>3,942</td>
</tr>
<tr>
<td>2011</td>
<td>3,161</td>
<td>462</td>
<td>222</td>
<td>3,845</td>
</tr>
<tr>
<td>2012</td>
<td>6,618</td>
<td>342</td>
<td>110</td>
<td>7,070</td>
</tr>
<tr>
<td>2013</td>
<td>6779</td>
<td>289</td>
<td>53</td>
<td>7,121</td>
</tr>
<tr>
<td>2014</td>
<td>6247</td>
<td>405</td>
<td>62</td>
<td>6,714</td>
</tr>
<tr>
<td>2015</td>
<td>6330</td>
<td>290</td>
<td>74</td>
<td>6,714</td>
</tr>
<tr>
<td>2016</td>
<td>382</td>
<td>97</td>
<td>16</td>
<td>495</td>
</tr>
<tr>
<td>2017</td>
<td>6102</td>
<td>282</td>
<td>38</td>
<td>6,422</td>
</tr>
<tr>
<td>2018</td>
<td>7144</td>
<td>346</td>
<td>27</td>
<td>7,517</td>
</tr>
<tr>
<td>Total</td>
<td>54,270</td>
<td>4,724</td>
<td>1,239</td>
<td>60,233</td>
</tr>
</tbody>
</table>
DISCUSSION

In the present study, total numbers of 306,406 cases were studied, reported to the emergency department of Abbasi Shaheed Hospital, civil hospital and Jinnah postgraduate medical centre from January 2007 to December 2018. Predominant cases of assault were noted, following to assault were of intoxication. Poisoning outnumber among the intoxication cases. This might be due to the easy availability of the desired substance, low cost and also awareness of the effect of the substance. There is a gradual increase in the intoxication cases with the passage of years since 2007 till 2013. The number of intoxication was also eminent in year 2014 & 2015 but there was remarkable decline in the year 2016. Repeatedly the number of intoxication cases ascent in the year 2017 and 2018. After the intoxication cases we have accident cases, RTA being the highest. As Conditions of city roads are not perfect, untrained drivers and condition of the vehicle are also the factors that contribute the number of 30,896 RTA cases among accident cases.

In the first national injury survey in Pakistan, the yearly overall incidence of injury was found to be 41 injuries for every 1,000 persons converse to the low incidence in the western world.14 RTIs have a yearly incident of 15 injuries for every 1000 individuals and take lives of 500 and hurt 12,000 people in Pakistan every year.15 This is contrary to the low incidence in England and Wales where injury rate is 6.4/100,000 residents.16 Road traffic accidents may be associated to non-existence of safety rules, horrific road infrastructure, avoidance of helmets and seat belts use, lack of implementation of traffic laws and legislations, careless, rash and negligent driving and availability of limited trauma care facilities in Pakistan.17-18

According to 2011 and 2010 local public health data, the annual count of firearm deaths and injuries in New York City exceeded 2000; there were 366 firearm fatalities, 999 firearm hospitalizations and 691 firearm injury emergency department visits.19 Multiple factors leading into preeminent number of assault cases could be situation of the city, increase terrorism, suicidal bomb attacks, snatching, unemployment and above all are stress factors. Due to any of these we are in exasperating life and people are ready to beat, injured or even kill someone on minute quarrels. Easy availability of object of assault contributes a lot. Study conducted by Romana et al on 3105 medico-legal cases revealed RTA (38%) followed by physical assault (32%) and sharp weapon injury (19%).20 These findings were homogenous with the study conducted at Nepal.21 On the contrary study conducted in UK, where
The prevalence of penetrating trauma was on highest with 86.8% and firearm injuries with 13.3%.16 Talha et al recognized that amongst the medico-legal cases at Bahawalpur, blunt weapon contributed 55% while firearm cases added only 2% to the total.22 Malik et al reporting 33% blunt injuries and 4% firearm injuries in medico-legal cases at Rawalpindi.23 Among the sexual assault medico-legal cases, we have rape and sodomy cases. Also constituted the age determination cases in both male and female. In the 12 year study period we have 5,505 rape cases and 1,318 sodomy cases. Saeed et al24 revealed that maximum number of medico-legal cases had the injuries due to physical assault 717(85.66%) followed by sexual assault in 54 (6.45%) cases in one-year study period of 2012. In Pakistan, the rape rate is 16.8 per 100,000 women with 10% being gang rapes according to 2013 National Crime Data Report. Worldwide the incidence is 225 rapes per 100,000 women in South Africa, 58 rapes per 100,000 women in United States and 22,000 rapes per year in India.25 In USA, 683,000 women are raped per year. This is in spite of the fact that sexual assault is the least reported of the violent crimes with only 16-39% being reported to the police.

CONCLUSION

Injuries can be prevented by proper education, awareness and training of safety standards which are required to be implemented strictly. Teaching and training facilities should be more improved for the staff which will be a benefaction for our population. Doctors who are involved in handling medico-legal cases need to be more trained.

Due to increase in violence and accidents the requisite for round the clock availability of medical experts in casualty and emergency departments to deal with the medico-legal cases is required. Emergency should be well equipped with the required equipments, antidotes, drugs and other remedies which are used for the treatment of victim especially in cases of poisoning and assault.

Providing facts about sexual abuse is one of the ways to raise awareness. Attentiveness of the facts is one of the several preventive measures that can be taken to assist you in making better decisions to keep you and someone you know safe.

Author’s Contribution:

Concept & Design of Study: Roohi Ehsan
Drafting: M. Faiz-uddin
Data Analysis: Wasiq Ahmed
Revisiting Critically: Roohi Ehsan, Wasiq Ahmed
Final Approval of version: Roohi Ehsan

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

REFERENCES


Medical Student’s Performance and Satisfaction with Online Theory Exams during the Covid-19 Pandemic

Muhammad Suleman Sadiq Hashmi, Afifa Tabassum, Sobia Ali and Faiza Ambreen

ABSTRACT

Objective: To compare the performance of medical undergraduate students in online and traditional exams and to gauge student satisfaction regarding online exams.

Study Design: Cross Sectional study

Place and Duration of Study: This study was conducted at the Liaquat National Hospital and Medical College during the period of June-July 2020.

Materials and Methods: The target population was second year MBBS students who had given a paper based traditional exam in their first year of medical college and an online exam in second year. Scores of both the exams were compared. Students ‘opinions about the online exam were collected through an online survey. Data was analyzed using SPSS version-17.

Results: There were 88 students who had attempted both year 1 and 2 examinations. There were statistically significant differences amongst median scores of both exams [p=0.016]. Out of 78 responses received majority of the students were satisfied with the instructions and felt that the amount of proctoring was sufficient for a fair exam. Students were equally divided in term of technical or connectivity issues and background noise. Regarding the entire online examination most students reported similar concerns i.e. not fully prepared for the exam due to Covid-19 patients at home and lack of resources. As compared to traditional exam students found online exam difficult to attempt due to technical issues such as power outages, internet issues and software glitches.

Conclusion: With better performance in an online exam, students still prefer the traditional exam format better than online exams due to several reasons. This highlights the importance of investing in e-learning and e-assessment infrastructure.

Key Words: Students’ Performance, Online assessment, Traditional Exam, Medical Education


INTRODUCTION

Globally educational institutions are facing suspension of all academic activities due to pandemic. Institutes have a responsibility to their students to continue delivering education as these restrictions may be prolonged further. Especially institutions like medical university cannot remain suspended as there is growing demand of medical workforce in the face of COVID-19 pandemic. Hence the current circumstances have increased the utilization of modalities such as video conferencing, mobile apps, surveys, and WhatsApp messages.

Institutions are becoming more interested in engaging their students and delivering quality content.1,2 When Covid-19 was declared a pandemic by the WHO soon after medical institutions changed their academic and teaching strategies to meet the students’ needs during lockdown. Some medical institutions focus on online teaching while other emphasized on self-learning abilities of students. Assessment methods were also modified as some medical institute’s implemented pass/fail exams, online exams, and research projects while others postponed their final exams. In Pakistan, medical institutes began online lectures and altered the evaluation benchmarks for the foundation academic years to mainly depend on online examination, assignments and quizzes while the clinical rotations and final exams of the clinical years were postponed.3-5 Worldwide, online examinations are being used for assessment in both traditional and online learning. Due to the current Covid-19 pandemic their use has increased further.6 Online examinations come with both advantages and disadvantages. Advantages include time reduction, quick results, cost effectiveness and automated record keeping for item analysis.6,7 It also gives the student the luxury to give the exam in a non-threatening environment leading to decreased test anxiety among students.8
anxiety as compared to a traditional exam format with high test anxiety and stress. This is one important factor that is strongly related to student achievement\(^5\). In contrast disadvantages include technical problems, security concerns, external resources required, faculty and student resistance\(^7\). There is a small amount of literature evaluating student performance in online examination. Students’ opinions are also important in success and effectiveness of online exams.

Liaquat National Hospital and Medical College initiated the use of online exams in the context of the current pandemic. Online exams were utilized for conducting the Mid-term and Pre-prof exams of MBBS undergraduates. The current study aims to examine the academic accomplishment of students in online exams as compared to traditional exams and to gauge student satisfaction regarding online exams.

**MATERIALS AND METHODS**

This cross sectional study was conducted at Liaquat National Hospital and Medical College. The target population was second year MBBS students who had given a paper based traditional exam in their first year of medical college and an online exam in second year. The first year exam comprised of four modules i.e. Locomotor, Respiratory-1, Cardiovascular-1 and GIT&Liver-1, which were held during the period of July-September 2019. The second year midterm exam comprised of 3 modules i.e. Neurosciences-1, Special senses and Head & Neck which was held in June 2020. The scores of all students who had given both first year and second year exams were included. Those students who had given either one of the exams or were repeaters were excluded from the study. Both exams consisted of content from three areas: anatomy, physiology and biochemistry and had questions in the one best choice type format. The traditional paper based exam was conducted in the college premises. Students marked their answers on OMR sheets that were graded later electronically. The online exam was conducted via EDMODO and ZOOM. EDMODO was used to deliver the paper whereas ZOOM was used to monitor the exam. Since this was the first experience of students with online exam, a mock exam was held one day before the exam. Students logged on to both ZOOM and EDMODO from their homes on the day of the exam and they were briefed about the process again. If they encountered any problems they could communicate with administrator or post their query via ZOOM. Upon completion of the exam the papers were graded automatically in EDMODO.

The scores of all students in both the exams were recorded on an excel sheet. The overall maximum score of year 1 exam was 250 and of second year was 150. Student scores were converted to percentages. Data was analyzed using SPSS version-18. Statistical assumptions were evaluated using statistical tests. Students’ opinions about the online exam were collected through an online survey immediately after the exam. The survey consisted of 15 questions out of which 12 were closed ended and 3 were open ended questions. Frequencies were calculated for quantitative output response. Responses of open ended questions were analyzed and coded.

**RESULTS**

There were 88 students who had attempted both year 1 and year 2 examinations. As the data was non-normal, Mann-Whitney U Test was used to demonstrate statistical significance of data set. There were statistically significant differences amongst median scores of both exams \([p=0.016]\) (Table I).

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of students</th>
<th>Mean</th>
<th>Sum of Ranks</th>
<th>Median</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>First year traditional exam</td>
<td>88</td>
<td>79.23</td>
<td>6972.00</td>
<td>62.0</td>
<td>0.016</td>
</tr>
<tr>
<td>2nd year online exam</td>
<td>88</td>
<td>97.77</td>
<td>8604.00</td>
<td>63.5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Using Mann-Whitney U test with p value <0.05 as statistically significant

**Table No.2: Students’ perception of online examination**

<table>
<thead>
<tr>
<th>Question</th>
<th>Great</th>
<th>Pretty Good</th>
<th>OK</th>
<th>Not so Good</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How do you feel about online exam process?</td>
<td>12%</td>
<td>15%</td>
<td>33%</td>
<td>27%</td>
<td>13%</td>
</tr>
<tr>
<td>2. What was the level of difficulty of exam?</td>
<td>Very Easy</td>
<td>Easy</td>
<td>Neutral</td>
<td>Difficult</td>
<td>Very Difficult</td>
</tr>
<tr>
<td></td>
<td>3%</td>
<td>13%</td>
<td>47%</td>
<td>24%</td>
<td>13%</td>
</tr>
<tr>
<td>3. How do you feel about your performance in this exam?</td>
<td>Great</td>
<td>Pretty Good</td>
<td>OK</td>
<td>Not so Good</td>
<td>Terrible</td>
</tr>
<tr>
<td></td>
<td>4%</td>
<td>21%</td>
<td>40%</td>
<td>25%</td>
<td>10%</td>
</tr>
<tr>
<td>4. Is your performance in this exam a good indicator of how well you know/understand the topics/content?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>60%</td>
<td>40%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. How well did Zoom class rooms sessions, Edmodo activities</td>
<td>Not at all</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
<td>Really</td>
</tr>
</tbody>
</table>
and assignment/quizzes prepare you for this exam? (0) well (4) 14% 24% 26% 22% 14%

7. How much time did you spend studying for this exam? Weeks Days Hours 35% 55% 10%

11. How well did the Mock exam prepare you for this examination? Not at all (0) (1) (2) (3) Really well (4) 20% 23% 17% 17% 23%

12. Instructions and Pre-Requisites for this online exam were clear and communicated prior to exam? Yes No 90% 10%

13. Time allocated for the exam was sufficient Strongly Disagree Disagree Neutral Agree Strongly Agree 17% 13% 21% 18% 31%

14. The invigilation/proctoring was sufficient for conducting a fair exam? Strongly Disagree Disagree Neutral Agree Strongly Agree 9% 12% 17% 31% 31%

15. Did you face any technical or internet issues during the exam? Yes No 47% 53%

16. Online exam was better than traditional exam Strongly Disagree Disagree Neutral Agree Strongly Agree 34% 18% 23% 12% 13%

Open ended questions had varied response rates. Responses were analyzed and coded (Table 3).

Table No.3: Student responses on different aspects of online exam

<table>
<thead>
<tr>
<th>Question</th>
<th>Code</th>
<th>No. of responses</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you think your performance in this exam is a good indicator of how well you know/understand the topic/content?</td>
<td>Satisfied with their performance</td>
<td>14</td>
<td>31%</td>
</tr>
<tr>
<td></td>
<td>Couldn’t focus on paper due to technical issues or background noises</td>
<td>8</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>Disturbance due to Covid 19 patients at home</td>
<td>7</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td>Teaching sessions didn’t prepare well for exam</td>
<td>6</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Didn’t perform well due to less preparation time or less exam time</td>
<td>8</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>Lack of resources due to unforeseen events in pandemic</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>45</strong></td>
<td><strong>100</strong></td>
</tr>
<tr>
<td>If you could go back in time and study for this exam again, what would you do differently?</td>
<td>Organize study habits/ change learning strategies</td>
<td>27</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>Give more time to study</td>
<td>24</td>
<td>38%</td>
</tr>
<tr>
<td></td>
<td>Focus more on clinical sciences</td>
<td>7</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>Focus more on basic sciences</td>
<td>5</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>63</strong></td>
<td><strong>100</strong></td>
</tr>
<tr>
<td>Why was Online exam not better than traditional exam?</td>
<td>Technical issues (power outages, internet issues, software glitches)</td>
<td>24</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>Difficult to attempt as compared to traditional exam</td>
<td>11</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>Accessibility to unfair means</td>
<td>10</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>Back ground noise/ disturbance due to students as well as invigilators</td>
<td>10</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>Exam decorum cannot be maintained at home</td>
<td>5</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>More financial burden</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Fine with both versions of exam</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Less time was given to attempt exam</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>68</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

**DISCUSSION**

During the past 5 month of Covid-19 lockdown universities have been closed and students faced uncertainty regarding their academic future. For the first in both government and private institutions online examinations are being used by universities.

The objective of the present study was to examine the academic accomplishment of students in online exams as compared to traditional exams and to gauge student satisfaction regarding online exams. The study population was second year MBBS students who have attempted the traditional paper based exam in first year and online mid-term examination in second year with
similar subjects i.e. anatomy, physiology and biochemistry. Statistical testing showed that students performed significantly well in online examination as compared to tradition (p-value, 0.01) other studies conducted relating to online examinations have reported similar finding in regards to students satisfaction and performance. With regards to the logistics and operations including difficulty level, allocated time, overall feel, and their performance of online examination students’ reported neutral responses. Students were satisfied with the instructions, and Pre-Requisites reported it to be communicated clearly prior to exam and the amount of proctoring was sufficient for conducting a fair exam. In term of technical or connectivity issues students had an equal divide with almost half reporting facing issues with internet and back noise and more than a half percent did not face any such difficulty during exam. Students considered online examination to reflect their aptitude and a good indicator of how well they understand the content. Similar results have been reported by other studies conducted on related topic.

Students considered the technical assistance provided by the institute though the Zoom class rooms’ sessions, Edmodo activities and online assignments and quizzes as well as the Mock exam were sufficient to prepare them for the final online examination. On average students spends days to weeks on exam preparation. Although students scored better in online examinations (97, 77) as compared to traditional examinations (79, 23), based on the responses to question 16 majority students disagree that online exams are better than traditional method. Previous studies suggested students showed significant satisfaction and better performance with online examination. One study however reported that students performance and scores were far better with traditional method as compared to online. In another study result reported that students were satisfied with online examination however their performance did not show any correlation to that finding.

Students were asked to share their views regarding the entire online examination experience and most students reported similar concern, students share they were not fully prepare for the exam due to Covid-19 patients at home, lack of resources due to unforeseen event in pandemic. Students shared that if given the time they will be more organized, spend more time on studying. As compared to traditional exam students found online exam difficult to attempt due to technical issues such as power outages, internet issues, Edmodo glitches, accessibility to unfair means, background noise/disturbance due to students as well as invigilators. These difficulties and limitation in online learning and examinations are highlighted by similar studies previously conducted:

These finding highlight the importance of investing in E-learning infrastructure, assist in documenting the effects of changing academic paradigms, according to students though online examination is flexible, and easily assessable still there are some issues that are needed to be resolved.

CONCLUSION
With better performance in an online exam, students still prefer the traditional exam format better than online exams mainly due to technical issues. This highlights the importance of investing in e-learning and e-assessment infrastructure. Understanding the advantages and challenges of online exams will not only help us but other institutes to plan and execute this process really well.

Author’s Contribution:
Concept & Design of Study: Muhammad Suleman Sadiq Hashmi
Drafting: Afifa Tabassum, Sobia Ali
Data Analysis: Sobia Ali, Faiza Ambreen
Revisiting Critically: Muhammad Suleman Sadiq Hashmi, Afifa Tabassum
Final Approval of version: Muhammad Suleman Sadiq Hashmi

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

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Body Mass Index (BMI) and Ovarian Cancer: Impact on Tumor Stage
Anum Jafri¹, Sarwat Rizvi² and Rubar Haider³

ABSTRACT

Objective: To determine the frequency of high body mass index in ovarian cancer and to compare the stage of tumour in patients of ovarian cancers with normal versus high BMI.

Study Design: Descriptive, cross-sectional

Place and Duration of Study: This study was conducted at the Department of Pathology, King Edward Medical University, Lahore from September 2017 to March 2018.

Materials and Methods: One hundred and fourteen patients having ovarian cancer of age 15-55 years were included. Patients having metastatic ovarian carcinoma were excluded. Frequency of high BMI was recorded and two groups (A & B) were formed according to their BMI i.e. body mass index BMI ≥30 kg/m2 and body mass index BMI <30 kg/m2. Tumor stage of these cases was assessed by FIGO staging system.

Results: Mean age was 38.89±10.07 years. Most of the females, i.e. 66 (57.89%) were between 46 to 55 years of age. Mean duration of ovarian cancer was 9.12±3.68 months. Out of the 114 patients, 99 (86.84%) were married and 15 (13.16%) were unmarried. Frequency of high body mass index in ovarian cancer was found in 35 (30.70%) patients, whereas there was normal BMI in 79 (69.30%) patients.

Conclusion: Frequency of high body mass index in ovarian cancer is quite high. No statistically significant difference was noticed in stage of tumour in patients with normal versus high BMI.

Key Words: Ovarian tumours, Body mass index, Stage of tumour, Prognosis

Citation of article: Jafri A, Rizvi S, Haider R. Body Mass Index (BMI) and Ovarian Cancer: Impact on Tumor Stage. Med Forum 2020;31(10):177-180.

INTRODUCTION

Among the cancers of female genital tract, ovarian carcinoma carries the worst prognosis, having five-year survival rate of 37%.¹ Numerous researchers have assessed the effect of obesity on the risk of ovarian carcinoma using BMI as the measure of obesity.² Obesity or high BMI has been established as a risk factor for a number of hormone-related malignancies.³ However, its association with ovarian carcinoma has been contradictory in the literature. The relationship between obesity and ovarian carcinoma is quite probable, since obesity has been found to be associated with variation in hormonal levels and ovulation, polycystic ovarian syndrome, infertility and endometriosis, all of which are believed to raise the odds of having ovarian cancer.

Furthermore, increased BMI has also been associated with other hormonally related malignancies, such as endometrial and breast carcinomas.⁴ One of the most significant risk factors for epithelial ovarian carcinomas (EOC) particularly amongst post-menopausal females.⁵ While the evidence suggests that increased BMI is linked with the risk of many malignancies, the increasing epidemic of obesity has lead the researchers to believe that there is a need for implementation of guidelines for the weight management in order to prevent the risk of developing certain malignancies. The data from the literature points out obesity or high BMI is a cause of nearly 14% deaths due to cancer in males and almost 20% deaths in females.⁶ A study conducted by Erondu et al⁷ compared the BMI with stage of tumour i.e. stage I was recorded in 37.78% in patients with BMI <30 kg/m2 while 62.28% in women with ≥30 kg/m2, stage II was recorded in 48.48% versus 51.52% respectively, stage III in 41.07% versus 58.93% and stage IV in 38.10% vs 61.90% respectively.⁷

Although previous international studies are present but no local study was available on this and no researches have explicitly addressed the impact of obesity on ovarian carcinoma survival among Pakistani women, therefore we conducted this study to determine the relationship of BMI with stage of ovarian cancer in local population. The literature indicates that obesity worsens the prognosis of ovarian cancer as in obese patients ovarian cancers tend to be more aggressive and such patients present with a higher stage. Then based on
the results of my study, a protocol can be designed for multidisciplinary management of obesity which will be a prognostic factor in ovarian cancer patients. Also on the basis of this study, public awareness programs on national and regional levels will be arranged to create awareness among public regarding this major public health issue among women as well as treating clinicians for a better future outcome in every aspect to reduce morbidity and mortality of these particular patients.

MATERIALS AND METHODS

This descriptive, cross-sectional study was conducted at Department of Pathology, King Edward Medical University, Lahore from 6th September 2017 to 5th March 2018. Samples were received from the surgical units affiliated with King Edward Medical University, i.e. Lady Willingdon Hospital and Lady Aitchison Hospital, Lahore. Females with ovarian cancer diagnosed on the basis of histopathology and age 15-55 years were included. Patients having metastatic ovarian carcinoma and autolysed specimen (on gross examination) were excluded. A total of 114 females having ovarian cancers, diagnosed on the basis of histopathology, who fulfill selection criteria were enrolled. A thorough history of the patients was noted. Frequency of high BMI was recorded and two groups (A & B) were formed according to their BMI i.e. BMI ≥30 kg/m2 and <30 kg/m2. Tumor stage of these cases was assessed by FIGO staging system as described in operational definitions. All the data was recorded. The collected data was entered in SPSS-20.0 and analyzed. Chi square test was applied to determine the significance in both groups and p value ≤0.05 was taken as significant.

RESULTS

Mean age of the patients in this study was 38.89 ± 10.07 years with age ranging from 15 to 55 years. Majority of the females, i.e. 66 (57.89%) were between 46 to 55 years of age. Mean duration of ovarian cancer was 9.12 ± 3.68 months. Out of the 114 patients, 99 (86.84%) were married and 15 (13.16%) were unmarried. Frequency of high body mass index in ovarian cancer was found in 35 (30.70%) patients, whereas there was normal BMI in 79 (69.30%) patients as shown in Figure I.

When stratification of high body mass index in ovarian cancer was done on stage of tumour, it was established that there was no significant difference among various stages as shown in Table I while the stratification of high body mass index in ovarian cancer with regard to age groups is mentioned in Table II which also revealed no significant difference amid various age groups.

Table No.1: Stratification of high body mass index with respect to stage of tumour

<table>
<thead>
<tr>
<th>Stage of tumour</th>
<th>High body mass index</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>I</td>
<td>9 (27.27%)</td>
<td>24 (72.73%)</td>
</tr>
<tr>
<td>II</td>
<td>10 (34.48%)</td>
<td>19 (65.52%)</td>
</tr>
<tr>
<td>III</td>
<td>11 (45.83%)</td>
<td>13 (54.17%)</td>
</tr>
<tr>
<td>IV</td>
<td>5 (17.86%)</td>
<td>23 (82.14%)</td>
</tr>
</tbody>
</table>

Table No. 2: Stratification of high body mass index with respect to age groups

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>High body mass index</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>15-35</td>
<td>15 (31.25%)</td>
<td>33 (68.75%)</td>
</tr>
<tr>
<td>36-55</td>
<td>20 (30.30%)</td>
<td>46 (69.70%)</td>
</tr>
</tbody>
</table>

DISCUSSION

Pooled and meta analyses carried out among chiefly white populations revealed that obese females are at a higher risk for developing ovarian cancer and have worse survival rate after the diagnosis. According to some studies, for African American women, a risk factor for ovarian carcinoma is obesity. The age range in the current study was from 15 to 55 years with mean age of 38.89±10.07 years. Majority of females, i.e. 66 (57.89%) were between 46 to 55 years of age. Frequency of high body mass index in ovarian cancer was found in 35 (30.70%) patients, whereas there was normal BMI in 79 (69.30%) patients. In a meta-analysis, there were 25% cases of ovarian cancer with high BMI ≥30 kg/m². Multivariate risk of ovarian carcinoma for overweight patients with BMI ≥30 kg/m², in comparison with females having normal weight (BMI 18.5–24.9 kg/m²) in the cohort on the whole was 1.25 (95%-CI=0.93–1.68). The multivariate risk for overweight as opposed to females with normal weight was 1.80 (95%-CI=1.16–2.80) amongst females who never used Hormone Replacement Therapy. On the contrary, no relationship between body mass index and ovarian carcinoma was evident in females who took Hormone Replacement Therapy (MVRR=0.96; 95%-CI=0.64–1.43; P-interaction = 0.02). An association between body mass index and carcinoma of the ovary was noticed amid females with no family history of ovarian carcinoma (MVRR comparing obese versus females with normal weight =1.36; 95%-CI=0.99–1.85) has also been suggested, however no association with Body Mass Index was found in females who had a
positive family history of ovarian carcinoma (MVRR=0.73;95%-CI=0.34–1.60;P:interaction=0.02).  
In 3 prospective cohorts in USA, Italy and Sweden, a case-control study was carried out in which case subjects included the diagnosed cases of epithelial ovarian carcinoma (n = 122) whose diagnosis was made twelve months or later after being recruited in the respective cohort. An inverse association was observed between BMI and the risk of ovarian carcinoma. Odds ratio for increasing quartiles of body mass index higher than the lowest, were 0.62 (0.32-1.21), 0.59 (0.30-1.17) and 0.46 (0.23-0.92), p = 0.03. When overweight females (BMI > 30) were contrasted to thin females (BMI < or = 23), the inverse relationship turned out to be strong, having an odds ratio of 0.38 (0.17-0.85), p<0.02. Some proof of association of carcinoma of the ovary with height was also observed, which was restricted to tumors diagnosed earlier than age 55.  
No evidence of relationship between body mass index and ovarian carcinoma-related survival in a cohort study was found. Nevertheless, significant effect modification was observed by stage (P interaction <0.01). In contrast with normal pre-diagnosis body mass index (18.5–24.9 kg/m²), females who were overweight before the diagnosis (BMI≥35 kg/m²), ovarian cancer-related survival rate was worse in the patients at stages I and II (hazard ratio (HR): 3.40; 95% (CI): 1.16–9.99), however raised in the patients with stage IV tumor (HR: 0.58; 95% CI: 0.35–0.96).  
A study by Kuper and colleagues described 57% amplification in possibility of developing ovarian carcinoma that was restricted to overweight, premenopausal females, though the outcomes were not significant statistically. Intriguingly, postmenopausal females exhibited no tendency for increased risk, even though the females who were postmenopausal for less than ten years revealed higher risk compared with females who had been postmenopausal for ten years or more, once more highlighting the modifying impact of menopausal status.  
A survey carried out by Erondu et al compared the body mass index with tumor stage i.e. stage I was documented in 37.78% in patients with body mass index <30 kg/m² whereas 62.28% in females with ≥30 kg/m², stage II was registered in 48.48% versus 51.52% respectively, stage III in 41.07% versus 58.93% and stage IV in 38.10% versus 61.90% respectively.  
Farrow et al study of ovarian carcinoma linked to body mass index established a noteworthy increase in risk amongst the most overweight, premenopausal females with serous and endometrioid histological subtypes of ovarian cancer. Nevertheless other investigators established maximum risk among borderline tumors and invasive serous, mucinous, and undifferentiated subtypes. An analysis of ten case-control studies brought forward the fact that relationship among parity and OCP use and the risk of developing carcinoma is comparatively consistent among various histological types of tumor. On the contrary, body mass index demonstrated increased heterogeneity in anticipating the risk of carcinoma among serous, mucinous, and endometrioid subtypes.  
A prospective cohort study showed an inverse relationship among survival time and body mass index in females with ovarian carcinoma. Pavelka et al demonstrated that for females having advanced ovarian carcinoma, obesity was independently associated with both lesser time in recurrence and on the whole survival. These researchers endorsed under dosage of chemotherapy as a likely contributing cause. In a sub-cohort of 149 females having tumor stage III or IV, a considerable fashion was acknowledged supporting increased body mass index as an independent negative factor for overall (P = 0.02) and disease free (P = 0.02) survival. In the SCOTROC I trial, in which chemotherapeutic doses were not restricted based on body weight, the researchers came across no difference among BMI subgroups and general rate of survival.  
There were 2 studies including a meta-analysis that described the link between survival rate of increased body weight and survival of ovarian carcinoma. Protani et al., reported that obese patients of ovarian carcinoma showed worse survival than lean patients with ovarian cancer. Nevertheless, this association was applicable only to females with body mass index ≥30. Yang et al., established that obesity early in adulthood happens to be linked to increased mortality in patients having ovarian carcinoma.  

**CONCLUSION**  
The frequency of high body mass index in ovarian cancer is quite high with statistically no significant difference among stage of tumour in patients of ovarian cancers with normal versus high BMI. So we recommend that public awareness programs on national and regional levels should be arranged to create awareness among public regarding this major public health issue of obesity among women as well as treating clinicians for a better future outcome in every aspect to reduce morbidity and mortality of these particular patients.

**Author’s Contribution:**

- **Concept & Design of Study:** Anum Jafri
- **Drafting:** Sarwat Rizvi
- **Data Analysis:** Rubar Haider
- **Revisiting Critically:** Anum Jafri, Sarwat Rizvi
- **Final Approval of version:** Anum Jafri

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


Prevalence and Antimicrobial Susceptibility of Aerobic Bacterial Pathogens in Chronic Suppurative Otitis Media
Kashif Waqas1, Muhammad Idris Mazhar2, M Saeed Razi3, Khalid Mahmood4 and Syed Zeeshan Haider5

ABSTRACT

Objective: To determine the prevalence of aerobic bacterial organisms in chronic suppurative otitis media (tubotympanic variety), difference in isolation of aerobic bacterial organisms and to establish pattern of antimicrobial sensitivity of these isolates.

Study Design: Prospective comparative study

Place and Duration of Study: This study was conducted at the Department of Microbiology, Institute of Molecular Biology & Biotechnology, The university of Lahore, Pakistan from January 2015 to December 2015.

Materials and Methods: Two hundred patients with chronic suppurative otitis media were included. An ear swab was taken from the middle ear by insertion of nichrome wire loop and conventional sterile swab separately.

Results: Thirty-six (18%) were <10 years of age, 104 were females. Only a few cases were seen in higher age groups. Hundred samples were collected using nichrome wire loop and conventional sterile swabs each. Yield ratio of organisms was 94.5% of samples. Nichrome wire loop showed no advantage over the conventional sterile swab. Staphylococcus aureus was the most common organism isolated, followed by Pseudomonas aeruginosa and Proteus species. 92.9% of the organisms were susceptible to ciprofloxacin and only 20.1% were susceptible to trimethoprim-sulfamethoxazole.

Conclusion: Bacterial isolates from ear samples with conventional sterile swab were found to be identical to those with nichrome wire loop. Conventional sterile swab was as good as nichrome wire loop for collection of ear samples.

Key Words: Chronic suppurative otitis media (CSOM), Ear swab culture & sensitivity pattern


INTRODUCTION

The term CSOM, chronic suppurative otitis media, is employed when discharge from middle ear continues beyond duration of more than 8 weeks. It is still prevalent around the world and is a source of concern to the treating physician and patients/families. Chronic suppurative otitis media may occur at any age. Western literature quotes the incidence rate of this condition as 15-20% in the paediatric population.

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membrane and the middle ear sample can be collected.\textsuperscript{8,9} In this method specimen is aspirated through the perforation in the tympanic membrane, using 2 ml disposable syringe fitted with 24 gauges or 18 gauge needle covered by plastic cannula. The tip of the needle is bent to avoid accidental trauma.\textsuperscript{10} The presence of multiple strains of both Gram negative and Gram positive aerobes were seen to be the rule rather than exception.\textsuperscript{11} Infective complications of CSOM range from mastoiditis, ossicular damage, meningitis to cerebral abscess with resulting disability and handicap and developing cholesteatoma.\textsuperscript{6} In CSOM, both aerobic Gram positive, Gram negative and anaerobes are found but Pseudomonas aeruginosa, Staphylococcus aureus and Enterobacteriacea are the most frequently isolated micro-organisms.\textsuperscript{12}

**MATERIALS AND METHODS**

This prospective comparative study was conducted at Department of Microbiology, Institute of Molecular Biology & Biotechnology, The University of Lahore, Pakistan from 1\textsuperscript{st} January 2015 to 31\textsuperscript{st} December 2015. Two hundred patients with CSOM of tuberculosis type, seen in ENT and Paediatric Clinics were eligible. Diagnosis of tubotympanic type of CSOM was established on the basis of history, ear examination and otoscopic examination of tympanic membrane, showing tubotympanic type of (central) perforation. Patients having marginal tympanic membrane perforation, showing cholesteatoma, granulation tissue or polyp were excluded from the study. Similarly, patients on topical or systemic antibiotic therapy were also excluded. Demographic information was collected including, age, sex, weight, place of residence, number of family members, number of rooms in the house and socioeconomic conditions. A detailed history of present illness, its duration and the symptomatology was recorded. External auditory canal was mopped dry using sterile ear swab. The samples for bacteriological studies were obtained from the middle ear by insertion of nichrome wire loop and the conventional sterile swab separately. The swabs were inoculated on chocolate agar, blood agar and MacConkey agar, incubated aerobically at 37\textdegree{}C, and read after 24 hours. Laboratory standard operating procedure for the identification of these organisms include colonial morphology, Gram staining, catalase, DNase, oxidase, motility, citrate and where needed API identification system of Biomerieux France was used.\textsuperscript{7} A Gram stain was done on all specimens gathered. Microorganisms were characterized and identified by using conventional scheme.\textsuperscript{13} A rapid method of identification for Candida albicans and Candida species in general was based on its ability to form germ tubes within two hours of incubation in human serum at 37\textdegree{}C.\textsuperscript{14} Antibiotic susceptibilities were determined using a comparative disc method. Control organisms included Staphylococcus aureus NCTC6571 and Escherichia coli NCTC10418 susceptibility were confirmed by determining MIC’s of these drugs. Data were checked for completeness, entered and analyzed by using SPSS-20.

**RESULTS**

There were 104 females and 96 males patients. 20% patients fell in the upper income group, 62% in the middle, and 18% in lower income group. Thirty patients (24 males and 12 females) were 1-10 years old, 50 were 11-20 years old (22 males and 28 females) and 52 were 21-30 years old (24 males and 28 females), 20 were 31-40 years old (with 8 males and 10 females) and 24 were 41-50 years old (10 males and 14 females) respectively (Table 1). Swabs were classified according to their nature of discharge; ear discharge was mainly thick and non-odourous in 90 patients (45%) cases. Mucopurulent ear discharge in 68 patients (34%) and mucopurulent with smell in 18 patients (9%). Discharge was watery in 16 patients (8%) and blood tinged discharge was seen in only 8 patients (4%). No discrepancy was observed in both types of samples (Table 2). Staphylococcus (coagulase negative) species were isolated from 30 patients with conventional swabs accounting for 6.7% of total isolates and in 12 patients with nichrome wire loop, accounting 2.8% of total isolates. Streptococcus pyogenes was observed in samples from 30 patients taken with nichrome wire loop and sterile swab, representing 7.2% and 6.7% of total isolates respectively (Table 3).

Single organism was isolated in 38 patients with nichrome wire loop and in 24 patients with conventional sterile swab. Two organisms (double growth) were isolated in 120 patients with nichrome wire loop and in 130 patients with conventional sterile swabs samples. With nichrome wire loop growth of three organisms was obtained in 30 cases and four organisms were in 12 cases. While with conventional sterile swab, three organism growths were observed in 34 patients and four organism growth in 12 patients (Table 4). Staphylococcus aureus, as a single isolate was observed in 24 out of 38 patients (63.15%), of those presenting with single organism growth with nichrome wire loop while in 18 out of 24 patients (75%) with sterile swab ear samples. Pseudomonas aeruginosa as a single pathogen isolates were seen in 10of total patients (26.33%), nichrome wire loop culture and in 6 patients (25%) with conventional sterile swab isolates. Proteus species, Streptococcus pyogenes both were observed as a single pathogenic organism in one patient (5.2%) each with nichrome wire loop isolates (Table 5).

Methicillin resistance in Staphylococcus aureus was observed in 20 patients (7.89%) out of 252 patients' isolates whereas remaining 140 isolates showed
Prevalence of microorganism along with their sensitivity pattern was studied in 200 patients of tubotympanic type of CSOM. There were 104 females and 96 males. Few studies showed similar finding in gender distribution as observed in our study.\textsuperscript{14,15} Whereas western literature also quotes a significant male preponderance.\textsuperscript{16} This difference may be attributed to more common swimming habits in males in west as compared to our population.

Patients were arranged in different age groups, 36 patients were seen in 1-10 years age group. In the 11-20 and 21-30 age groups, there were 50 and 52 patients respectively. Number of patients decreased with increasing age and only 20 and 24 patients fell in 31-40 and 41-50 years age group. While only few cases were seen in higher age group. CSOM has been reported to be more common in third decade of life (30\% to 35\%) cases that is comparable in our study and other studies in the world.\textsuperscript{4,17}

In the present study, ear discharge was thick and non-odourous in 90 patients (45\%) cases mucopurulent in 68 (34\%) and mucopurulent with smell in 18 patients (9\%). Discharge was watery in 16 patients (8\%) and blood stained in 8 patients (4\%). Two other different studies in which non-odourous and thick discharge was reported in 42.5\%, mucopurulent 30\%, mucopurulent with smell 11.5\%, 10\% watery and 6\% blood stained samples.\textsuperscript{18,19}

Nichrome wire loop samples yielded 208 isolates as compared to conventional sterile swab samples which yielded 221 isolates. Isolates both with Nichrome wire loop and conventional sterile swab were almost identical in 94.5\% and samples showing same type of growth by both methods. The results were comparable with the observation of Raju et al\textsuperscript{17} who reported 88\%
isolates of same type by both methods in a study of 25 isolates.

The commonest organism was Staphylococcus aureus (40%) cases followed by Pseudomonas (28%), Proteus species (11%), Streptococcus pyogenes (5%) and Staphylococcus species (1%) with decreasing frequency. Many workers have reported similar incidences in which Staphylococcus aureus was isolated 30.3-40.3% of cases, Pseudomonas 24-30%, Proteus species 8-11%. In the present study, 60% of cultures yielded 2 organisms and 19% single organism whereas 15% and 6% yielded 3 and 4 organisms respectively. Earlier workers have also reported 40-85% of cases yielding 2 organisms. Whereas Aslam et al (1998) from Aligarh (India) have reported monobacterial isolates in 87% and polybacterial only in 13%. Maximum samples yielded 2 organism growth. This was followed by one, three and four organism growth in decreasing order of frequency.

In cases with two organisms’ growth Staphylococcus aureus and Pseudomonas were the commonest associated infecting organisms and were isolated in 27% cultures which were followed by Staphylococcus aureus and Proteus association (7%). Many workers had reported Staphylococcus aureus and Pseudomonas association in 20-30% cases, Staphylococcus aureus and Proteus species association 5-8% cases. Based on in vitro sensitivity the most effective antimicrobial agent, if all isolates are taken into account was observed to be ciprofloxacin (susceptibility 92.9%) followed by sparfloxacin (92.4%), cefpirome (91.9%), ofloxacin (91.4%) and imipenem, cefepime (90.4%). Septran was the least effective antimicrobial showing 20.1%. The results reported by Deosthale is comparable with the results of our study, who reported ciprofloxacin >85 %, and gentamicin >81 % effective. When vancomycin and teicoplanin were tested against Staphylococcus aureus and Staphylococcus species, both were found to be 100% effective. As in the present study no vancomycin resistance was observed among 1829 Staphylococcus isolates from United States and Canada collected from January to June 1997. Similarly, all these strains were also sensitive to teicoplanin. Methicillin resistance was seen in 7.9% of Staphylococcus aureus isolates in the present study. Methicillin resistant strains of Staphylococci emerged by the late 1970s have become increasingly more prevalent as nosocomial pathogens. In Italy, the incidence of methicillin resistant Staphylococcus aureus among Staphylococcus aureus strains isolated at the Institute of Microbiology of the University Hospital of Genova exceeds 35%. In France (Saint-Joseph Hospital), the incidence of methicillin resistant Staphylococcus aureus in 1992, was reported to be 44%. Other reports show that the proportion of methicillin resistant Staphylococcus aureus in hospitals in Spain, France and Italy ranges to the rate of 30-40%. In Lahore, the overall prevalence of methicillin resistance in Staphylococcus aureus isolates from indoor cases in the year 2000 was 46.5%. In present study, methicillin resistant Staphylococcus aureus is 7.89% and Staphylococcus species is 16.6% only (Table 13) which is very low as compared to the other studies. Low level of methicillin resistant Staphylococcus aureus in current study is due to the fact that samples are collected from the community patients attending outpatients and were not exposed to the ward/ ICU environment.

CONCLUSION

Conventional sterile swab was as good as nichrome wire loop for collection of ear samples. Staphylococcus aureus, Pseudomonas aeruginosa and Proteus species continue to be the major infecting pathogens in chronic suppurative otitis media. Sensitivity pattern of isolates shows that all organisms are sensitive to commonly used drugs.

Author’s Contribution:
Concept & Design of Study: Kashif Waqas
Drafting: Muhammad Idris Mazhar
Data Analysis: Khalid Mahmood, Syed Zeeshan Haider
Revisiting Critically: Kashif Waqas, Muhammad Idris Mazhar
Final Approval of version: Kashif Waqas

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

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6. Tiedt NJ. Paediatric chronic suppurative otitis media in the Free State Province: Clinical and
Laparoscopic Finding in Infertile Females: A Study at a Tertiary Care Hospital

Sarwat Rizvi¹, Anum Jafri² and Rubar Haider³

ABSTRACT

Objective: To study the laparoscopic findings in infertile females.

Study Design: Descriptive cross sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology, Lady Willingdon Hospital, Lahore from January 2018 to January 2020.

Materials and Methods: One hundred and fifty patients with either primary or secondary infertility who underwent diagnostic laparoscopy and fulfilled the inclusion criteria were included.

Results: The mean age of the participants was 32.15 ranging from 20 to 45 years. Mean age of the patients with primary infertility was 26.15 years and those with secondary infertility were 31.3 years of age. Amongst these females, 107 (71.3%) had primary infertility, whereas 43 (28.6%) females had secondary infertility. Forty-seven (31.3%) cases turned out to have normal findings. Anomalous findings were noticed in 103 (68.7%) patients. Among the patients with abnormal findings, the leading cause of infertility was found to be tubal blockade which was seen in 40 (31.3%) cases. This was followed by endometriosis in 30 (29.1%) cases. The third leading cause in our study population was pelvic adhesions found in 28 (27.1%) cases. Polycystic ovarian disease was noticed in 3 (2.9%) and fibroid in 2 (1.9%) cases.

Conclusion: The most common factor leading to infertility among females in our study was tubal blockade. This was followed by endometriosis, pelvic adhesions, PCOD and fibroids.

Key Words: Laparoscopic finding, Infertile female, Tertiary care.

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INTRODUCTION

Infertility is a major global public health predicament. It is defined as failure to conceive after one year of regular unprotected intercourse. Sub fertility has been a problem in nearly 60-80 million couples worldwide. Infertility is seen in 10-15% married couples of reproductive age. The prevalence of infertility in Pakistan is 21.9% of which primary infertility cases are 3.5% and secondary infertility cases are 18.4%.¹ Numerous factors lead to infertility including physiological, anatomical and genetic factors. Fertility is also influenced by several environmental and acquired factors. Among these the most common causes are menstrual irregularities and ovulation dysfunction.

In different parts of the world the prevalence and causes of infertility are different. This inconsistency is owing to existence of variation in environmental factors related to reproductive practices, for instance age at marriage, smoking and alcohol abuse, lifestyle and diet.² The term primary infertility is used if conception has never taken place; secondary infertility is defined as failure to get pregnant after having achieved an earlier conception. Most favorable age group which has the maximum chances of conception is 20-35 years in females. Above 40 years of age, there is a significant reduction in fertility rate and an increase in the risk of chromosomal and other anomalies.³ Infertility has been documented as a grave, expensive and troublesome dilemma for distressed families. The stigma in society of being childless even today can lead to seclusion and rejection in several countries.⁴ Various causes of infertility were explored in this study. The major hurdle in assessing global estimation in the epidemiology of infertility is the paucity of local population based researches. Consequently, precise measurement of the occurrence of infertility with epidemiological data is needed so as to prepare suitable plan for prevention and treatment of infertility and its devastating socio-economic cost. Thus, in this population-based study we intended to recognize the prevalence and causes of primary infertility in a group of females in reproductive age.

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² Department of Pathology, King Edward Medical University, Lahore.
³ PG Resident, Shaikh Zayed Hospital, Lahore.
MATERIALS AND METHODS

This was a descriptive cross sectional study carried out in the department of gynecology and obstetrics, Lady Willingdon hospital, Lahore. From the outpatient department, 150 female patients who presented with infertility from January 2018 to January, 2020 were included in the study. These patients were collected through purposive sampling after a thorough history including demographics, obstetrical and gynecological and medical and surgical history. History was followed by detailed physical examination, baseline investigations, hormonal profile (serum FSH, LH, TSH) and pelvic ultrasound of the patients. Male factor was ruled out. Patients from the age group 20 to 45 years, with primary or secondary infertility were included in the study. The patients who had a previous history of laparoscopy, abdominal surgeries, or those who were deemed unfit for anesthesia were excluded from the study. Patients who refused to give consent for the procedure or whose husbands had abnormal semen analysis were also excluded. Written informed consent was obtained from the patients. Laparoscopy procedure was carried out under general anesthesia. Mostly single port was used however accessory port had to be used in several patients. Those patients who underwent this procedure were admitted a day earlier and discharged on the second post op day. The data was analyzed by using SPSS version 20.

RESULTS

The mean age of the participants was 32.15 ranging from 20 to 45 years. Mean age of the patients with primary infertility was 26.15 years and those with secondary infertility were 31.3 years of age. Amongst these females, 107 (71.3%) had primary infertility, whereas 43 (28.6%) females had secondary infertility. Forty-seven (31.3%) cases turned out to have normal findings. Anomalous findings were noticed in 103 (68.7%) patients. Among the patients with abnormal findings, the leading cause of infertility was found to be tubal blockade which was seen in 40 (31.3%) cases. This was followed by endometriosis in 30 (29.1%) cases. The third leading cause in our study population was pelvic adhesions found in 28 (27.1%) cases. Polycystic ovarian disease was noticed in 3 (2.9%) and fibroid in 2 (1.9%) cases (Table 1).

<table>
<thead>
<tr>
<th>Laparoscopic Findings</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>40</td>
<td>31.3</td>
</tr>
<tr>
<td>Tubal blockade</td>
<td>40</td>
<td>31.3</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>30</td>
<td>29.1</td>
</tr>
<tr>
<td>Pelvic adhesions</td>
<td>28</td>
<td>27.1</td>
</tr>
<tr>
<td>PCOD</td>
<td>3</td>
<td>2.9</td>
</tr>
<tr>
<td>Fibroid</td>
<td>2</td>
<td>1.9</td>
</tr>
</tbody>
</table>

DISCUSSION

The mean age of the patients in this study was 32.15 years. Mean age of the patients with primary infertility was 26.15 years and those with secondary infertility were 31.3 years of age. This is comparable to the study carried out by Al-Turk, where patients who came up with secondary infertility belonged to an older age group compared to the one with primary infertility.

In our study the leading type of infertility we came across was primary infertility (71.3%). Similar results were seen in the study carried out by Tamrakar and Benksim et al where primary infertility was also the main type of infertility. However, in other studies the rate of secondary infertility was higher than primary infertility. This difference could be due to demographic factors like higher age of marriage in certain parts of the world.

The mean duration of patients who presented with the complaint of infertility was 5.4 years. This is in contrast to a study conducted in USA where the patients’ mean duration of infertility was 3.5 years. This difference could be due to lack of medical care and reliance on traditional medicine in our part of the world.

Our study revealed that the major reason for infertility in our study population was tubal ligation followed by endometriosis. This is in accordance with the study conducted by Wani et al where tubal pathology was the leading cause of infertility and the second common cause was endometriosis. Similar results were also reported in another study by Shetty, which also revealed tubal blockade as the foremost cause of infertility.

The prevalence of endometriosis in the study carried out by Aziz was 12.5% whereas in the current study this prevalence was found to be higher, i.e. 29.1%. Frequency of fibroids in this study was 1.9%. In a study by Olive et al, fibroids are routinely found in infertile patients.

In this study tubal adhesions were seen in 27.1% patients. This is in contrast with the study by Bonneau et al, where 40% patients turned out to have pelvic adhesions.

In our study PCOD was observed in 2.9% cases whereas 6.6% cases came up with PCOD in the study by Jain.

CONCLUSION

The leading cause of infertility in developing world is tubal pathology. Hence laparoscopy ought to be performed earlier in management of infertility. This can avoid the emotional and physical toll it takes on an infertile couple. Early diagnosis can also assist in recognizing patients who can be benefitted from assisted reproductive technology (ART). In this study we attempted to assess the factors leading to primary or secondary infertility. We can conclude that...
laparoscopy has emerged as an invaluable method for detailed assessment of infertility in females. Moreover, it aids in treating the underlying cause.

Author's Contribution:
Concept & Design of Study: Sarwat Rizvi
Drafting: Anum Jafri,
Data Analysis: Rubar Haider
Revisiting Critically: Sarwat Rizvi, Anum Jafri
Final Approval of version: Sarwat Rizvi

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

REFERENCES
Impact of Blended Learning Environment on Self-Directed Learning Skill Development Among Post Graduates of Health Professions Education

Saira Waqqar¹, Aasma Qaiser² and Amna Ahmed Noor³

ABSTRACT

Objective: The study aims to identify impact of blended learning environment on self-directed learning skill development among post graduates of Masters in Health Professions Education.

Study Design: Qualitative Study

Place and Duration of Study: This study was conducted at Riphah International University from September 2019 to February 2020.

Materials and Methods: Semi-structured interviews of all participants were audio recorded and transcribed verbatim. Later manual thematic analysis was performed to get meaning within the data.

Results: Three major themes 1) Self-paced E learning, 2) motivation and satisfaction, 3) project-based teaching and learning were identified from ten sub-themes. The main factors like flexibility and convenience given to them in their learning, structured assessment policy, time management, self-pacing, more access to resources, and ease of communication have a major role to develop self-directed learning skill. Health professions Education is an emergent, interesting master degree program under blended learning environment that offers a great opportunity to be a lifelong learner to those who have completed their bachelor degree under traditional curriculum, in fact, most of the participants were rote learner are were not familiar to integration.

Conclusion: Health Professions Education is an emergent Master degree program with pure blended learning environment, providing platform for health professionals to polish their soft and management capabilities through development of self-directed learning skill. This program enables the students to define and achieve their set goals within specific timeline. In fact, making students self-directed and lifelong learners in their continuing professional education.

Key Words: Blended learning; Health profession education post graduate students; learning effectiveness; Motivation, Self-directed learning.

Citation of article: Waqqar S, Qaiser A, Noor AA. Impact of Blended Learning Environment on Self-Directed Learning Skill Development Among Post Graduates of Health Professions Education. Med Forum 2020;31(10):189-193.

INTRODUCTION

In recent decades, with innovation in technology and digital communications there has been an increasing trend towards blended learning and wholly online educational approach.¹ In higher education institutes, instead of one-on-one teaching and learning, there has been rising interest towards internet-based methodologies of teaching and learning like blended learning.² Blended learning has become a popular approach that assist learning.²,³ It is a blend of traditional person to person and online teaching. This has changed student’s way of assessing and expand knowledge, critical thinking and updating skills at workplace.⁴ In blended learning environment, self-directed learning is thought to be one of the crucial skills that help students in their continuous professional development.¹ There has been much debates related to trends and preferences for online teaching and learning in higher educational institutes. Using information and communication technology to enhance students self-directed learning,² perceptions of self-directed learning and digital technology usage in professional development,¹ blended environment and student satisfaction,² educational strategies associated with

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problem solving, critical thinking and self-directed learning experiences during training, enhancing teaching skill through blended learning environment and integrating blended learning in higher education. Previous studies have shown that high self-directed learning skills are pivotal for effective online learning, but there is a mini debate on effect of blended learning environment on development of self-directed learning skills among students of Masters in Health Professions of Education. Usage of these learning technologies combined with traditional person to person learning and its impact on self-directed learning skills of postgraduate students was the main aim of this study.

MATERIALS AND METHODS

A qualitative study was carried out from September 2019 to February 2020 in Riphah International University.

Sampling technique: The 9 post graduates who were completed their MHPE and willing to participate in the study were selected through purposive, homogenous sampling technique.

Data collection: All the participants were clarified about research consequences and a written informed consent was obtained from all participants. An interview guide (IG) was prepared and pilot tested, having validated interview questions. The questions in IG were written in full sentences but in reality, their formulation and order were adjusted according to situation during interview. Later, semi structured one-on-one interviews of all participants were conducted using interview guide. Interviews lasted for 60-90 minutes until data saturated. Both male and female postgraduates of MHPE program were included in this study. All interviews were conducted in a safe and comfortable environment. Notes were also taken during the interview. Data was audio recorded and then transcribed verbatim.

Data Analysis Procedure: Data analysis started early during data collection process. Thematic analysis was employed to generate codes. After reading through the interviews several times and the generated codes, data was categorized to develop themes. Themes were further refined after discussions with all the authors.

RESULTS

Participants (n=09) were post graduates of health professions education. They Belonged to different health care professions (Table 1). They have recently completed their MHPE degree program and shared their experiences how their self-directed learning habit was influenced by this blended learning environment.

<table>
<thead>
<tr>
<th>Participant No</th>
<th>Basic Qualification</th>
<th>Age</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MBBS</td>
<td>33</td>
<td>M</td>
</tr>
<tr>
<td>2</td>
<td>MBBS</td>
<td>46</td>
<td>M</td>
</tr>
<tr>
<td>3</td>
<td>MBBS</td>
<td>43</td>
<td>F</td>
</tr>
<tr>
<td>4</td>
<td>MBBS</td>
<td>36</td>
<td>F</td>
</tr>
<tr>
<td>5</td>
<td>MBBS</td>
<td>45</td>
<td>M</td>
</tr>
<tr>
<td>6</td>
<td>NURSING</td>
<td>36</td>
<td>F</td>
</tr>
<tr>
<td>7</td>
<td>Physiotherapist</td>
<td>37</td>
<td>F</td>
</tr>
<tr>
<td>8</td>
<td>BDS</td>
<td>40</td>
<td>M</td>
</tr>
<tr>
<td>9</td>
<td>BDS</td>
<td>43</td>
<td>M</td>
</tr>
</tbody>
</table>

In one on one semi structured interview participants identified a number of factors that proved to be helpful in improvement of their self-directed learning skills. Three main themes derived after data analysis were 1) Self-paced E learning, 2) Motivation and satisfaction 3) Project based teaching and learning. Five attributes relating to themes are described in (Table 2). Remaining five are briefly described below:

Theme 1. Self-paced E learning

Use of technology: Innovation in digital technologies brought tremendous change in teaching and learning. Most of the participants indicated that use of digital technologies during this course not only improved their critical thinking skill but also have a great positive impact on their self-directed learning skill. “I highly appreciate to the Moodle platform that provide opportunity of full time accessibility to the course with its relevant materials to follow and understand it” (participant #6).

Theme 2. Motivation with satisfaction

Reflection: Reflection is an integral part of blended learning, significant tool for engaging students and is helpful in enhancing student’s behavioral, emotional and cognitive processes. Most of the participants were in favor of daily self-reflection activity they did during their 10 days contact session. “We were bound to write reflection daily, what we learn, about our lectures and daily activities, teaching strategies used and behavior of our instructors and fellows. This enabled me to critically analyze my whole day activities, what I had learn and what are my strength and weaknesses and how I can improve them, infect it was a source of my internal motivation” (P#4)

Theme 3. Project-based teaching and learning

3.1. Use of metacognitive strategies: Metacognition is considered to be a set of learning skills that make students responsive how to evaluate their self and acclimatize progressively with metacognitive skills to become an effective learner. Projects and different learning activities enabled students to use metacognitive strategies.

“I was not familiar with the term metacognition, we were taught about metacognitive strategies but I learn..."
best by interacting with peers who were more advanced than me. I observed their proficient use of a metacognitive skills and try to follow them” (P#5)

“Self-directed learning enabled me to do literature search from authentic sources to find out the answer of particular question that is related to my task. For finalization the task, I take time to review it critically, without the instructor support that sort of thing” (P#9)

3.2. Developing own learning objectives: It was the opinion of participants that during their master’s degree program with blended learning environment they practiced how to write learning objectives. Writing of these specific statements helped us to evaluate our progress and what we are going to achieve at the end of project.

“I think practice of writing own learning objectives means actually you are polishing your self-direction skill. Leaning objectives served as road map towards your goal, so in order to achieve a given task set your goal, write your objective, monitor progress, evaluate and finally you will find results” (P#3)

3.3. Sense of responsibility: Self-directed learning is directly associated with sense of responsibility. In blended learning environment you have a contact session of only ten days, remaining two months before next contact session students have to take the responsibility of their own learning.

“After contact session, our instructors gave us assignments and explained how we have to complete this task with in a given time. These home task created a sense of responsibility and I was bound to manage my time and other activities in order to complete the task in time” (P#6)

Table No.2: Impact of blended learning environment on development of SDL skills

<table>
<thead>
<tr>
<th>Themes</th>
<th>Subthemes</th>
<th>Quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-paced E-learning</td>
<td>Conducive and flexible learning environment</td>
<td>“For me it was a very conducive and flexible learning environment, more comfortable to learn at my own pace, enabled me to figure out things personally, took initiative to make my own decisions rather than a class where everyone is expected at a same rate” (P#4)</td>
</tr>
<tr>
<td>Motivation with satisfaction</td>
<td>Peer communication</td>
<td>“As we have interaction with our teachers only during contact session but on Moodle and discussion forum we interact with our fellows and discus and express our views” (p#1)</td>
</tr>
<tr>
<td></td>
<td>Constructive and timely feedback</td>
<td>“I was a rote learner, but time bound assignments and timely constructive feedback from teachers motivated me, how I have to learn on my own and improve my grades” (P3#)</td>
</tr>
<tr>
<td>Project based teaching and learning</td>
<td>Time management/task management</td>
<td>“The most important aspect of BL environment was time bound assignment; we learn how to manage time and to complete task in a given time” (P#6)</td>
</tr>
<tr>
<td></td>
<td>Critical thinking process activation</td>
<td>“While presentations assigned to me during course, searching literature, application of information and to complete task improved my critical thinking skill” (P#2)</td>
</tr>
</tbody>
</table>

DISCUSSION

Our study highlights the different views of post graduates on their self-directed learning skills, recently completed their master degree program with blended learning environment. Comparing with the previous studies, our findings regarding self-directed learning skills development are less or more similar with a little bit of differences. In our study, conducive and flexible environment and time bound assignments and reflection were the main factors that have positive impact on self-directed learning skills of students. While in the previous study, design of working environment, feedback from instructor were effective in terms of improving self-directed learning of students. Blended Learning, a recent trend of higher educational institutes that provides an educational environment with various forms of communication by combining face-to-face learning with technologically enhanced online learning so that instruction and learning takes place both in the classroom and online. Flexible learning means increased focus of students on personalization of learning experiences and utilization of maximum opportunities available during the learning process. Majority of participants appreciated the flexibility given to them in their learning and assessment. They noted that blended learning offered convenience, time management, self- pacing, more access to resources,
and ease of communication, but few participants still prefer face-to-face teaching. Behavior, self-efficacy, environment and motivation affect learning process of a learner.\textsuperscript{15} It was opinion of participant that traditional courses are mostly theoretical and quite boring. My attention and motivation for the course increased as MHPE course provided both theoretical and practice-based applications along with giving us studying environment different from the traditional classroom. Communication and interactions with the peers in class and discussion forum on Moodle, after every assignment positive and constructive feedback from teachers was a source of motivation among post graduates. Writing reflection on daily basis was a part of contact session and it was opinion of participants that reflection on our daily activities was helpful to motivate us for future activities.

Active participation of learner, using active learning strategies can improve the learning process and performance.\textsuperscript{16} The emergence of numerous computer technologies allows use of multimedia content and multimedia communication for education, and provides learning material anywhere, anytime. Participants described self-directed learning as requisite characteristic, that is, taking the “initiative” to manage one’s own learning. Recognizing personal learning needs, establishing an approach, pursue information and resources to address that learning need. Some participants valued face to face component of this learning program, micro teaching, projects in small group and discussions with peers broadened their knowledge and provide more experience and ideas. Metacognition, an important aspect of human intelligence, higher learning and closely related to critical thinking. Metacognition means awareness, regulation, monitoring and reflection on any learning process that makes a learner an independent learner. Use of metacognitive strategies in completion of a given task /assignments, time management was a crucial component of this blended learning hence develop a sense of responsibility in participants.

Medical education being a vast field, the essential component to achieve the set goals is appropriate time management. A participant shared that after first contact session he could not manage time with frequent assessments. This mismanagement of time led to first-time failure which was shocking for him. Another participant was unable to focus on studies due to house responsibilities and was unable to perform in a better way. Later, time bound assignments with constructive feedback from supervisors create sense of responsibility and hence I improved my grades. Literature also emphasizes on the need to develop skills such as time management to be a life-long learner.\textsuperscript{17}

CONCLUSION

Health Professions Education is an emergent Master degree program with pure blended learning environment. It is providing flexible and conducive platform for health professionals to polish their soft and management capabilities through development of self-directed learning skill i.e. time management, effective communication, Critical thinking and task planning. Different instructional strategies, micro teaching, small group discussions and time bound assignments, self-paced and E-learning were the identified factors that promoted self-directed learning skill among post graduates of health professions education. This program enables the students to define and achieve their set goals within specific timeline. Infect, making students self-directed and lifelong learners in continuing professional education.

Acknowledgement: We are highly obliged to the institute and the participants who participated in this study.

Author’s Contribution:
Concept & Design of Study: Saira Waqqar
Drafting: Aasma Qaiser
Data Analysis; Amna Ahmed Noor
Revisiting Critically: Saira Waqqar, Aasma Qaiser
Final Approval of version: Saira Waqqar

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

REFERENCES


Vitamin Cobalamin in Metformin Treated Type 2 Diabetics Presenting at a Tertiary Care Hospital of Sindh
Muhammad Akbar¹, Akram Munir² and Fatima Qureshi²

ABSTRACT

Objective: To determine vitamin cobalamin (VC) in metformin treated type 2 diabetics compared to no metformin treated type 2 diabetics.

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Isra University Hospital, from March 2019 to February 2020.

Materials and Methods: A sample of 221 diabetics taking metformin (Group A - cases) and 200 diabetics (no metformin) (Group B - control) were selected through non-probability convenient sampling. Blood was centrifuged to get sera for analysis. Cobalamin was detected by ELISA assay kit (Chemiluminescence Technique). Data was analyzed and tabulated on SPSS (version 21.0) at 95% CI.

Results: Mean VC levels in group A (diabetics taking metformin) and group B (diabetic not taking metformin) were found at 139.5±15.7 and 302.5±58.51 pg/dl respectively (P=0.0001). VC deficiency was found in 83.3% in diabetics taking metformin compared to 71.5% in diabetic not taking metformin.

Conclusion: We found cobalamin deficiency in 83.3% diabetics taking metformin compared to 71.5% diabetic not taking metformin.

Key Words: Cobalamin, Metformin, Type 2 Diabetics.

INTRODUCTION

World burden of type 2 diabetes mellitus was 463 million diabetics in 2019 that is estimated to rise 700 million by the year 2045 as reported by the International Diabetes Federation (IDF).¹ Second National Diabetes Survey of Pakistan (NDSP) 2016 – 2017 showed the DM prevalence was 26.3%.¹² Metformin is the first line of hypoglycemic drugs recommended by the American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD) and the IDF.¹³ Previous studies have revealed metformin therapy is associated with vitamin cobalamin (VC) deficiency.⁴ Previous studies⁵,⁶ reported VC deficiency occurrence in 9% to 52% of type 2 diabetics and metformin has been an alleged drug. VC is necessary for the re-methylation reaction of homocysteine (Hcy) to methionine.

VC is essential for this methylation reaction of Hcy and VC deficiency may cause hyperhomocysteinemia – that is a risk factor for the vascular complications in type 2 diabetics.⁷ Vitamin cobalamin insufficiency or deficiency has emerged as an epidemic in metformin treated diabetics. Long term intake of metformin is reportedly interferes with intestinal cobalamin absorption. Cobalamin deficiency is associated with hematological disorders, immune dysfunction, hyperhomocysteinemia, vascular and neurological complications.⁸ Metformin induced cobalamin deficiency has been categorized as minor (type B) drug induced condition of clinical significance. Metformin when taken chronically for average >5 years manifests low serum cobalamin levels. Deficiency occurs for >5years duration till hepatic deposits is depleted. Metformin belongs to the biguanide class of anti – diabetic drug widely used because of low cost.⁹ Metformin augments insulin sensitivity and inhibits hepatic gluco-neogenesis.¹⁰ It has very good safety profile having gut intolerance as the major complaint.¹¹ In Pakistan, prevalence of DM has exponentially increased²,¹² compared to any other country affecting rural and urban populations equally. Metformin, being cost effective drug, is widely used in the country. Risk of VC deficiency in long term metformin intake diabetics needs further studies as the risk of VC deficiency is multiplied by dietary insufficiency.¹³ In this context the present observational study was conducted to analyze the serum cobalamin in type 2
MATERIALS AND METHODS

The present observational study was conducted at the Department of Medicine, Isra University Hospital. Study took place from March 2019 to February 2020. Study was approved by the institute’s ethical review committee (ERC). A sample of 221 diabetics taking metformin (Group A- cases) and 200 diabetics (no metformin) (Group B - control) were selected through non-probability convenient sampling. Sample size was calculated by proportions for the sample size. Inclusion criteria for group A were; diagnosed cases of DM, volunteers, age 40 – 60 years, metformin intake for ≥5 years and metformin dose 1-2 grams daily. Inclusion criteria for group B were; diagnosed cases of DM, volunteers, age 40 – 60 years, who had no history of metformin intake. Exclusion criteria were; age <40 or > 60 years, meat intake, liver or liver extract intake in last 3 months, hypothyroid, alcoholics, chronic liver disorders, renal disease, chronic malabsorption syndrome and taking proton pump inhibitors. Patients taking multivitamins and vitamin-mineral pills were excluded. Signing of consent form was mandatory. Duration of diabetes mellitus, metformin intake, relevant clinical history, and other drug intake was taken. Clinical history was taken by researcher to fulfill the inclusion and exclusion criteria. Volunteers were interviewed of their full consent, signing of proforma and willingness of blood sampling. They were asked to abide by the study protocol study. They were informed that the expenses of blood investigations will be paid by the researcher. Volunteers were informed the confidentiality of information is secured by the researcher, and blood laboratory investigations will never by publicized, only results will be published in a medical journal. A pre-structured proforma was designed for data collection to be entered and saved in. Volunteers were taken 3 ml blood from skin vein, preferably from the ante- cubital fossa under proper aseptic conditions. 3 ml BD disposable syringe drew blood; 3 ml was put into Sodium fluoride tube, and 2 ml was centrifuged to get sera. Hematolgoical parameters were performed in Cobas hematology analyzer. Sera were used for vitamin cobalamin (VC) estimation by ELISA assay kit (Abbot Architect -1000) by Chemiluminescence Technique. Cobalamin levels were categorized as; <100 pg/ml - severe VC deficiency, <170 - >100 pg/dl VC deficiency, 170-239.9 pg/ml – mild deficiency and ≥240pg/ml normal vitamin cobalamin levels. Statistical analysis of variables was performed on SPSS (version 21.0) using Student t – test and results were presented as mean and standard deviation (SD). Gender distribution was analyzed by Chi-square and results (frequency and %). Results were taken statistically significant at 95% CI (P ≤ 0.05).

RESULTS

Mean age of subjects in Group A (Diabetics) was 48.5±7.5 compared to Group B (control) 47.5±11.5 years. Group A comprised of 221 study subjects; 119 (53.8%) were male and 102 (46.1%) were female (P<0.05). While Group B comprised 200 study subjects; male were 101(50.5%) and female were 99 (49.5%)(P>0.05). Mean vitamin cobalamin levels in group A (diabetics taking metformin) and group B (diabetic not taking metformin) were found at 139.5±15.7 and 302.5±58.51 pg/dl respectively (P=0.0001).

Table No.1: Cobalamin levels in study groups

<table>
<thead>
<tr>
<th>Cobalamin</th>
<th>Group A, Diabetics (n=221)</th>
<th>Group B, Control (n=200)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 pg/dl</td>
<td>70.5±15.1</td>
<td>97.1±2.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>&lt;170 - &gt;100 pg/dl</td>
<td>111.1±5.6</td>
<td>165.2±37.5</td>
<td></td>
</tr>
<tr>
<td>170-239.9 pg/dl</td>
<td>191.3±11.5</td>
<td>276.3±34.3</td>
<td></td>
</tr>
<tr>
<td>≥240 pg/ml</td>
<td>615.1±13.7</td>
<td>935.7±26.7</td>
<td></td>
</tr>
</tbody>
</table>

Table No.2: Frequency of cobalamin deficiency in study groups

<table>
<thead>
<tr>
<th>Cobalamin</th>
<th>Group A, Diabetics (n=221)</th>
<th>Group B, Control (n=200)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 pg/dl</td>
<td>99 (44.7%)</td>
<td>78 (39%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>&lt;170 - &gt;100 pg/dl</td>
<td>49 (22.1%)</td>
<td>38 (19%)</td>
<td></td>
</tr>
<tr>
<td>170-239.9 pg/dl</td>
<td>34 (17%)</td>
<td>27 (13.5%)</td>
<td></td>
</tr>
<tr>
<td>≥240 pg/ml</td>
<td>39 (15.3%)</td>
<td>57 (28.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>221 (100%)</td>
<td>200 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Graph No.1: Gender distribution in study groups

Table 1 shows the vitamin cobalamin distribution in study groups. In group A, vitamin Cobalamin levels; severe deficiency (<100 pg/dl), mild deficiency (170-240 pg/dl), deficiency (<170 pg/dl) and normal (>240 pg/ml) levels were found in 49.5%, 24.5%, 17% and

19.5% compared to group B that revealed severe deficiency (<100 pg/dl), mild deficiency (170-240 pg/dl), deficiency (<170 pg/dl) and normal (≥240 pg/ml) levels in 39%, 19%, 13.5% and 28.5% respectively (table 2 and graph 2) (P=0.0001). Graph 3 shows the vitamin Cobalamin distribution in groups A and B. Normal and deficient cobalamin was found in 16.2% and 83.3% in group A (diabetics taking metformin) compared to 28.5% and 71.5% in group B (diabetic not taking metformin).

DISCUSSION

The present observational study was conducted at our tertiary hospital Liaquat University, Jamshoro. Serum cobalamin levels were compared between diabetics taking metformin versus diabetics not taking metformin. Metformin is a cost effective drug hence prescribed as first line drug for glycemic control in type 2 diabetics. It is prescribed as single pill or combined with other anti – diabetic drug. Gut intolerance is the common side effect of metformin; however, long term therapy in diabetics has been implicated in causing vitamin cobalamin (VC) deficiency. One postulated mechanism of VC deficiency is retardation of cobalamin-intrinsic factor endocytosis in the terminal ileum. In present study, cobalamin deficiency was found in 83.3% group A (diabetics taking metformin) compared to 71.5% in group B (diabetic not taking metformin). The findings are in agreement with previous studies. A recent study from Pakistan reported 68% VC deficiency in gestational DM compared to 40% in control. They reported that the vitamin cobalamin deficiency is very common nutritional deficiency. Another recent study from Pakistan has reported the VC insufficiency is frequent findings in metformin treated type 2 diabetics that may progress to frank VC deficiency. They found association of VC deficiency causing peripheral neuropathy. The findings of above studies are in agreement with present study. However, 83.3% group A (diabetics taking metformin) is a new finding showing the true prevalence of metformin – induced VC deficiency. Still another recent study has reported 41% VC deficiency in metformin treated type 2 diabetics compared to 20% in metformin naïve patients. The findings of above study are in keeping with present study finding of VC deficiency. However, frequency of 83.3% cobalamin deficiency is very high and is being reported for the first time. This may be because of nutritional deficiency that is prevalent among the general population of Pakistan. We think the nutritional VC deficiency is very high in the society and metformin – induced addition shows high VC deficiency. This is the most probable justification of VC deficiency. Another justification of high VC deficiency is the 71.5% VC deficiency in no-metformin diabetics that points to the severe nutritional deficiency. A previous study reported 27.5% VC deficiency in metformin treated diabetics. The finding of VC deficiency is a consistent finding but the high frequency of 83.3% was found in present study. Another reason of severe VC deficiency is duration of metformin as the present study selected those diabetics with history of ≥ 5 years metformin therapy. Nutritional deficiency is more prevalent and this may be superadded by the metformin therapy causing severe VC deficiency. A previous study reported 31% VC deficiency in metformin treated diabetics that is in contrast to 83.3% VC deficiency in present study. This controversy is because of duration of metformin therapy. Above study analyzed VC at 3 months that is in contrast to ≥5 years metformin duration of present study. Another previous study found 31% VC deficiency in metformin treated diabetics compared to 9% no-metformin therapy. In present study, cobalamin deficiency was found in 83.3% diabetics taking metformin compared to 71.5% diabetic not taking metformin. This indicates prevalent nutritional deficiency in the country. A previous study have reported 38.1% VC deficiency in their diabetic population. However, the study sample of above study was small. Hence findings are incomparable. In present study, the mean vitamin cobalamin levels in group A (diabetics taking metformin) and group B (diabetic not taking metformin) were found at 139.5±15.7 and
302.5±58.51 pg/dl respectively (P=0.0001). The findings are in agreement with a previous study\textsuperscript{24} that reported VC deficiency in range of 125–250 pg/ml. A previous study\textsuperscript{25} found VC deficiency that was severe enough causing megaloblastic anemia in metformin treated diabetics. The findings are sufficiently keeping with the present study. A previous study showed VC deficiency <150 pmol/l that is in agreement as the present study found <100 pg/dl VC concentration in both study groups. One of the major limitations of present study is that the nutritional deficiency might have affected the results towards severe VC deficiency that needs further studies.

CONCLUSION

Vitamin cobalamin deficiency is observed in diabetics taking metformin therapy for long duration. We found cobalamin deficiency in 83.3% diabetics taking metformin compared to 71.5% diabetic not taking metformin. Diabetics taking metformin for long duration must be checked vitamin cobalamin and should get vitamin supplements.

Author’s Contribution:
Concept & Design of Study: Muhammad Akbar
Drafting: Akram Munir
Data Analysis: Fatima Qureshi
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

Effects of Different Dosage of Calcium on Gentamicin-Induced Nephrotoxicity in Rabbits

Nauman Idris Butt¹, Mohammad Rafique³, Umra Imran², Anum Imran², Faryal Azhar² and Muhammad Usama Faruqui⁴

ABSTRACT

Objective: To Study the Effects of Different Dosages of calcium on Gentamicin-Induced Nephrotoxicity in Rabbits.
Study Design: Experimental Study
Place and Duration of Study: This study was conducted at the Idris Teaching Hospital Sialkot and DHQ Teaching Hospital Faisalabad during Feb 2020 to April 2020.
Materials and Methods: Fifty-four Rabbits were included in this experimental study. Different doses of Calcium and Gentamicin were given to rabbits and Blood urea nitrogen (BUN), Serum Creatinine, Urine Protein, Kidney SOD and histopathology of kidney were recorded. The Ethical Committee Permission was taken before start of the study and data published in Medical Journal. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 14.0 package. The data were expressed as mean ± standard deviation (SD). Student's unpaired t-test, analysis of variance (ANOVA), and Wilcoxon Rank Sum test were used for parametric and non-parametric data, respectively. P <0.05 was considered significant.

Results: Rabbits: Effect on BUN, serum Creatinine, urinary proteins and kidney SOD: The levels of BUN, serum creatinine, urinary proteins, and kidney SOD were compared between the five groups, on day 7, after six days of consecutive treatment with respective drugs. The baseline values were similar in all groups on day 0. Results showed that BUN, serum creatinine, and urinary proteins were significantly elevated (P <0.05) and kidney SOD levels were significantly reduced (P <0.05) in group II (Gentamicin-treated group). While calcium 0.5 g/kg/day and calcium 1.0 g/kg/day significantly reduced (P <0.05) the elevated BUN, serum creatinine, urinary proteins, and significantly elevated (P < 0.05) the SOD levels when administered with gentamicin in group V, respectively. There was a significant dose-dependent relationship between group 4 with group 5 (calcium 1.0 g/kg/day) showing more significant effect on above parameters when compared to group V.

Histopathological effects: The histopathological picture of animals in group I, III, and IV revealed normal architecture of glomeruli and mesangium. Basement membrane of the tubules was found to be intact. However, animals in group II (gentamicin only) showed numerous patches of focal and diffuse necrosis of tubular cells. Basement membrane breaks were found in tubule sections. Glomerular changes of grade 4 were seen with occasional infiltration. The renal histopathology picture in group V (calcium 0.5 g/kg/day) revealed normal architecture of glomeruli and mesangium with few areas of focal necrosis while group V (calcium 1.0 g/kg/day) revealed normal architecture of glomeruli and mesangium. Basement membrane of the tubules was found to be intact in both groups. Basement membrane breaks were found in tubule sections. Glomerular changes of grade 4 were seen with occasional infiltration

Conclusion: The administration of calcium 1.0 g/kg/day is more efficacious than calcium 0.5 g/kg/day in preventing Gentamicin-induced Nephrotoxicity in rabbits. Further, there is no species sensitive variation in results that could be extrapolated to humans.

Key Words: Rabbits, Gentamicin, Calcium, Nephrotoxicity.


INTRODUCTION

Aminoglycosides are utilized in the administration of genuine and hazardous gram-negative bacterial contaminations in light of their synergism with beta-lactam anti-toxins, their stamped post-anti-toxin impact, and their quick fixation subordinate murdering impact. Be that as it may, nephrotoxicity especially on delayed organization is seen in 10–20% of hospitalized patients who create intense harmful renal failure. Various investigations completed so far have demonstrated that in 39% of instances of intense renal disappointment, earlier organization of medications was the reason for failure. More disturbing was the way that gentamicin organization was answerable for the same number of as 89% of these cases. Nephrotoxicity is answerable for

INTRODUCTION

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more and all the more exorbitant hospitalizations and potentiates the poison levels of other drugs. An expanding assemblage of proof shows that the systems engaged with gentamicin-initiated nephrotoxicity are multifaceted. The atomic and pathophysiological instruments of gentamicin-instigated nephrotoxicity are all around described. Gentamicin is disguised through the mammoth endocytic complex that is specially communicated in renal proximal cylindrical fragments S1 and S2. In these cells, gentamicin is for the most part amassed in lysosomes, the Golgi contraption and endoplasmic reticulum, delivering lysosomal phospholipidosis, unfurled protein reaction and different impacts, in this way turning on apoptotic and necrotic passing pathways.

Past decade has seen a colossal examination on rodents and bunnies all the while to perceive any confusions initiated by gentamicin inside the renal tubule cells, accordingly forestalling basic cell nephrotoxicity upgrading potential. Past examinations utilizing calcium channel blockers, for example, verapamil have demonstrated opposing outcomes in gentamicin-induced nephrotoxicity with some indicating an advantag.

MATERIALS AND METHODS

Fifty-four Rabbits were included in this experimental study. Different doses of Calcium and Gentamicin were given to rabbits and Blood urea nitrogen (BUN), Serum Creatinine, Urine Protein, Kidney SOD and histopathology of kidney were recorded. The Ethical Committee Permission was taken before start of the study and data published in Medical Journal. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 14.0 package. The data were expressed as mean ± standard deviation (SD). Student’s unpaired t-test, analysis of variance (ANOVA), and Wilcoxon Rank Sum test were used for parametric and non-parametric data, respectively. P <0.05 was considered significant.

RESULTS

Rabbits

Effect on BUN, serum creatinine, urinary proteins and kidney SOD

The levels of BUN, serum creatinine, urinary proteins, and kidney SOD were compared between the seven groups, on day 7, after six days of consecutive treatment with respective drugs. The baseline values were similar in all groups on day 0. Results showed that BUN, serum creatinine, and urinary proteins were significantly elevated (P < 0.05) and kidney SOD levels were significantly reduced (P < 0.05) in group II (Gentamicin-treated group). Calcium 1.0 g/kg/day and verapamil 7.0 mg/kg/day had no significant effect on above parameters when administered with gentamicin in group III and group IV, respectively (Table 1) while calcium 0.5 g/kg/day and calcium 1.0 g/kg/day significantly reduced (P < 0.05) the elevated BUN, serum creatinine, urinary proteins, and significantly elevated (P < 0.05) the SOD levels when administered with gentamicin in group V and group VI, respectively. [Table 2] There was a significant dose-dependent relationship between group V and group VI with group VI (calcium 1.0 g/kg/day) showing more significant effect on above parameters when compared to group V. Table 2

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
</tr>
<tr>
<td></td>
<td>(Control, normal saline)</td>
</tr>
<tr>
<td>Blood urea nitrogen (BUN) (mg/dl)</td>
<td>17.95 +_ 1.2390</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>0.5 +_ 0.083</td>
</tr>
<tr>
<td>Urinary proteins (mg/dl)</td>
<td>0.24 +_ 0.43</td>
</tr>
<tr>
<td>Kidney superoxide dismutase (SOD) (U/ml)</td>
<td>0.161 +_ 0.0162</td>
</tr>
</tbody>
</table>

P<0.05 as compared to group 1. SOD= Superoxide dismutase level, BUN= Blood urea nitrogen, SD= Standard deviation.
Table No. 2: Effect of gentamicin, gentamicin + calcium (0.5 g/kg/day), gentamicin + calcium (1.0 g/kg/day), on blood urea nitrogen (BUN), serum creatinine, urinary proteins, and kidney SOD in rabbits

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Group 5 (Gentamicin 80 mg/kg/day, i.m. + calcium 0.5 g/kg/day, p.o.)</th>
<th>Group 5 (Gentamicin 80 mg/kg/day, i.m. + calcium 1.0 g/kg/day, p.o.)</th>
<th>BUN (mg/dl)</th>
<th>Serum Creatinine (mg/dl)</th>
<th>Urinary proteins (mg/dl)</th>
<th>Tissue superoxide dismutase (SOD) (U/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mg/dl)</td>
<td>125.95 + 3.97</td>
<td>92.95 + 4.97</td>
<td>20.96 + 1.72</td>
<td></td>
<td>0.34 + 0.04</td>
<td>0.17 + 0.035</td>
<td>0.56 + 0.04</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>4.58 + 0.60</td>
<td>2.20 + 0.47</td>
<td>0.47 + 0.06</td>
<td></td>
<td>1.25 + 0.21</td>
<td>0.24 + 0.035</td>
<td>0.39 + 0.01</td>
</tr>
<tr>
<td>Urinary proteins (mg/dl)</td>
<td>2.07 + 0.93</td>
<td>1.12 + 0.028</td>
<td>0.24 + 0.035</td>
<td></td>
<td>0.17 + 0.021</td>
<td>0.17 + 0.015</td>
<td>0.17 + 0.015</td>
</tr>
<tr>
<td>Tissue superoxide dismutase (SOD) (U/ml)</td>
<td>0.04</td>
<td>0.39 + 0.01</td>
<td>0.17 + 0.015</td>
<td></td>
<td>0.20 + 0.018</td>
<td>0.20 + 0.015</td>
<td>0.17 + 0.015</td>
</tr>
</tbody>
</table>

P<0.05 as compared to group 2. P<0.05 compared to group 5. SOD= Superoxide dismutase level, BUN= Blood urea nitrogen, SD= Standard deviation.

Table No. 3: Effect of normal saline, gentamicin, calcium, on histopathology in rabbit kidney

<table>
<thead>
<tr>
<th>Histopathology scores</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Mean rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=16) normal saline 2.0 ml/kg</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6.5</td>
</tr>
<tr>
<td>Group 2 (n=16) Gentamicin 80 mg/kg, i.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6.5</td>
</tr>
<tr>
<td>Group 3 (n=16) Calcium 1.0 g/kg, p.o.</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6.5</td>
</tr>
</tbody>
</table>

P<0.05 as compared to group 1

Table No. 4: Effect of gentamicin, gentamicin + calcium (0.5 g/kg/day), gentamicin + calcium (1.0 g/kg/day) on histopathology in rabbit kidney

<table>
<thead>
<tr>
<th>Histopathology scores</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Mean rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2 (n=16) Gentamicin 80 mg/kg, i.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.95</td>
<td>9.4</td>
</tr>
<tr>
<td>Group 4 (n=16) Gentamicin 80 mg/kg, i.m. + calcium 0.5 g/kg, p.o.</td>
<td>1.98</td>
<td>3.98</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.2</td>
</tr>
<tr>
<td>Group 5 (n=16) Gentamicin 80 mg/kg/day, i.m. + calcium 1.0 g/kg/day, p.o.</td>
<td>4.96</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.0</td>
</tr>
</tbody>
</table>

P<0.05 as compared to group 2

Table No. 5: Effect of normal saline, gentamicin, calcium, on blood urea nitrogen (BUN), serum creatinine, urinary proteins, and kidney superoxide dismutase (SOD) in rabbits

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Group 1 (Control, normal saline, 2.0 ml/kg)</th>
<th>Group 2 (Gentamicin 80 mg/kg/day, i.m.)</th>
<th>Group 3 (Calcium 1.0 g/kg/day, p.o.)</th>
<th>BUN (mg/dl)</th>
<th>Serum Creatinine (mg/dl)</th>
<th>Urinary proteins (mg/dl)</th>
<th>Kidney SOD (U/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mg/dl)</td>
<td>18.95 + 1.50</td>
<td>130.07 + 3.80</td>
<td>19.80 + 2.01</td>
<td>0.34 + 0.04</td>
<td></td>
<td>1.25 + 0.21</td>
<td>0.17 + 0.021</td>
<td>0.20 + 0.018</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>0.34 + 0.04</td>
<td>3.90 + 0.15</td>
<td>0.29 + 0.32</td>
<td>0.17 + 0.021</td>
<td></td>
<td>0.15 + 0.092</td>
<td>0.21 + 0.021</td>
<td>0.21 + 0.021</td>
</tr>
</tbody>
</table>

P<0.05 as compared to group 1. SOD= Superoxide dismutase level, BUN= Blood urea nitrogen, SD= Standard deviation.

Histopathological effects: The histopathological picture of animals in group I, III, and IV revealed normal architecture of glomeruli and mesangium. Basement membrane of the tubules was found to be intact. However, animals in group II (gentamicin only) showed numerous patches of focal and diffuse necrosis of tubular cells. Basement membrane breaks were found in tubule sections. Glomerular changes of grade 4 were seen with occasional infiltration. (Table 3) The renal histopathology picture in group V (calcium 0.5 g/kg/day) revealed normal architecture of glomeruli and mesangium with few areas of focal necrosis while group VI (calcium 1.0 g/kg/day) revealed normal architecture of glomeruli and mesangium. Basement membrane of the tubules was found to be intact in both groups (Table 4). However, the animals in group VII (gentamicin + verapamil) showed patches of focal and diffuse necrosis of tubular cells. Basement membrane breaks were found in tubule sections. Glomerular changes of grade 4 were seen with occasional infiltration (Table 5).

Rabbits

Effect on BUN, serum creatinine, urinary proteins, and kidney SOD: The levels of BUN, serum creatinine, urinary proteins, and kidney SOD were compared between the five groups on day 7 after 6 days of consecutive treatment with respective drugs in a manner similar to those in rabbits. The baseline values were similar in all groups on day 0. The results were identical to results obtained in rabbits with group II (gentamicin only) showing a significant elevation (P < 0.05) of BUN, serum creatinine, urinary proteins, and significant reduction (P < 0.05) of kidney SOD when compared to control group [Table 5].
This investigation was directed to think about the impacts of various doses of calcium on Gentamicin-prompted Nephrotoxicity in hares. Gentamicin 80 mg/kg/day i.e. for six days in hares is known to deliver morphological and biochemical adjustments in kidneys like the signs in human kidney.\(^\text{11}\) Hence, Gentamicin was utilized in our investigation for acceptance of Nephrotoxicity in hares in comparative portion and term. In clinical settings, intense renal disappointment is analyzed based on BUN and serum Creatinine. They are considered as the most solid and practical markers of renal capacity among some other renal parameters.\(^\text{12}\) Therefore BUN, serum Creatinine, and urinary proteins were evaluated for estimation of kidney work in our investigation. Different lysosomal compounds like decreased glutathione, SOD, malondialdehyde, and histopathological changes. Thus, we additionally evaluated superoxide dismutase levels and histopathological changes as boundaries for estimating renal poisonousness. These boundaries have been effectively utilized by different analysts in past studies.\(^\text{13}\)

The outcomes showed in hares, calcium when regulated alone for six days in bunches III and IV, individually, didn't build the BUN, serum Creatinine, urinary proteins, or decreased kidney SOD levels, demonstrating that these medications are not nephrotoxic without anyone else. Then again, gentamicin particularly expanded the BUN, serum creatinine, urinary proteins, and diminished the kidney SOD levels when directed for six days in bunch II in hares. These outcomes were steady with recently directed examinations in which gentamicin has been demonstrated to be exceptionally nephrotoxic.\(^\text{14}\) Gentamicin extraordinarily upgrades the age of receptive oxygen metabolites in the mitochondria. Histopathological changes of evaluation 4 reminiscent
of cylindrical rot and glomerular harm were likewise found in Gentamicin-rewarded hares in bunch II affirming the nephrotoxic capability of Gentamicin saw in before examine. In our examination we found that low portions of calcium, for example 0.5 g/kg/day had the option to forestall nephrotoxicity actuated by gentamicin in a huge way when contrasted with bunch II creatures regulated gentamicin alone. There was a noteworthy decrease in BUN, serum creatinine, urinary proteins, and rise of kidney SOD levels when contrasted with hares given Gentamicin alone. Histopathological assessment likewise demonstrated less rounded and glomerular harm when contrasted with hares given gentamicin alone. Calcium in a high portion of 1.0 g/kg/day alongside Gentamicin demonstrated huge decrease in BUN, serum creatinine, urinary proteins, and rise of kidney SOD in bunch V when contrasted with Gentamicin alone The histopathological assessment additionally indicated typical engineering in creatures co-rewarded with calcium 1.0 g/kg/day and gentamicin. The portion of calcium 1.0 g/kg/day was altogether more useful than calcium 0.5 g/kg/day in normalizing the disturbed biochemical boundaries and forestalling the morphological modifications in tubules and glomerulus of kidney. These outcomes were like a previous investigation directed indicating a portion subordinate defensive impact of calcium. Some laborers have shown that oral Ca2+ load notably decreases the gentamicin-prompted renal disappointment in people and rabbits. Others anyway have neglected to record a Ca2+-incited enhancement in gentamicin nephrotoxicity in bunnies. While still others have detailed Ca2+ to potentiate intense renal disappointment in people rewarded with gentamicin. Calcium has nephroprotective activity by either reducing practical hemodynamic modifications at the glomerular level or forestalling basic cell harm at the rounded level. Others propose that the defensive activity of Ca2+ might be intervened either (a) by initiating metabolic changes during oral Ca2+ loading, (b) by easing back renal cortical collection, or (c) by upgrading the discharge of gentamicin.

In this investigation, we didn't discover any adjustment in the BUN, serum creatinine, urinary proteins, and SOD levels in bunnies regulated with gentamicin. Further histopathology indicated numerous regions of extreme central corrosion and rounded harm in gentamicin gathering. Likewise, there was no huge increment in the harmfulness on attending gentamicin yet not at all like the examination did by Ali et al., 2002 which indicated improve the impacts of gentamicin.

CONCLUSION

The administration of calcium 1.0 g/kg/day is more efficacious than calcium 0.5 g/kg/day in preventing Gentamicin-induced Nephrotoxicity in rabbits. Further, there is no species sensitive variation in results that could be extrapolated to humans.

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Revisiting Critically: Nauman Idris Butt, Mohammad Rafique
Final Approval of version: Nauman Idris Butt

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

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