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Abstract

Objective: To determine the patterns of antimicrobial drug resistance among gram negative bacterial pathogens in intensive care unit in a tertiary care hospital, Lahore

Study Design: Cross-sectional study.

Place and Duration of Study: October 2016-September 2018, Sharif Medical City Hospital.

Methodology: A total of 371 clinical specimens received in microbiology lab, SMCH for culture and sensitivity from Intensive care unit patients showing signs and symptoms of infections were included in the study. All other specimens were inoculated on Blood agar (Oxoid UK) and Mac Conkey agar (Oxoid UK) and urine was inoculated on CLED (Oxoid UK). The culture plates were incubated for 18-24 hours at 37°C. The bacterial isolates were identified by colony morphology, gram staining and biochemical profile. The antibiotic susceptibility of Gram negative bacteria isolated was assessed by Kirby-Bauer disk diffusion technique in accordance with guidelines of Clinical Laboratory Standard Institute (CLSI).

Results: Out of 371, 172 (46.36%) specimens yielded positive cultures and 199 (53.68%) specimens were negative. 90 (52.3%) of the pathogens isolated were Gram negative bacteria, 56 (32%) were gram positive cocci and the remaining were candida species 26 (15.1%). Among GNRs, E.coli showed the highest prevalence of 46 (51.1%) followed by Pseudomonas aeruginosa 18 (20%), Acinetobacter sp. 10 (11.1%), Klebsiella sp. 9 (10%), Proteus sp. 5 (5.5%) and Enterobacter sp. 2 (2.2%). Enterobacteriaceae showed least resistance to carbapenems. Only 28.2% of E.coli was resistant to imipenem and 21.7% to meropenem. As far as Klebsiella pneumoniae is concerned 44.4% isolates were resistant to imipenem and meropenem. However, Pseudomonas aeruginosa and Acinetobacter sp didn't exhibit good susceptibility for carbapenems as 72.2% Pseudomonas aeruginosa and 100% Acinetobacter sp were resistant to imipenem and meropenem. Much poor susceptibility was observed for other β-lactams such as ampicillin, co-amoxiclav, cephalexins etc.

Fluoroquinolones again proved to be poor choice for gram negative bacteria as 100% Acinetobacter, Klebsiella, Enterobacter sp, 72.2% Pseudomonas, 80% Proteus and 91.3% E.coli were fluoroquinolone resistant.

Conclusion: Majority of the gram negative isolates showed a high resistance to the commonly used antimicrobials like penicillins, cephalexins, fluoroquinolones, β-lactam combinations etc. Only carbapenems and aminoglycosides showed moderate sensitivity. Acinetobacter sp are highly resistant to all commonly used drugs and only doxycycline showed a hope for treatment of infections with acinetobacter sp.

Keywords: Antibiotic susceptibility, Kirby-bauer disk diffusion technique, Intensive care unit
A n intensive care unit (ICU) is a potential source of infection. As the patients with weak immune status and poor host defense requiring invasive manipulations such as tracheal intubation, mechanical ventilation, intravascular catheterization, I/V line access are being managed there, they are more prone to be infected. The closed ICU setups and immuno-compromised patients permit virulent as well as opportunistic microorganisms to establish, multiply and hence cause disease. Despite better care and hygiene practices in ICU than other areas of hospital, there is a consistent rise in ICU infections. This is true even for countries where infection prevention policies are followed. The most commonly encountered ICU infections are ventilator associated pneumonia and surgical site infections. These are then followed by urinary tract (UTI), bloodstream (BSI) and gastrointestinal tract infections. The spectrum of microbial pathogens isolated from ICUs shows wide variation among different countries and even among various hospitals of the same region. However, more frequently isolated bacteria include gram negative microbes like Escherichia coli, Klebsiella sp., Pseudomonas sp., Acinetobacter sp., Enterobacter sp., Proteus sp., Citrobacter sp., and gram positive microbes such as Staphylococcus aureus, enterococcus sp., and even Candida sp. For many years, control of gram positive pathogens have been primarily emphasized by designing new antibiotics and infection control plans. Meanwhile, the prevalence of gram-negative infections have shown a significant increase in intensive care units (ICUs). Various studies reveal E.coli, Klebsiella sp, Pseudomonas aeruginosa and Enterobacter sp. constituting the major bulk for ICU infections, E. coli being on the top of the list.

Treatment of ICU infections have become a challenge because of development of multi drug resistance. This calls for the right understanding of MDR and XDR microbes and drags the attention of clinicians and physicians for the judicious use of antibiotics. If this emerging resistance is not addressed promptly and the irrational antimicrobial usage is not ceased, we might fall back to pre-antibiotic era. Particularly the gram negative bugs are becoming increasingly resistant to the best available antibiotics, hence worsening the clinical outcome due to therapeutic failure. The high rate of ICU infections caused by MDR gram negative pathogens results in high morbidity, prolonged hospitalization, increased mortality and ultimately heavy economic burden.

Hence, the need of hour is to gather regional data for determining the commonly encountered bacterial pathogens in ICUs and assess their resistance pattern. So, this study was designed to identify the most common pathogens in ICUs of a tertiary care hospital, Lahore and evaluate their resistance pattern. This would definitely contribute to redesign local antibiotic policies and better patient outcome.

**Objective:**

To determine the common gram negative bacterial pathogens and their patterns of antimicrobial drug resistance in intensive care unit in a tertiary care hospital, Lahore

**METHODOLOGY:**

This study was conducted in Sharif Medical City Hospital over a period of 2 years from October 2016-September 2018. It included 371 specimens received in microbiology lab, SMCH for culture and sensitivity from ICU patients showing signs and symptoms of infections. The specimens were urine, blood, CSF, peritoneal, ascitic, pleural fluids, pus, wound swabs, CVP tip, tissues etc. Institutional ethical and research committee approved the project for research purpose.

All other specimens were inoculated on Blood agar (Oxoid UK) and Mac Conkey agar (Oxoid UK) and urine was inoculated on CLED (Oxoid UK). The culture plates were incubated for 24 hours at 37°C. The bacterial isolates were identified by colony morphology, gram staining and biochemical profile. Analytical profile index API-20E (Biomeerieux, France) was used to identify members of
Enterobacteriaceae family according to manufacturer's protocol. The antimicrobial sensitivity of the isolates was assessed by Kirby Bauer disc diffusion method using CLSI guidelines\(^{(11)}\) Following commercially available antibiotic discs (Oxoid/UK) were used in this study.

Amoxicillin/clavulanic acid (20/10μg), ceftriaxone (30μg), cefotaxime (30μg), ceftazidime (30 μg), cefipime (30μg), imipenem (10 μg), meropenem (10 μg), gentamicin (10 μg), Amikacin (30 μg), ciprofloxacin(5μg), trimethoprim/ sulfamethoxazole(1.25/23.75μg), piperacillin/tazobactam(100/10μg). The zones of inhibition of all drugs for the isolated bacteria were measured and reported according to the CLSI guidelines.\(^{(11)}\) S. aureus (ATCC 25923) and E. coli (ATCC 25922) were used as reference strains.

**DATA ANALYSIS**

The data was entered and analyzed by Statistical Package for Social Sciences (SPSS) version 24. Frequencies and percentages were evaluated for the study variables. The p-value of ≤ 0.5 was taken as statistically significant.

**RESULTS**

A total of 371 specimens from ICU patients consisting of urine, sputum, CSF, pleural fluid, ascitic fluid, CVP tip, blood, pus, wound swabs, tissue etc were included in the study. Out of 371, 172 (46.36%) specimens exhibited positive cultures and 199 (53.68%) specimens turned out negative for any bacterial pathogen. 52.3% (90) of the pathogens isolated were Gram negative bacteria.

Figure 1 shows number of all specimens from ICU which were included in the study. A total of 371 specimens were proceeded for culture and sensitivity. Out of those 96 were urine, 87 blood and 80 were pus or wound swabs. The remaining specimens were constituted by fluids, CVP tip etc as shown in the figure.

Figure 2 represents various Gram negative rods isolated from ICU. The bar chart shows that out of total 90 GNR isolates, 46 (51.1%) were E.coli followed by Pseudomonas aeruginosa 18 (20%). 10(11.1%) were Acinetobacter sp, 9(10%) Klebsiella sp, 5(5.5%) Proteus sp and 2(2.2%) were Enterobacter sp.

**FIG 1: Specimens From ICU**

**FIGURE 2: GNR isolated from ICU Specimens**

Table 1 exhibits the specimens along with the pathogens isolated. It is evident from the table that E.coli was the commonest isolated pathogen from urine specimens followed by Klebsiella and Pseudomonas aeruginosa.96 specimens of urine were proceeded and 19 revealed E.coli. Klebsiella sp and Pseudomonas aeruginosa were isolated from 2 specimens. Only 1 urine culture revealed Proteus sp and 1 Enterobacter. Similarly E.coli was again the predominant pathogen isolated from pus/wound swabs. Out of 80 pus specimens, E.coli was isolated from 21 specimens, Pseudomonas aeruginosa from 6, Klebsiella sp from 4 specimens, Acinetobacter sp and Proteus sp were isolated from 2 specimens each. Among pathogens isolated from sputum, 5 were
Pseudomonas aeruginosa and 4 turned out to be acinetobacter sp. In CVP tip, again the non-fermenters were predominant as 4 specimens yielded Pseudomonas aeruginosa followed by acinetobacter sp. in 2 specimens. Majority of the blood cultures were negative with only 2 yielding gram negative bacteria.

The antibiotic drug resistance pattern of enterobacteriaceae is shown in Table 2. A very poor susceptibility is observed for Amoxicillin-clavulinate, cephalosporins and ciprofloxacin. Out of aminoglycosides, amikacin showed better results. Only 39.1% E.coli, and none of the Enterobacter showed resistance to amikacin. However, 66.7% Klebsiella sp. and 60% Proteus were amikacin resistant. Carbapenems showed promising results for E.coil and Enterobacter as only 28.2% and 21.7% E.coli were resistant to imipenem and meropenem respectively and none of the Enterobacter sp exhibited resistance to the two tested carbapenems. But Klebsiella sp and Proteus sp showed high resistance to this group of drugs.

Table 3 represents the resistance pattern of non fermenters i-e Pseudomonas aeruginosa and Acinetobacter sp. to the commonly used antibiotics. 100% Acinetobacter sp was found to be resistant to third and fourth generation cephalosporins, fluoroquinolones and aminoglycosides. Only 2 isolates were sensitive to tazobactam-piperacillin. Doxycycline showed good activity with only 3 Acinetobacter isolates being resistant to it. As far as Pseudomonas aeruginosa is concerned, a poor susceptibility is obtained.55.5% of Pseudomonas were resistant to ceftazidime and piperacillin-tazobactam. 72.2% were resistant to fluoroquinolones and 61.1% and 66.7% showed resistance to imipenem and mero-

**Table 1: Specimens and the GNR Isolated**

<table>
<thead>
<tr>
<th>SPECIMENS</th>
<th>E.coli</th>
<th>Klebsiella sp</th>
<th>Proteus sp</th>
<th>Enterobacter sp</th>
<th>Pseudomonas aeruginosa</th>
<th>Acinetobacter sp</th>
</tr>
</thead>
<tbody>
<tr>
<td>URINE</td>
<td>19</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>Nil</td>
</tr>
<tr>
<td>PUS/WOUND SWAB</td>
<td>21</td>
<td>4</td>
<td>2</td>
<td>Nil</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>SPUTUM</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>CSF/PLEURAL/ASCITC FLUID</td>
<td>3</td>
<td>nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>1</td>
</tr>
<tr>
<td>CVP TIP</td>
<td>nil</td>
<td>1</td>
<td>nil</td>
<td>Nil</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>TISSUE</td>
<td>nil</td>
<td>nil</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>BLOOD</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 2: ANTIMICROBIAL RESISTANCE PATTERN OF ENTEROBACTERIACEAE**

<table>
<thead>
<tr>
<th>ANTIBIOTICS</th>
<th>E.COLI n=46</th>
<th>K.PNEUMONIAE n=9</th>
<th>ENTEROBACTER sp n=2</th>
<th>PROTEUS SP. n=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMOXICILLIN/CLAVULANATE</td>
<td>41(89.1%)</td>
<td>9(100%)</td>
<td>2(100%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>CEFIXIME</td>
<td>42(91.3%)</td>
<td>9(100%)</td>
<td>2(100%)</td>
<td>5(100%)</td>
</tr>
<tr>
<td>CEFOTAXIME</td>
<td>42(91.3%)</td>
<td>9(100%)</td>
<td>2(100%)</td>
<td>5(100%)</td>
</tr>
<tr>
<td>CEFTAXONE</td>
<td>42(91.3%)</td>
<td>9(100%)</td>
<td>2(100%)</td>
<td>4(80%)</td>
</tr>
<tr>
<td>CEFTAZIDIME</td>
<td>40(86.9%)</td>
<td>9(100%)</td>
<td>1(50%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>CEFIPIME</td>
<td>40(86.9%)</td>
<td>9(100%)</td>
<td>1(50%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>PIPERACILLIN/TAZOBACTAM</td>
<td>27(58.7%)</td>
<td>7(77.8%)</td>
<td>0(0%)</td>
<td>4(80%)</td>
</tr>
<tr>
<td>GENTAMICIN</td>
<td>24(52.2%)</td>
<td>7(77.8%)</td>
<td>0(0%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>AMIKACIN</td>
<td>18(39.1%)</td>
<td>6(66.7%)</td>
<td>5(0%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>CIPROFLOXACIN</td>
<td>42(91.3%)</td>
<td>9(100%)</td>
<td>2(100%)</td>
<td>4(80%)</td>
</tr>
<tr>
<td>DOXYCYCLINE</td>
<td>25(54.3%)</td>
<td>6(66.6%)</td>
<td>2(100%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>SULFAMETHOXAZOLE/TRIMETHOPRIM</td>
<td>43(93.5%)</td>
<td>8(88.9%)</td>
<td>2(0%)</td>
<td>4(80%)</td>
</tr>
<tr>
<td>NITROFURANTOIN (ONLY URINE)</td>
<td>13(51%)</td>
<td>1(50%)</td>
<td>2(0%)</td>
<td>2(40%)</td>
</tr>
<tr>
<td>IMIPENEM</td>
<td>13(28.2%)</td>
<td>4(44.4%)</td>
<td>0(0%)</td>
<td>4(80%)</td>
</tr>
<tr>
<td>MEROPENEM</td>
<td>10(21.7%)</td>
<td>4(44.4%)</td>
<td>0(0%)</td>
<td>4(80%)</td>
</tr>
</tbody>
</table>
penem respectively.

**DISCUSSION**

In the current study, among 172 pathogens isolated from ICU specimens, gram-negative bacteria were more prevalent than gram-positive bacteria. This finding is similar to a study conducted in Shifa International hospital in 2015 and another research by Al-Jawady et al. in 2012. This predominance might be because of wide spread presence and survival of multi-drug resistant gram negative bacteria in the hospital environment.

In our study among 90 GNRs isolated, E. coli showed the highest prevalence 46 (51.1%) followed by Pseudomonas aeruginosa 18(20%) and Acinetobacter sp. 10(11.1%). This is unlike findings of a study conducted by Amira and her colleagues in 2016 which showed that Acinetobacter sp was the commonest isolated pathogen. However, our results are comparable to those of Rajan, et al. However, our results are different from a prospective study conducted in 2015 in Romania, that showed that the respiratory tract infections have highest incidence (58.7%) among ICU infections and the commonest pathogen in that study was Klebsiella sp (17.6%) followed by Acinetobacter sp (14.2%).

As for as the drug resistance pattern is seen, an alarmingly high resistance rate was obtained among enterobacteriaceae for the commonly used drugs like amoxicillin-clavulanate, cephalexin and ciprofloxacin. E.coli showed 89.1% resistance to Amoxicillin-clavulanate, 91.3% to cefixime, ceftriaxone, cefotaxime and ciprofloxacin, 86.9% to ceftazidime and cefepime . Klebsiella, enterobacter and proteus sp. also exhibited a very poor susceptibility to these antimicrobials. Ibrar and his colleagues similarly got a high resistance for these drugs. E.coli showed 73% resistance to cefixime, 66.6% to ceftazidime, and 57.7% to ciprofloxacin.

Out of aminoglycosides, amikacin showed better susceptibility results. Only 39.1 % E.coli, and none of the Enterobacter sp. showed resistance to amikacin. The results are comparable to other studies in Pakistan and India which showed a low amikacin resistance 6.6% and 30% respectively. However, 66.7% Klebsiella sp. and 60% Proteus were amikacin resistant in our study. Hence identification of the causative pathogen in each clinical case and determination of its antimicrobial susceptibility is of utmost importance for prompt patient treatment.

Carbapenems gave promising results for E.coli and Enterobacter as only 28.2% and 21.7% E.coli showed resistance to imipenem and meropenem respectively and none of the Enterobacter sp was resistant to the two tested carbapenems. Even a better susceptibility is observed in a study in Taiwan that only reported 8.7% of Enterobacteriaceae among UTI causing bacteria E.coli showed the highest percentage. urine cultures revealed E.coli followed by Pseudomonas aeruginosa and Klebsiella sp., each isolated in 2 urine specimens. These results are comparable to those of Rajan, et al.

<table>
<thead>
<tr>
<th>ANTIBIOTICS</th>
<th>PSEUDOMONAS AERUGINOSA N=18</th>
<th>ACINETOBACTER SP. N=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEFTRIAXONE</td>
<td>-</td>
<td>10(100%)</td>
</tr>
<tr>
<td>CEFOTAXIME</td>
<td>-</td>
<td>10(100%)</td>
</tr>
<tr>
<td>CEFAZIDIME</td>
<td>10(55.5%)</td>
<td>10(100%)</td>
</tr>
<tr>
<td>CEFEPIME</td>
<td>11(61.1%)</td>
<td>10(100%)</td>
</tr>
<tr>
<td>PIPERACILLIN/TAZOBACTAM</td>
<td>10(55.5%)</td>
<td>8(80%)</td>
</tr>
<tr>
<td>GENTAMICIN</td>
<td>13(72.2%)</td>
<td>10(100%)</td>
</tr>
<tr>
<td>AMIKACIN</td>
<td>11(61.1%)</td>
<td>10(100%)</td>
</tr>
<tr>
<td>CIPROFLOXACIN</td>
<td>13(72.2%)</td>
<td>10(100%)</td>
</tr>
<tr>
<td>LEVOFLOXACIN</td>
<td>13(72.2%)</td>
<td>10(100%)</td>
</tr>
<tr>
<td>IMIPENEM</td>
<td>11(61.1%)</td>
<td>6(60%)</td>
</tr>
<tr>
<td>MEROPENEM</td>
<td>12(66.7%)</td>
<td>7(70%)</td>
</tr>
<tr>
<td>DOXYCYCLINE</td>
<td>-</td>
<td>3(30%)</td>
</tr>
<tr>
<td>AZTREONAM</td>
<td>14(77.8%)</td>
<td>10(100%)</td>
</tr>
</tbody>
</table>
isolates from ICUs being resistant to carbapenems. But Klebsiella sp and Proteus sp showed high resistance to this group of drugs. Other studies also reported a high carbapenem resistance among Klebsiella sp. Yi Li, Hui Shen et al reported 48.1% Klebsiella carbapenem resistant strains in 2019. In another study conducted on carbapenem non-susceptible pathogens (Carb-NS), 42.6% of entire Carb-NS enterobacteriaceae was constituted by Klebsiella sp. This rising resistance is of particular concern in critically ill patients as in intensive care units and calls for cautious use of carbapenems.

The resistance pattern of the non-fermenters, Pseudomonas aeruginosa and Acinetobacter sp. is quite upsetting as very low percentage of the isolates were susceptible to the tested antimicrobials. 55.5% Pseudomonas aeruginosa was non-susceptible to the anti-pseudomonal drugs like ceftazidime and tazobactam–piperacillin and 61.1% to cefpirome. Aminoglycosides and fluoroquinolones even showed poorer results. 72.2% and 61.1% strains exhibited ciprofloxacin and amikacin resistance respectively. The results for tazobactam–piperacillin are somewhat similar to a study conducted in Peshawar showing 66.2% tazobactam–piperacillin non-susceptibility. However, our results for other drugs are unlike this study in Peshawar as 92.86% Pseudomonas aeruginosa isolates were susceptible to amikacin, 71% to ceftazidime and 66.2% to ciprofloxacin. Our results are comparable to a study conducted in Karachi showing 57.3% Pseudomonas aeruginosa resistant to cefepime, 53.9% to ceftazidime and 53% to amikacin. Impenem and meropenem didn’t prove to be good choice in our study as 61.1% and 66.7% Pseudomonas aeruginosa were resistant to imipenem and meropenem respectively. The rise of such multi drug resistant strains might be attributed to development of cross-resistance between various drugs and the exposure of ICU patients to a number of drug resistant pathogens during invasive diagnostic and therapeutic procedures while they stay in ICU.

The antimicrobial resistance pattern of acinetobacter sp. gave worst and most disappointing results as the 10 isolated strains (100%) were non-susceptible to ceftriaxone, cefotaxime, ceftazidime, cefepime, ciprofloxacin, levofloxacin, gentamicin and amikacin. A similar study conducted by Ayesha et al showed highly resistant acinetobacter with 100% non-susceptibility to ceftazidime, 95% to amikacin, and 100% to ciprofloxacin. Our study results for carbapenems are again quite tormenting as 60% isolates were resistant to imipenem and 70% to meropenem. These findings are not much different from those of Rajan, et al. who showed 52% carbapenem resistance among Acinetobacter sp and Ayesha et al showing even poorer pattern of 100% resistance to this important group of drugs.12 Only doxycycline showed a ray of hope as 7 (70%) out of 10 acinetobacter isolates were found susceptible to this drug.

**CONCLUSION**

Majority of the gram negative isolates showed a high resistance to the commonly used antimicrobials like penicillins, cephalosporins, fluoroquinolones, β-lactam combinations etc. Only carbapenems and aminoglycosides showed moderate sensitivity. Acinetobacter sp are highly resistant to all commonly used drugs and only doxycycline showed a hope for treatment of infections with acinetabacter sp.

**LIMITATIONS**

The study was conducted on the ICU patients of only one tertiary care hospital. A study with larger group of population and increased duration might give much vivid picture of the entire population of this area.

**RECOMMENDATIONS**

1. Future studies enrolling patients from multiple hospitals should be conducted.
2. Further, newer drugs like colistin, meropenem-vaborbactam should be evaluated for efficacy by MIC determination. This could help in development of new antibiotic policies and provide a rationale for empirical therapy of ICU patients.
REFERENCES


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PATIENT SATISFACTION WITH PHLEBOTOMY SERVICES IN A TERTIARY CARE HOSPITAL IN LAHORE

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Abstract

Background: Phlebotomy services are an integral component of the laboratory services and patient satisfaction is a reliable indicator to monitor the quality of these services.

Aim: The purpose of this study was to assess the patient satisfaction with phlebotomy services at Mayo Hospital Lahore, a tertiary care hospital.

Design & Setting: A total of 241 patients from different wards of Mayo Hospital were evaluated in terms of personal experience about phlebotomy services by means of specifically designed questionnaire based on protocol of these services.

Methods: A qualitative analysis approach was used to interpret the data generated by the survey form filled by the patients admitted in medical, surgical and allied wards. The data was entered in SPSS-22 using quantitative variables and descriptive statistics including frequency distribution tables.

Results: The study revealed that 65% of the patients were very satisfied with courtesy and behavior of collecting staff while only 43% admitted that staff provided requisite information about procedure of sample collection.

Conclusion: The overall level of patient satisfaction was average. However, there were areas which need our attention for example information provided by staff about phlebotomy procedure and delivery of results needs improvement.

Key Words: Mayo Hospital, Phlebotomy, questionnaire, satisfaction.

Patient satisfaction denotes the extent to which patient’s expectations of ideal health care are fulfilled. It is an important criterion for evaluating the quality of health care services. Various problems faced by patients during delivery of the phlebotomy services are highlighted. Research work regarding the patient satisfaction is earning a lot of repute because of its role in improving various health care services.¹

Phlebotomy is the most important component of laboratory services having direct patient encounter. Due care must be taken so as to provide maximum comfort to the patient during needle pricking. Individual patient attitude and demographics may affect patient perception of satisfaction. Maximum patient satisfaction is possible only when phlebotomists are well aware of the procedure and its protocols.² Various factors which monitor patient satisfaction with phlebotomy services include waiting time, communication skill of the staff, cleanliness of the collection area and competency of the phlebotomist.³ ⁴ Recklessness of worker including multiple pricks and bruises may influence the patient compliance with the procedure. A study conducted by Gupta at all to analyze patient satisfaction with phlebotomy services at NABH in 2014 revealed a

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satisfaction of 94%. However, local data is lacking in this prospect. That’s why we conducted this study at Mayo Hospital, Lahore to measure patient satisfaction with phlebotomy services of the laboratory. The aim of study is to highlight the major contributing factors which are affecting the level of patient satisfaction with phlebotomy services in our setup.

METHODS

This was a cross-sectional descriptive study performed at Mayo Hospital Lahore from May, 2018 to July, 2018. Sample size of 241 patients is estimated by using 95% confidence level 3% margin of error with expected percentage of patient satisfaction with phlebotomy services in Mayo Hospital as 94%.²

It was a non-probability purposive sampling. All patients admitted in medical, surgical and allied wards were included in the study whereas children, unwilling and psychiatric patients were excluded. A written informed consent was taken from every patient. All the researchers obliged themselves to practice in accordance to Helsinki Declaration 1964 and its later amendments. The study was approved by the institutional review board of KEMU. Data was collected using pre-designed, pre-tested questionnaire which was validated after discussion with the academic members and subject specialists for its content validity. Questionnaire covered different aspects of Phlebotomy protocol. Interview was conducted by the same research team member in an estimated duration of 6min. Data was entered into SPSS-22. Quantitative variables like age were presented as mean ± standard deviation. Qualitative variables like responses were presented as frequency and percentages. Association between medical and surgical wards was calculated by help of chi square test. P value < 0.05 was considered significant.

RESULTS

After explaining the purpose and significance of research, the researchers got filled 241 perform as by the patients. There were 184 male patients and 57 female patients who participated in the survey. Mean age of the respondents was 39 ± 6.94years. Demographic profile and questions related to patient satisfaction with phlebotomy services are mentioned in table 1 & table 2 respectively. Out of 241 patients, 156 (65%) were very satisfied with courtesy and behavior of collecting staff. And 166 (68.8%) respondents expressed their full satisfaction regarding the waiting time of their turn. Only 100 (41.5%) patients were guided properly about how and when to receive their lab results.

DISCUSSION

In pursuit of providing patients with best health care services, the first priority is to improve the system and standard of services by simply getting feedback from the patients. Assessing the level of patient satisfaction has gained the top priority in this era. Our country is lacking research work in this respect. Our project on Patient satisfaction with phlebotomy services at Mayo Hospital is first of its type regarding phlebotomy practices in Mayo Hospital.

This study highlights the deficient areas of phlebotomy services in our setup. Almost less than half of the respondents reported that staff does not

<table>
<thead>
<tr>
<th>Table 1:</th>
</tr>
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<tbody>
<tr>
<td>Education</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Mean Age</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td>Females</td>
</tr>
</tbody>
</table>

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provide the prerequisite information about the phlebotomy procedure. Similarly other factors depicting patient satisfaction are listed in table no. 1.

In our study 58.9% patients were very satisfied with ability of staff to answer the queries. This is in comparison with the research conducted at Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia which showed that 41% of the respondents were very satisfied with the ability of staff to answer their queries.\textsuperscript{12,13} 68.4% respondents expressed their full satisfaction with the communication skills of staff. A similar study done by Koh YR et al. depicted that only 42.9% patients were satisfied by the communication skills.\textsuperscript{6} This could be due to certain deficit areas in the training of phlebotomy staff about patient dealing.

A higher level of satisfaction (65%) was observed on courtesy and behavior of staff which is an important parameter determining patient satisfaction. It is in contrast with the results of previously published data by Gupta A et al and CAP Q-probe study (24.5% and 52.7% respectively).\textsuperscript{2,10}

In present study, the overall level of satisfaction of participants on the ability of staff to provide information about procedure of sample collection was 43%. The finding was higher than the studies conducted by Gupta et al, Abera RG et al and Belay M et al which found level of satisfaction as 32%, 31.9% and 6.9% respectively.\textsuperscript{2,11,13} Some earlier studies done by Oja PI et al in University of Oulu, Finland have shown satisfaction level of 67.2% on information provided by staff for report collection. But in our study it was found to be 41.5%, significantly lower than previous studies.\textsuperscript{7}

Taking staff availability during working hours as a parameter determining patient satisfaction, the result was 68.4% in the present study while only 20% in a study designed at Nekemte Referral Hospital, Western Ethiopia.\textsuperscript{8}

In this study, a relatively high number of parameters were employed to evaluate the patient satisfaction level with phlebotomy services. All these parameters have considerable importance in determining patient satisfaction. Other healthcare workers including nurses can also be involved in this survey in future studies.\textsuperscript{10}

Some limitations of this study are worth to be mentioned here. Firstly, the responses of patients

<table>
<thead>
<tr>
<th>Table 2: Questionnaire</th>
<th>Very satisfied</th>
<th>Satisfied</th>
<th>Neutral</th>
<th>dissatisfied</th>
<th>Very dissatisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whether the staff was in proper uniform?</td>
<td>182(75%)</td>
<td>57(23.6%)</td>
<td>1(0.5%)</td>
<td>1(0.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Whether the behavior and courtesy of staff during collection was reasonable?</td>
<td>156(65%)</td>
<td>69(28.5%)</td>
<td>2(1%)</td>
<td>11(4.5%)</td>
<td>3(1%)</td>
</tr>
<tr>
<td>Whether the waiting time of your turn was satisfactory?</td>
<td>166(68.8%)</td>
<td>55(22.8%)</td>
<td>13(5.4%)</td>
<td>6(2.5%)</td>
<td>1(0.4%)</td>
</tr>
<tr>
<td>Whether the staff gives information about procedure of sample collection?</td>
<td>105(43%)</td>
<td>65(27%)</td>
<td>14(5.8%)</td>
<td>52(21.6%)</td>
<td>5(2%)</td>
</tr>
<tr>
<td>Whether the sample was collected? 1 prick=v.sat 2 pricks=sat 3 pricks=neutral 4 pricks=dissatisfied 5&amp;so on=v.dissatisfied</td>
<td>185(76.7%)</td>
<td>34(14.1%)</td>
<td>10(4.2%)</td>
<td>8(3.3%)</td>
<td>4(1.6%)</td>
</tr>
<tr>
<td>Whether you felt any inconvenience/ swelling / bruising/ fainting attack/ persistent pain during sample collection?</td>
<td>163(67.6%)</td>
<td>47(19.5%)</td>
<td>6(2.5%)</td>
<td>20(8.3%)</td>
<td>5(2%)</td>
</tr>
<tr>
<td>Whether the staff was available during working hours?</td>
<td>165(68.4%)</td>
<td>55(22.8%)</td>
<td>9(3.7%)</td>
<td>8(3.3%)</td>
<td>4(1.6%)</td>
</tr>
<tr>
<td>Whether they responded well to your questions?</td>
<td>142(58.9%)</td>
<td>53(21.9%)</td>
<td>38(15.7%)</td>
<td>6(2.5%)</td>
<td>2(0.8%)</td>
</tr>
<tr>
<td>Whether the respect of your privacy and confidentiality was maintained by the staff?</td>
<td>136(56.4%)</td>
<td>54(22.4%)</td>
<td>48(19.9%)</td>
<td>20(8.2%)</td>
<td>1(0.4%)</td>
</tr>
<tr>
<td>Are you satisfied with skill of collecting staff?</td>
<td>168(70%)</td>
<td>56(23.2%)</td>
<td>7(2.9%)</td>
<td>7(2.9%)</td>
<td>3(1.2%)</td>
</tr>
<tr>
<td>Are you satisfied with communication of collecting staff?</td>
<td>165(68.4%)</td>
<td>62(25.7%)</td>
<td>3(1.2%)</td>
<td>8(3.3%)</td>
<td>3(1.2%)</td>
</tr>
<tr>
<td>Whether staff provided information on how and when to receive lab results?</td>
<td>100(41.5%)</td>
<td>64(26.5%)</td>
<td>11(4.5%)</td>
<td>61(25.3%)</td>
<td>5(2%)</td>
</tr>
<tr>
<td>Are you satisfied with cleanliness of collection area?</td>
<td>154(63.9%)</td>
<td>57(23.6%)</td>
<td>6(2.5%)</td>
<td>22(9.1%)</td>
<td>2(0.8%)</td>
</tr>
</tbody>
</table>
depend greatly upon their socioeconomic statuses and perceptions. In our study, most of the patients were illiterate and belonged to rural areas. Therefore care must be taken while comparing the results as they are largely dependent upon sociodemographic profile of respondents. Secondly, the study was conducted among patients admitted in wards, where phlebotomy procedure was being performed on bedside not in lab premises.

This is first ever cross sectional study to evaluate patient satisfaction with phlebotomy services in our setup. Health authorities can use its results to monitor the deficient areas of phlebotomy services in various hospitals.

CONCLUSION

This study provides an insight to the overall patient experience about phlebotomy services and highlights its deficient areas. Phlebotomy is the most commonly performed procedure in the hospital. So it should be taken on preference list in terms of training of phlebotomist and taking feedback from the patients about their experience. Other aspect of the study can be seen as it provides awareness in the community about the proper phlebotomy practices. Therefore, it’s strongly recommended to enhance the standard training workshops for the phlebotomy procedures and conduct different types of studies for the improvement of the field.

REFERENCES

Abstract
Evaluation of anemia particularly iron deficiency in patients with cancer is difficult. RET-He results can help physicians better identify and monitor therapy in iron deficiency and iron deficiency anemia. The RET-He test is simple, reliable and available at a minimum cost. It is automatically reported as part of the comprehensive complete blood count evaluation. It has been shown to be an early indicator of either decreasing or increasing iron availability in the bone marrow. Physicians may be able to monitor a patient's response to therapy in days instead of weeks and adjust the plan of care accordingly. Use of RET-He as a screening test can reduce unnecessary iron studies and can be cost effective for patients. Studies regarding role of RET-He in detecting iron deficiency in cancer patients has not been done in Pakistan.

Objective: To determine the diagnostic accuracy of haemoglobin content of reticulocytes (RET-He) as a screening test for iron deficiency anemia taking transferrin saturation as a gold standard in patients with cancer.

Material & Methods: This prospective cross sectional study was conducted at department of Hematology in collaboration with department of Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore for 6 months i.e. from 4 April,2016 to 4 October,2016. The non-probability consecutive sampling technique was used in this study. All the data was entered and analyzed on SPSS version 20. Patients were entered into the study based on the existence of concurrent laboratory test requests for CBC and serum iron studies.

Results: In our study the mean age of the patients was 37.51±12.36 years, the male to female ratio of the patients was 1.4:1. The sensitivity of RET-He was 74.55% with specificity of 80% and the diagnostic accuracy of 77.5% taking transferrin saturation as gold standard.

Conclusion: It has been proved in our study the RET-He can be used as screening test for iron deficiency with sensitivity of 74.55%, specificity of 80%, NPV value of 78.79% with diagnostic accuracy of 77.5% taking transferrin saturation as gold standard in a cancer hospital setting. RET-He is a cost effective test and may reduce unnecessary iron studies.

Keywords: Iron Deficiency anemia(IDA), Reticulocytes, Hemoglobin Content, Diagnostic accuracy, transferrin saturation, cancer

Reticulocytes are the youngest erythrocytes released into the circulating blood from bone marrow. They mature for 1 to 3 days in the bone marrow and circulate in 1 to 2 days before becoming mature erythrocytes. Red cell and reticulocyte cellular indices provide an essential support to the diagnosis and monitoring of haematological diseases. Modern haematology analyzers provide
additional data on these parameters and quantify parameters of reticulocytes as well.\(^2\) Reticulocyte parameters such as haemoglobin content of reticulocytes has shown value in haematological conditions.\(^3\) The reticulocyte hemoglobin content provides direct information on bone marrow iron availability and on its use for hemoglobin synthesis.\(^4\)

Microcytic hypochromic anemia can be present in both iron deficient anemia and functional iron deficiency as a result of its blockage in macrophages (anemia of chronic disease) in oncology patients.\(^4\) Functional iron deficiency is a condition in which there is insufficient iron incorporation in erythroid precursors despite adequate body iron stores.\(^5\) Microcytic hypochromic anemia due to beta thalassemia trait is also common in Pakistani population.\(^6\) \(\beta\)-thalassemia carriers were estimated to be 8 million in Pakistan.\(^6\)

Advanced reticulocyte indices such as the cellular hemoglobin content of reticulocytes designated as CHr and RET-He, are reportable parameters on Siemens ADVIA 2120 and Sysmex XE and XN series automated hematology analyzers respectively.\(^7\) These indices correlate with iron deficient erythropoiesis and are useful markers in iron deficiency in infants and children,\(^7\) blood donors,\(^8\) geriatric patients,\(^9\) pregnant women\(^10\) and patients with chronic kidney disease undergoing haemodialysis.\(^3\)

Iron is essential for many metabolic processes.\(^11\) Iron depletion causes tiredness, decreased exercise tolerance, neurocognitive changes\(^12\) and restless leg syndrome.\(^13\) Iron deficiency reduces the responsiveness of erythroid precursors to erythropoietin apparently through an iron-aconitase-isocitrate pathway.\(^14\) Iron deficiency is the leading cause of anemia worldwide. However the anemia of chronic disease is more common in patients with cancer.\(^15\)

Anemia of chronic disease is often accompanied by acute phase response. The standard biochemical markers for iron metabolism as serum iron, ferritin and transferrin are under influence of acute phase response. Differentiating between iron deficiency and anemia of chronic disease is sometimes difficult.\(^16\)

RET-He is also reduced in thalassemias and thalassemic haemoglobin variants. A study found that RET HE, MCH, MCV together with ferritin and erythrocyte count to be powerful in identifying thalassemias and thalassemic haemoglobin variants in children and adults with high prevalence of iron deficiency. These parameters cannot replace DNA based diagnosis in haemoglobinopathy and are not guiding tool for clinicians.\(^17\)

The importance of this study lies in the fact that prevalence of iron deficiency and iron deficiency anemia is more in Pakistan as compared to developed countries.\(^16\) Approximately 39% of adolescents, 30% boys and 54% girls, 47% of the children, 30% of the adult females, 40-50 % of preschool and primary school children and 69% children <2 years were reported to be affected by IDA in Pakistan.\(^18\) Haemoglobin content of reticulocytes (RET-HE) is helpful in detecting early iron deficiency prior to development of anemia.\(^19\) Therefore it is important to rule out iron deficiency anemia in patients with cancer who are being considered for therapy with ESA.\(^20\) Approximately 30% to 50% of patients with cancer with chemotherapy-related anemia have been reported to experience poor response to ESA and iron therapy has been shown to improve the response in some of these patients.\(^15\)

This study focuses on utility of RET-HE for identifying early iron deficiency and also excluding iron deficiency defined by biochemical markers as serum iron less than 37ug/dl in women and less than 59ug/dl in men and transferrin saturation less than 20%. Although bone marrow examination is the conventional gold standard for assessing iron stores. It is not performed routinely at our center for the sole purpose of identifying iron deficiency because of its invasive nature.

Transferrin saturation is a particularly useful biochemical marker of iron deficiency since it reflects the interrelationship between bone marrow iron stores, iron absorption and the availability of
iron in circulating blood. In our study we will not use serum ferritin; another marker of iron deficiency as it is an acute phase reactant and is less helpful in cancer patients. I will take transferrin saturation as gold standard to label iron deficiency as in a study done in New York defined iron deficiency anemia on the basis of transferrin saturation < 20 % and then compared it with RET-HE.

METHODS

Prospective cross sectional study conducted during period from 4th April, 2016 to 4th October, 2016 at department of Haematology of SKMCH & RC Lahore. A total of 120 consecutive patients taken referred from department of oncology for CBC and iron studies belonging to all age groups, both genders, all types of cancers irrespective of stage and treatment and having Hb of 11g/dl in men and 10g/dl in women were included. Patients already taking iron supplements were excluded from the study. All data was collected by using a proforma. Written consent was obtained from the patients. After fulfilling the inclusion criteria, a 5 ml whole blood was collected by aseptic venipuncture in purple topped (EDTA) and red topped vial. Blood in purple vial was run on automated haematology analyzer XN 20 for estimation of RET-HE in haematology department and red topped vial was sent to chemical pathology department for serum iron studies. Bone marrow procedure was not performed to see iron stores as it is an invasive procedure.

Operational Definitions:

Haemoglobin content of Reticulocytes(RET-HE) is content of haemoglobin in immature erythrocytes. It is measured by sysmex automated haematology analyzer on XN 20 mode. RET-HE <28pg/l labelled as iron deficiency and RET-HE > 28pg/l labelled as negative for iron deficiency.

Anemia was defined as Hb <11g/dl in men and Hb <10g/dl in women.

Cancer Patients: All types of cancer patients (haematological and non haematological) irrespective of the stage and treatment

Transferrin Saturation was defined as the ratio of serum iron divided by total iron binding capacity multiplied by 100. Transferrin saturation <20% labelled as iron deficient and >20% labelled as negative for iron deficiency.

True positive when transferrin saturation less than 20% and RET-HE <28 pg/cell positive for iron deficiency

True negative when transferrin saturation more than 20 % and RET-HE equal to and >28 pg/cell negative for iron deficiency

False positive when transferrin saturation more than 20% negative for iron deficiency and RET-HE < 28 pg/cell positive for iron deficiency

False negative when transferrin saturation is less than 20 % positive for iron deficiency and RET-HE equal to and >28 pg/cell negative for iron deficiency

Sensitivity number of true positives/number of true positives+number of false negatives (TP/TP+FN)

Specificity: number of true negatives/number of true negatives+number of false positives

Positive predictive value (PPV) number of true positives/ number of true positives+number of false positives(TP/TP+FP)

Negative predictive value (NPV) number of true negatives/number of true negatives+number of false negatives(TN/TN+FN)

RESULTS

Out of 120 cases the transferrin saturation diagnosed anemia in 65(54.17%) patients. Fig#1

Fig#1: Frequency Distribution of Transferrin Saturation Diagnosed IDA
The study results showed that the sensitivity of RET-HE was 74.55% with specificity of 80%, PPV value was 75.93%, NPV value was 78.79% with diagnostic accuracy of 77.5% taking transferrin saturation as gold standard. Table #1

**Table 2: Comparison of RET-HE with Transferrin Saturation Stratified by Age**

<table>
<thead>
<tr>
<th>RET-HE</th>
<th>≤40</th>
<th>&gt;40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>79.41%</td>
<td>66.67%</td>
</tr>
<tr>
<td>Specificity</td>
<td>77.5%</td>
<td>84%</td>
</tr>
<tr>
<td>PPV</td>
<td>75%</td>
<td>77.78%</td>
</tr>
<tr>
<td>NPV</td>
<td>81.58%</td>
<td>75%</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>78.38%</td>
<td>76.09%</td>
</tr>
</tbody>
</table>

The study results showed that in ≤40 years patients, the sensitivity, specificity and diagnostic accuracy of RET-HE was 79.41%, 77.5% and 78.38% respectively taking transferrin saturation as gold standard, similarly in >40 years patients the sensitivity, specificity and diagnostic accuracy of RET-HE was 66.67%, 84% and 76.09% respectively taking transferrin saturation as gold standard. Table #2

**Table 3: Comparison of RET-HE with Transferrin Saturation Stratified by Gender**

<table>
<thead>
<tr>
<th>RET-HE</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>76.67%</td>
<td>72%</td>
</tr>
<tr>
<td>Specificity</td>
<td>80.49%</td>
<td>79.17%</td>
</tr>
<tr>
<td>PPV</td>
<td>74.19%</td>
<td>78.26%</td>
</tr>
<tr>
<td>NPV</td>
<td>82.5%</td>
<td>73.08%</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>78.87%</td>
<td>75.51%</td>
</tr>
</tbody>
</table>

The study results showed that in male patients, the sensitivity, specificity and diagnostic accuracy of RET-HE was 76.67%, 80.49% and 78.87% respectively taking transferrin saturation as gold standard, similarly in female patients the sensitivity, specificity and diagnostic accuracy of RET-HE was 72%, 79.17% and 75.51% respectively taking transferrin saturation as gold standard. Table #3

**Table 4: Comparison of RET-HE with Transferrin Saturation Stratified by Diagnosis**

<table>
<thead>
<tr>
<th>RET-HE</th>
<th>Hematological cancer</th>
<th>Non-Hematological cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>78.26%</td>
<td>71.88%</td>
</tr>
<tr>
<td>Specificity</td>
<td>80%</td>
<td>80%</td>
</tr>
<tr>
<td>PPV</td>
<td>75%</td>
<td>76.67%</td>
</tr>
<tr>
<td>NPV</td>
<td>82.76%</td>
<td>75.68%</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>79.25%</td>
<td>76.12%</td>
</tr>
</tbody>
</table>

The study results showed that in hematological cancer patients, the sensitivity, specificity and diagnostic accuracy of RET-HE was 78.16%, 80% and 79.25% respectively taking transferrin saturation as gold standard, similarly in non-hematological cancer patients the sensitivity, specificity and diagnostic accuracy of RET-HE were 71.88%, 80% and 76.12% respectively taking transferrin saturation as gold standard. Table #4

**DISCUSSION**

This prospective cross sectional study was carried out at Department of Haematology in collaboration with Department of Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore to determine the diagnostic accuracy of RET-HE as a screening test for iron deficiency anemia taking transferrin saturation as a gold standard in patients with cancer. Anemia is a major cause of morbidity in patients with cancer. There are multiple causative factors, including absolute iron deficiency due to blood loss and/or nutritional deficiencies, anemia of chronic disease, and myelosuppressive effects of chemotherapy, as well as metastatic infiltration of the bone marrow. The
identification of iron deficiency in patients with cancer is particularly important in patients being considered for therapy with erythropoietin stimulating agents ESA. In our study the sensitivity of RET-HE was 74.55% with specificity of 80%, PPV value was 75.93%, NPV value was 78.79% with diagnostic accuracy of 77.5% taking transferrin saturation as gold standard.

A study by Ellinor I. B. Peerschke et al revealed that the use of RET-He supports in the evaluation of iron deficiency in a cancer care setting. RET-He ruled out iron deficiency with a negative predictive value (NPV) of 98.5% and 100%, respectively, in the study population (n=209) and in a subpopulation of patients with low reticulocyte counts (n = 19). Compared with our reference study in which negative predictive value (NPV) was 98.5%, my study showed negative predictive value of 78.79% this may be because of sample size difference.

A study by Carlo Brugnara et al revealed that with a Ret He cutoff level of 27.2 pg, iron deficiency could be diagnosed with a sensitivity of 93.3%, and a specificity of 83.2%. They concluded Ret He is a reliable marker of cellular hemoglobin content and can be used to identify the presence of iron-deficient states.

A study by Kudelienė R et al showed that the Reticulocyte hemoglobin content, ferritin and transferrin saturation had sensitivity and specificity of 76.6% and 78.4%, 81.3% and 81.9%, 85.9% and 87.9%, respectively. Reticulocyte hemoglobin content is comparable test with ferritin and transferrin saturation and can be used to detect iron deficiency in 6-24-month-old children. However ferritin is an acute phase reactant and can be increased in many malignancies, so underlying iron deficient states can be missed. In cancer hospital setting RET-HE is a more reliable indicator of underlying iron deficiency.

The diagnostic accuracy of reticulocyte parameters has been tested by many authors, especially to diagnose iron deficiency in patients submitted to dialysis. Measurement of the haemoglobin content of reticulocytes (RET-HE) is helpful in detecting early stages of iron deficiency prior to the development of anaemia. Another study by Ana Beatriz Barbosa Torino et al concluded in their study that the erythrocyte and reticulocyte indices are moderately good to identify absolute iron deficiency in patients with anaemia of chronic disease.

Different authors described that the measurements of reticulocyte hemoglobin content have been shown to provide useful information in diagnosing functional iron deficiency (FID) during erythropoietin therapy, iron-deficient states in infancy and response to iron therapy.

In short, data supports the use of RET-HE to rule out iron deficient erythropoiesis, reduce unnecessary iron studies and provide rapid diagnostic tool when automated CBC and reticulocyte counts are reported.

The limitation includes of falsely positive results in some cases of anaemia of chronic disease and beta thalassaemia trait in which it is expected to be low.

Although in Pakistan incidence of beta thalassaemia trait is high but in our study we do not have the data of beta thalassaemia trait. So further studies are required to determine the role of RET-HE in distinguishing iron deficient haematopoisis and beta thalassaemia trait in Pakistani population.

CONCLUSION

It has been proved in our study the RET-HE can be used as a screening test for iron deficiency with sensitivity of 74.55%, specificity of 80%, NPV value of 78.79% with diagnostic accuracy of 77.5% taking transferrin saturation as gold standard in a cancer hospital setting. RET-HE is a cost effective test and may reduce unnecessary iron studies.
REFERENCES


ASSOCIATION OF B BLOOD GROUP ANTIGEN WITH ESPHAGEOAL SQUAMOUS CELL CARCINOMA: A CASE CONTROL STUDY AT SINGLE CANCER CENTER IN PAKISTAN

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Abstract

Esophageal cancer is a cancer arising from the esophagus—the muscular tube that extends from throat (pharynx) to stomach. Squamous cell carcinoma of esophagus is the most common presentation of esophageal cancer in Pakistan. Since it is an aggressive cancer with poor survival that is why many risk factors are being studied to have any association with it and blood group is one of them. Blood groups have been found to have association with many diseases and cancers worldwide but not much work has been done in Pakistan.

Objective: To determine association of B blood group antigen with squamous cell carcinoma of esophagus.

Material and Methods: This case control study was carried out at department of Hematology in collaboration with Department of Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore for 6 months from 12th April, 2016 to 12th October 2016. After fulfilling inclusion criteria for cases and controls, about 2ml blood was collected by aseptic venipuncture. ABO blood typing was carried out with tube as well as gel method. Presence of B antigen in cases and controls was noted as per operational definitions. All the data was entered and analyzed on SPSS version 20.

Results: In our study the mean age of the patients was 45.67±14.75 years, the male to female ratio of the patients was 1:1.02. Among cases, B antigen was present in 79 (43.9%) patients whereas in control group, B antigen was present in 62 (34.4%) individuals. Statistically there is 1.489 times more risk of association of squamous cell carcinoma esophagus with presence of B antigen i.e. OR=1.489 [95% CI; 0.973-2.279].

Conclusion: It has been proved in our study that B blood group antigen has significant association with squamous cell carcinoma of esophagus.

Keywords: Carcinoma, Squamous, Antigen, esophagus, Case
Blood groups vary markedly with ethnicity, race, geographical area, population migration, and external environment. The study of blood groups is not only important for effective blood bank services and blood transfusion but accumulating evidence has suggested its role in forensic pathology, genetics, tracing of human ancestry and population migration patterns. Blood groups have been studied to have association with different diseases as glaucoma, infections e.g. hepatitis C, vascular disease, thromboembolism and many more, due to which the need of having knowledge about blood group distribution has increased.

As blood groups are determined by genetics and their genes are located on chromosome 9(9q34) and 1 respectively, considerable work has been done to find association of blood groups with numerous cancers. Studies have shown that blood group A is associated with breast cancer, pancreatic cancer, and gastric cancer, non O blood groups are associated with colorectal cancer and lung cancer, blood group AB is associated with acute leukemia and blood groups with B antigen (B and AB) are associated with epithelial ovarian cancer and squamous cell carcinoma of esophagus. All these cancers have been found to show increased incidence with one type of blood group or the other. Blood groups have also been found to be related to prognosis in various cancers. Esophageal cancer is the 6th most frequent cancer worldwide. It is a lethal malignancy with poor survival rate because of advanced stage at presentation. Squamous cell carcinoma is the most common subtype reported in Pakistan.

A study conducted in Iran showed that there was statistically significant difference in distribution of B blood group between patients of squamous cell carcinoma of esophagus and control group, there was higher percentage of blood group B (25.9%) and blood group AB (9.3%) in cases compared to controls with blood group B (21.2%) and AB (6.1%). Another study conducted in India also showed similar results with higher percentage of B antigen (59.17%) in patients of squamous cell carcinoma of esophagus than in controls (46.04%).

The importance of this study lies in the fact that esophageal cancer is relatively more common in Pakistan being the seventh most common cancer in men in Karachi and third most common cancer in Quetta and study has shown poor survival in Pakistani patients because of late presentation. The aim of this study is to determine association of B blood group antigen with squamous cell carcinoma of esophagus and compare them with hospital controls. This study focuses on finding any association between ABO blood groups and risk of squamous cell carcinoma of esophagus in a single cancer hospital in Pakistan because blood grouping is an easily available and cost effective technique and to our knowledge, this association has not been studied in Pakistan so far. If significant association is found then blood groups can be used as a pre-clinical marker and a risk stratification tool especially in patients with positive family history and it might be helpful in early diagnosis of this lethal malignancy and hence in better chances of cure.

METHODS

Case control study conducted at Department of Hematology in collaboration with Department of Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center for six months from 12th April 2016 to 12th October 2016. A total of 180 cases of registered esophageal squamous cell carcinoma patients of both genders in age groups 20-75 years were enrolled from out-patient clinic as well as in-patient ward by monitoring histopathology results and 180 controls of both genders in age group 20-75 years who were either healthy blood donors or registered patients of malignancies other than squamous cell carcinoma of esophagus were enrolled via non-probability consecutive sampling. The patients having more than one malignancy or having blood disorders were excluded from controls. All data was collected by using a proforma. Written
consent was obtained from the patients and controls. After fulfilling the inclusion criteria, a 2ml blood was collected by aseptic venipuncture. ABO blood typing was carried out with tube as well as gel method. Agglutination (clumping after 5 minutes) is considered positive for the presence of a blood group antigen whose antibody has been added and absence of agglutination is taken as absence of blood group antigen. Presence of B antigen in cases and controls was labelled.

**OPERATIONAL DEFINITIONS**

**Blood groups with B antigen**

In blood group A, antigen present on surface of red cells is A. In blood group B, antigen present is B. In blood group AB, both A, B and AB surface antigens are present on RBCs and if neither A nor B antigen is present on red cells, blood group is O. So blood groups with B antigen are B and AB.

**Esophageal squamous cell carcinoma**

Squamous cell carcinoma of esophagus is diagnosed on esophageal biopsy showing undifferentiated / primitive basal cells, large flat squamous cells and keratinized foci and have intercellular bridges

**Data Analysis:**

Statistical analysis was performed according to Statistical Package for Social Science (SPSS) version 20.0. Quantitative variables such as age was presented as mean ± SD. Qualitative variables were presented as frequency and %age e.g gender, B blood group antigen, type of blood group (A, B, AB, O). Odds ratio was calculated to determine the association between B blood group antigen and squamous cell carcinoma of esophagus OR>= (more than or equal to) 1 was taken as significant. Data was stratified for age, gender and blood group (B/AB) to deal with effect modifiers.

**RESULTS**

In our study the mean age of the case group patients was 45.67±14.75 years and in control group was 38.94±13.82 years. There were 91 males in case group while 89 females. In control group, there were 106 males and 74 females. In case group, 47 (26.1%) patients had blood group A, 23 (12.8%) had blood group AB, 56 (31.1%) had blood group B and 54 (30.0%) had blood group O. In control group, 47 (26.1%) individuals had blood group A, 12 (6.7%) had blood group AB, 50 (27.8%) had blood group B and 71 (39.4%) had blood group O. Table#1

In our study the B antigen was present in 141(39.17%) individuals and it was absent in 219(60.83%) individuals. Fig#1

**Table 1: Characteristics of patients in both groups**

<table>
<thead>
<tr>
<th></th>
<th>Case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>180</td>
<td>180</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.67±14.75</td>
<td>38.94±13.82</td>
</tr>
<tr>
<td>Male</td>
<td>91</td>
<td>106</td>
</tr>
<tr>
<td>Female</td>
<td>89</td>
<td>74</td>
</tr>
<tr>
<td>Blood group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>47(26.1%)</td>
<td>47(26.1%)</td>
</tr>
<tr>
<td>B</td>
<td>56(31.1%)</td>
<td>50(27.8%)</td>
</tr>
<tr>
<td>AB</td>
<td>23(12.8%)</td>
<td>12(6.7%)</td>
</tr>
<tr>
<td>O</td>
<td>54(30.0%)</td>
<td>71(39.4%)</td>
</tr>
</tbody>
</table>

Among cases, B antigen was present in 79 (43.9%) patients whereas in control group, B antigen was present in 62 (34.4%) individuals. Statistically there is 1.489 times more risk of association of squamous cell carcinoma esophagus with presence of B antigen i.e. OR=1.489 [95% CI; 0.973-2.279]. Table#2

**DISCUSSION**
ASSOCIATION OF B BLOOD GROUP ANTIGEN WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA

### Table 2: Association of B Antigen with Squamous Cell Carcinoma

<table>
<thead>
<tr>
<th>B Antigen</th>
<th>Study Groups</th>
<th>Total</th>
<th>p-value</th>
<th>OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>79(43.9%)</td>
<td>62(34.4%)</td>
<td>141</td>
<td>0.066</td>
</tr>
<tr>
<td>Absent</td>
<td>101(56.1%)</td>
<td>118(65.6%)</td>
<td>219</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>180</td>
<td>180</td>
<td>360</td>
<td></td>
</tr>
</tbody>
</table>

In cancer patients, the relative incidence of B blood group is more frequent in squamous cell carcinoma of esophagus. Cancer patients with presence of B antigen (B and AB blood group) were higher, whereas in controls, absence of B antigen (A and O blood groups) was in higher frequency. Worldwide, cancer of esophagus is the sixth most common cause of cancer related mortality. Iran is located in the esophageal cancer belt of Asia and esophageal cancer is one of the most frequent solid tumors in Iran.

This case control study was done to determine association of B blood group antigen with squamous cell carcinoma of esophagus. According to our study results statistically there is 1.489 times more risk of association of squamous cell carcinoma esophagus with presence of B antigen i.e. OR=1.489 [95% CI; 0.973-2.279]. In this study, B antigen was present in 79 (43.9%) cases and 62 (34.4%) controls. Among cases, the most frequent blood group was B that was 31.1% as compared to controls with blood group B (27.8%) and among controls the most frequent blood group was O (39.4%) as compared to cases (30%) and this difference in blood group distribution was most pronounced for blood group AB that was 12.8% in cases as compared to 6.7% in controls.

As homozygosity or heterozygosity of blood group alleles is determined by genotyping which was not done in our study, so based on our findings we can hypothesize that blood group O may have protective effect against squamous cell carcinoma of esophagus and it is heterozygous trait of B antigen as in blood group AB that plays major role in development of esophageal cancer which further needs to be investigated.

Blood group B was determined by serology in our study so we don’t know if homozygous blood group B (BB) was more or heterozygous (OB) was more in our study groups. As we hypothesize that blood group O has protective effect against squamous cell carcinoma of esophagus based on our findings, we assume it is heterozygous B blood group that is more prevalent in our study groups which further needs to be investigated by genotyping.

A study conducted in Iran showed that there was statistically significant difference in distribution of ABO and Rh blood groups between patients of squamous cell carcinoma of esophagus and control group, there was higher percentage of blood group B(25.9%) and blood group AB(9.3%) in cases compared to controls with blood group B (21.2%) and AB (6.1%). This study also shows that frequency of B antigen (blood group B and AB) in cases is higher (35.2%) than that in control group (27.3%) and in terms of individuals with B antigen (blood groups B and AB) and without B antigen (blood group A and O), this difference became more prominent (Odds ratio=1.24) and presence of Rh antigen was about 4.2% more prevalent in cases (92%) that that in control group (87.8%).

One more study by Kumar N et al resulted that the OR (95% CIs) was 1.69(1.31-2.19) for presence of B antigen allele relative to its absence (P<0.0001); in female subgroup OR (95% CIs) observed at 1.84(1.27-2.65) was statistically significant (P = 0.001). SCC of esophagus shows significant difference in comparison to general population; blood group B is found to be higher in incidence (P = 0.0001).

Another study from China shows that in esophageal cancer patients, 33.1% blood group A, 31.7% blood group O, 25.9% blood group B, and 9.3% blood group AB were reported. Rh antigen was present in 92% and absent in 8% of the patients. ABO blood group B is associated with the incidence of Cardiac cancer in male individuals and carcinoma in the upper third esophagus.

Mourant and his colleagues reported that blood groups A and B were both associated with esophageal...
geal cancer based on the data from 31 districts in 13 countries and 7 districts of 6 countries, respectively. In esophageal cancer, the association between blood group A and B and increased incidence of B blood group have been reported. In previous studies, contradictory reports are available about the association of esophageal cancer with any blood group. Increased B blood group in the esophageal squamous cell carcinoma and increased O blood group for adenocarcinoma of esophagus have been reported.

These results suggest that genetic mutations in the vicinity of blood group gene locus play a role in development of esophageal cancer. The association of B blood group antigen with squamous cell carcinoma of esophagus is based on the grounds that it can mask immune system for the cancer cell having an antigen similar to B blood group antigen. It has been shown that cell motility, resistance to apoptosis and immune escape may be altered by modified expression of blood group antigens on the surface of tumor cells.

However, environmental, geographic and racial concerns can never be neglected while discussing associations of ABO blood groups with cancer. Therefore, recognition of all these factors with a better sample size can provide understanding of carcinogenesis and control of cancer.

CONCLUSION

The results of our study suggest that B blood group antigen has significant association with squamous cell carcinoma of esophagus. Additionally, more research is needed to further study the association of ABO blood group and the genetic and biological features of esophageal squamous cell carcinoma.

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ASSOCIATION OF B BLOOD GROUP ANTIGEN WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA


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EMOTIONAL BEHAVIORAL PROBLEMS AND SELF-ESTEEM IN CHILDREN WITH ABSENT FATHERS

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Abstract

Objective: To explore the relationship between emotional behavioral problems experienced during adolescence and self-esteem in children with absent fathers.

Methods: Cross sectional research design was used to carry out the research study in 10 different government schools of Lahore for boys and girls. The sample comprised of 200 students (94 boys and 106 girls) of age ranging between 13-17 years (M = 15.03, SD =1.22). There were 93 children with deceased father and 107 children with emigrant father in the study. Purposive sampling technique was used to collect the data. Two indigenous measures used namely School Children Problems Scale (Saleem and Mahmood, 2011) and Self-Esteem Children Scale (Saleem & Mahmood, 2011) along with demographic Performa.

Results: The results showed that emotional behavioral problems like anxiety, aggression, academic problems, somatic complaints, withdrawal, rejection had inverse relationship with positive self-esteem (p< .001) and positive relation with low self-esteem (p< .001). The results also revealed that children of emigrant father experience more aggression (p< .001) as compared to children with deceased father, whereas children of deceased father experience more somatic complaints (p<.005).

Conclusion: The present study is a seminal work carried out to understand the emotional behavioral problems of children with absent father. It is deemed necessary to take a healthy step towards the prevention and promotion of mental health school children to boast their self-esteem.

Key words: Children with deceased father, children with emigrant father, emotional and behavioral problems, self-esteem.

The paternal influence on children has become a more important area of research these days. And many social experts have explored this phenomenon in regard with the child development. Farrell (2001) utter that the father’s role is very important for the children throughout their life.¹ Like father’s absence, father’s presence can affect child’s life in a different way ie if father is estranged or offensive, then the child’s development can be better without his presence.² Many theories also tell us about the child’s development in different domains. In Freud’s theory, Oedipus conflict played an important role whereby the child needs sexually the opposite sex parent and also denied its desire by the other parent. According to Freud, father is responsible for the development of rules and regulations regarding the society, inside the child. It has been reported that due to the father’s absence, the child sees himself as askew in society.³ Father’s involvement is no less important than the mother’s whereas his absence

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creates many emotional, behavioral and psychological problems.

Parenting is most important activity for passing on their social and spiritual values to their children. It has a paramount effect on the development of the child’s personality in long and short run notably in different spheres of his life especially in mentally, physically and academically. Terms of both positive parenting and negative parenting have been used by different researchers. The positive parenting helps to enhance the child’s self-confidence whereby makes him/her competent socially and academically as well as protect them against disruptive behavior and substance abuse. In negative parenting practices, the child experiences rude behaviors, lack of child activities monitoring and guidance resulting in multiple children problems like delinquency, criminality, violence and substance abuse.

The role of mother is very important and is also explained in literature e.g., Smith (2011) clarified the role and association of a mother, the only individual who is initially attached. Parents have different natures of relationship with the children. According to Smith, children have more familiar and relaxed relationship with mother. Mother’s role increases with the growing age of children. Similarly, father is an important figure in the development of children in different areas socially, cognitively and emotionally. The dynamic role of father makes the stronger connection between him and his kids. Fathers’ role is essential in different aspects of raising up the child. They play and explore the world together through gaming which is important in upbringing of their children.

Propeone (1996) was the key person who first stressed about the significance of fathers in child development. He was a known sociologist who emphasized the involvement of a father in his child’s life because the presence of father brings constructive changes and benefits in children’s life. Fathers have a great impact on the well-being of their children. According to a US departmental survey, father’s contribution plays a major part in different fields of daughter’s life emotionally, socially and intellectually. Fathers are considered primary caregiver and add a sense of security. When fathers show their love and affection to their infants, it develops in them a secure and protective feeling. When father and child spend quality time together it increases their confidence, help them to cope with problems and take decisions and decrease their mental tension.

Following study was carried out in 2001 and investigated the fact that children with secure association with their fathers have strong nerves, high confidence, and lesser anxiety. The emotional, social and intellectual development of a child go side by side and several studies have proven that fathers endorse more autonomy and exploration of the outer world as compared to mothers.

Father’s participation also plays an imperative role in child’s development. Nowadays, fathers are well aware and do play an active role for their children so that they achieve perfection in their life. But the divorced fathers mostly disengage themselves from their children. Such children face a number of problems like low self-esteem and emotional or behavioral issues along with addiction in their life. In addition, those children whose fathers are absent for any reason, face many problems in adulthood like financial and social problems, unemployment and also face difficulties in relationships.

The attachment theory talks about the strong emotional and physical relationship with the primary caregiver which is very important for personal development of child. John Bowlby was the key person who introduced the attachment theory through studying the developmental psychology of children from different backgrounds. Mary Aimsworth investigated the phenomenon of child’s attachment behavior when they face stressful situations. Furthermore she described the four attachment styles as one is secure. She also stressed on three insecure attachment patterns namely avoidant, ambivalent and disorganized attachment styles. In
secure attachment style, the child will take parent as a secure base and the attachment figure is approachable, warm and accessible. But in avoidant style, the child will show a little response to separation and often avoid interaction. In ambivalent attachment style, the child will defy interaction and looks more concerned. Disorganized attachment style child shows utmost uncertainty, is puzzled and shows opposing behaviors. One of the major criticism on this theory is that the attachment theory just focused on the mother’s attachment with child and did not emphasize on the father’s.17

Similarly, the absence of a father creates problems in a child’s life. There are three categories of absent fathers namely deceased fathers, emigrant fathers and divorced fathers. As the name suggests, deceased fathers are those who passed away and their families had to bear their loss. The emigrant fathers are those whose left their country permanently for the purpose of better earning and to improve their family financial conditions. Amongst these are mostly middle class working men who live alone abroad leaving their family in their home countries and typically come back after one or two years to spend some time at home. Due to the migration of the head of the family, many emotional and behavioral problems are faced by the children left behind. In the absence of their fathers, children experience loneliness, physical hostility, sadness, difficulty in concentration, anxiety and lack of confidence or self-esteem etc. A huge number of Pakistani population is working abroad leaving their families here.18

Children under the age of 18 years experience many biological, psychological and social problems. As the child grows older, many physical changes occur which lead to the psychological and behavioral changes in the child. Hazel & Shinobu (1991) studied that the individual’s cultural milieu influences their view about themselves.19 The individualistic culture, which is prevalent in the west, creates the view of a separate identity. In collectivistic culture they have independent view of themselves but connected with each other. In collectivistic culture, as in Pakistan, children face less number of problems due to many positives aspects as compared to individualistic cultures. But sometimes excessive interference may disturb their lives, because parents’ absence cannot be fulfilled by others.

Due to the absence of fathers in children life, they can face emotional and behavioral problems. Achenbach and Edelbrock (1978) explained the terms of Internalizing and Externalizing for the emotional and behavioral problems in children and adolescents.20 These problems are experienced covertly and the others such as aggression, conduct problems and oppositional defiant behavior are expressed overtly.21 Children experiencing internalizing and externalizing problems leads to poor school performance, high dropout rate, shyness, nonsocial attitude, loneliness and lack of confidence in life. Externalizing and internalizing problems in children vary from culture to culture.

Coopersmith (1989) defined self-esteem as “an individual’s view of a value and worthiness of a person uttered in performance toward him and others.”22 Harter (1990) defined self-esteem as a degree to which an individual grants respect to himself and others as a person.23 Self-esteem is an essential part of a person’s behavior. In literature review, the researchers have shared many suggestions which are very helpful in a child’s development with absent fathers, but it should not be generalized. The impact of father’s absence is both emotional and cognitive and is quite different in both genders. There are very limited studies about these variables in reference to Pakistani culture.

In this study, the relationship of the father’s absence with the children’s self-esteem & sexual activity was studied in rural adolescents. 1409 samples (558 boys and 851 girls) were included in this study with the age ranging from 11 to 18 years. The Miller Self-Esteem Questionnaire (MSQ) was applied to determine the self-esteem. The results showed increased sexual activity in adolescence where fathers didn’t live at home but no significant
relationship was found between self-esteem and sexual activity. It also showed that father’s absence has a significant effect on the youngster’s lifestyle. This study also concluded that father’s presence may add variation in children’s way of life.

A study done by Saleem & Mahmood in 2011, explained the two variables, emotional and behavioral problems and self-esteem in perspective to school aged children. They used two indigenous and culturally appropriate scales, namely School Children’s Problem Scale (SCPS) and a Self-Esteem Scale for children (SESC). The sample was 1571 school aged children (boys 49% and girls 51%) between ages 13-17 years. These were administered in the scales of SCPS and SESC along with a demographic questionnaire. The problems found were anxiety, rejection which leads to poor school performance and low self-esteem. Existing literature about emotional behavioral problems (EBP) were important predictor of poor school performance and low self-esteem. Soomro &Clarbour (2012) determined the connection between emotional behavior and academic achievement in middle school children in Hyderabad, Pakistan. Emotional Behavioral Scale for Pakistani Adolescents (EBS-PA, Soomro, 2010), was used which assessed the social anxiety, male violent aggression, and social self-esteem scores. This also considered the emotional behavior in children based upon the Clarbour and Roger's (2004) model of emotional style, on which the EBS-PA scale is based. The outcome revealed that educational grades were definitely associated positively with self-esteem and negatively with male violent aggression.

A study of McLanahan & Sandefur (1994) explained the adverse effects of absence of fathers on academic achievement and sexual behavior in children. 2500 children were included in this research who had one parent. And the investigation showed that children had low grades, poor attendance and high rate of drop-out with absent fathers as compared to the children living with parents. Although, the trend of living away from the family and children due to jobs abroad is increasing day by day. This research study was carried out on national level only to know the role of fathers who are living in another country for the purpose of earning. And the result pointed out that father’s involvement can influence the children on social and cognitive level. The National Commission of Children pointed out that when parents are divorced or they get separated for any reason, children suffer a lot. Children with single parent (mostly mothers) are six times poor performer than children living with both parents. At present many students are dropped out of the school due to emotional, behavioral, and intellectual problems, alcohol and drug abuse, adolescent pregnancy and child-bearing, juvenile delinquency, mental illness, and suicide. The major reason of these problems are in their parents; either they are divorced, dead, living separately or are emmigrant. Children who are brought up with absent fathers look at the external world as insensitive, hostile and aggressive, which some time make them courageous and violent or coward and shy. In eastern world, particularly in Muslim society, the role of fathers is of utmost importance because boys take them as role models. They are taken as a sign of security and protection in our homes.

In Pakistani society, father is considered as the head and the owner of the house. Generally, he is the only earning figure in the house, so he is authoritative and commander as compared to his wife. In most of the houses in our society, mothers are housewives. Their most important duty is to bring up their children. Children are emotionally attached with their mothers and feel comfortable with them. They hesitate to express their emotions/feelings with their fathers. But this is not the case in every house; it varies from family to family.

**METHODS**

This cross sectional study was carried out in 10 government schools of Lahore for boys and girls. Purposive sampling technique was used to select...
school children. The sample size was determined on previous literature review. Formal permission from institute was obtained to carry out the research study. After obtaining informed consent from the school authorities’ data collection was carried out. Participants were assured about the confidentiality and anonymity. They were given right to withdraw at any stage of the research study. Debriefing was done at the end of test administration to resolve their queries.

The sample of 200 boys (47%) and girls (53%) was selected for this research study. In the current research study, children of absent father were included, which were divided into two categories (children with emigrant and deceased fathers). The participant’s age ranges from 13 to 17 years (M 15.03 SD 1.22), selected from grades 8th (36%), 9th (34%) and 10th. (31%). Only those children were included who had experienced father’s absence from 6 months till 1-year duration. Children of both working (51%) and non-working (149%) mothers were included in the sample. Children living in nuclear (101%) and joint (99%) family system were included in the sample. Children living with single parents were excluded from the current research study.

All agreed participants were given demographic Performa to get the personal information of the participants such as age, gender, family system, education of parents and family size. School children problems scale (SCPS, Saleem & Mahmood, 2011) was used to assess the emotional behavioral problems and it consisted of 44 items. It is also used as a self-report measure to report emotional and behavioral problems in school aged children. This scale contained rating options from 0-3 whereby “0 for Never, 1 for rarely, 2 for Sometimes and 3 for often”. Total six factors are included as Anxiousness, Academic Problems, Withdrawal, Rejections, Somatic Problems and Aggression. The scale has culturally relevant and psychometrically sound properties (a=.87). Self-esteem scale for children (SESC, Saleem & Mahmood, 2011) was used to assess the self-esteem in school children. Total 4 factors are included in which 3 factors are positive Academic Self-esteem (a=.74), Self-Confidence (a=.83), Social self-esteem (a=.70) and one negative factor is Low Self-Esteem (a=.74). It is a 5-point rating scale (0-4) was used to rate each problems options like “0 means Never, 1 means Rarely, 2 for to some extent, 3 means Very much and 4 means Always”.

Firstly, a pilot study was done on 20 school children (10 boys and 10 girls) to determine the user friendliness of both scales i.e School Children Problem Scale and Self-Esteem Children Scale (SCPS, SECS) that were used in this research study. The instructions were given in Urdu language and both the scales were easy to understand and comprehend.

Afterwards the study was carried out on 200 school children with absent father. Keeping in view the ethical and emotional sensitivity of the research participants, researcher sought the help of class teacher to identify the school children with absent father. After teacher’s identification and referral, the purpose of research was explained to school children and all those participants who were willing were given the scales. The study was carried out in the group setting, each group comprised of 10-15 research participants. After the test administration participants were debriefed about their queries. Then data was entered in the Statistical package for social science (SPSS) version 20.0 IBM to compute all the data and manually reviewed for discrepancies and missing data. To find out the relationship between emotional and behavioral problems and self-esteem correlation analysis was carried out. To find out the predictor of self-esteem, regression analysis was carried out. To find out the mean difference in expression of emotional and behavioral problems and self-esteem in child with emigrant father and children with deceased father, t-test was carried out.

RESULTS

The table 1 indicates that F1 Anxiousness has a positive relationship with academic problems, with-
EMOTIONAL BEHAVIORAL PROBLEMS AND SELF-ESTEEM IN CHILDREN WITH ABSENT FATHERS

Table 1: Summary of Inter-Factor Correlation, Means, Standard Deviations of the School Children (N=200) on SCPS and SECS

<table>
<thead>
<tr>
<th>Factors</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>SE1</th>
<th>SE2</th>
<th>SE3</th>
<th>SE4</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>---</td>
<td>.45***</td>
<td>.14ns</td>
<td>.54***</td>
<td>.14ns</td>
<td>.47***</td>
<td>-18ns</td>
<td>-26**</td>
<td>-10ns</td>
<td>.42***</td>
</tr>
<tr>
<td>F2</td>
<td>---</td>
<td>---</td>
<td>.40***</td>
<td>.37***</td>
<td>.40***</td>
<td>.21**</td>
<td>-27**</td>
<td>-11ns</td>
<td>-15ns</td>
<td>.40***</td>
</tr>
<tr>
<td>F3</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>.28**</td>
<td>.19*</td>
<td>.14ns</td>
<td>-12ns</td>
<td>-10ns</td>
<td>.20**</td>
<td></td>
</tr>
<tr>
<td>F4</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>31***</td>
<td>.39***</td>
<td>.71***</td>
<td>-12ns</td>
<td>-04ns</td>
<td>.30***</td>
<td></td>
</tr>
<tr>
<td>F5</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>30***</td>
<td>22***</td>
<td>.30***</td>
<td>.23**</td>
<td>.51**</td>
<td></td>
</tr>
<tr>
<td>F6</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>31***</td>
<td>30ns</td>
<td>.03**</td>
<td>.36**</td>
<td></td>
</tr>
<tr>
<td>SE1</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>.64**</td>
</tr>
<tr>
<td>SE2</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>.67**</td>
</tr>
<tr>
<td>SE3</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>.19</td>
</tr>
<tr>
<td>SE4</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
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</tr>
</tbody>
</table>

SD     7.80  5.05  4.95  4.42  3.85  3.13  5.57  7.92  6.06  5.53

df=199, *p<0.01, **p<0.05, ***p<0.001. Note. F1=Anxiety 1, F2=Academic,F3=Aggression,F4=Withdrawal,F5=Rejection, F6=Somatic complaints, SE1=Academic Self-Esteem, SE2=Self-confidence 2, SE3=Social Self-Esteem, SE4=Negative Self-Esteem

drawal, rejection, and low self-esteem, whereas it has inverse relationship with academic self-esteem, social self-esteem and self-confidence. Anxiety has no significant relationship with aggression and self-confidence. F2 Academic Problems has also a positive relationship with aggression, withdrawal, rejection, somatic complaints, low self-esteem and inverse relationship with academic self-esteem, social self-esteem and no significant relationship was found with self-confidence. F3 aggression has significant positive correlation with withdrawal, rejection, somatic complaints and low self-esteem but academic self-esteem, social self-esteem and self-confidence inversely related with aggression factor. The finding also suggests that there F4 withdrawal is positively correlated with low self-esteem, and negatively correlated with academic self-esteem, whereas no significant relationship was found with self-confidence and social self-esteem. F5 rejection has positive relationship with somatic complaints, academic self-esteem, social self-esteem and self-confidence. Low self-esteem has no significant association with rejection. F6 somatic complaints have positive relationship with academic problems. The result also showed academic self-esteem, self-confidence, and social self-esteem are positively correlated with each other and negatively correlated with low self-esteem.

Table 1: Hierarchical Regression Analysis of All Demographic Variables and School Children Problem Scale predicting Low Self-Esteem in Children with Absent Father

<table>
<thead>
<tr>
<th>Model</th>
<th>SEB</th>
<th>B</th>
<th>t</th>
<th>p&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1 (R=.23, ΔR²=.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>1.94</td>
<td>.10</td>
<td>1.10</td>
<td>.272(ns)</td>
</tr>
<tr>
<td>Gender</td>
<td>3.73</td>
<td>.14</td>
<td>1.45</td>
<td>.148(ns)</td>
</tr>
<tr>
<td>Class</td>
<td>2.29</td>
<td>.05</td>
<td>.54</td>
<td>.593(ns)</td>
</tr>
<tr>
<td>Step 2 (R=.26, ΔR²=.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother’s Occupation</td>
<td>4.24</td>
<td>-.05</td>
<td>.63</td>
<td>.531(ns)</td>
</tr>
<tr>
<td>No. of Siblings</td>
<td>.99</td>
<td>.10</td>
<td>1.36</td>
<td>.175(ns)</td>
</tr>
<tr>
<td>Family System</td>
<td>3.69</td>
<td>.04</td>
<td>.54</td>
<td>.590(ns)</td>
</tr>
<tr>
<td>Categories</td>
<td>4.03</td>
<td>-.16</td>
<td>1.10</td>
<td>.050(ns)</td>
</tr>
<tr>
<td>Step 3 (R=.61, ΔR²=.32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F1</td>
<td>.10</td>
<td>.15</td>
<td>1.10</td>
<td>.269(ns)</td>
</tr>
<tr>
<td>F2</td>
<td>.14</td>
<td>.13</td>
<td>1.72</td>
<td>.076(ns)</td>
</tr>
<tr>
<td>F3</td>
<td>.11</td>
<td>.10</td>
<td>1.43</td>
<td>.155(ns)</td>
</tr>
<tr>
<td>F4</td>
<td>.05</td>
<td>.04</td>
<td>.57</td>
<td>.569(ns)</td>
</tr>
<tr>
<td>F5</td>
<td>.43</td>
<td>.34</td>
<td>4.13</td>
<td>.001***</td>
</tr>
<tr>
<td>F6</td>
<td>.10</td>
<td>.18</td>
<td>.83</td>
<td>.405(ns)</td>
</tr>
</tbody>
</table>

Note. F1=Anxiety 1, F2=Academic,F3=Aggression, F4=Withdrawal, F5=Rejection, F6=Somatic complaints

In Table 2 In order to identify the significant predictors of low self-esteem in caregivers of children with absent father, hierarchical regression analysis was carried out. In Step I, demographic variables of the participants like age, gender and class were taken into account. In Step II mother's
occupation, no of siblings, family system and categories of children with deceased and emigrant children were entered. In step III factors of school children problem scale was entered. The results showed that in model 1 age, gender and class was not the significant predictor of low self-esteem in children with absent fathers. Similarly, in model 2 familial factors such as mother's occupation, no of siblings, family system does not contribute significantly in causing low self-esteem in children of absent father. Model 3 showed that overall independent variable is predicting 32 % change in the dependent variable. In the model rejection is found to be a significant positive predictor of low self-esteem in children with emigrant fathers.

### Table 1: Means, Standard Deviations, t and p values of Absent Father Categories and Emotional Behavioral Problems and Self-Esteem Factors

<table>
<thead>
<tr>
<th></th>
<th>Children with Emigrant Father</th>
<th>Children with Deceased Father</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>F1</td>
<td>15.04</td>
<td>7.08</td>
<td>16.77</td>
<td>8.42</td>
</tr>
<tr>
<td>F2</td>
<td>9.50</td>
<td>4.99</td>
<td>9.26</td>
<td>5.13</td>
</tr>
<tr>
<td>F3</td>
<td>10.63</td>
<td>5.17</td>
<td>8.26</td>
<td>4.42</td>
</tr>
<tr>
<td>F4</td>
<td>9.70</td>
<td>4.56</td>
<td>9.95</td>
<td>4.27</td>
</tr>
<tr>
<td>F5</td>
<td>3.37</td>
<td>3.65</td>
<td>4.43</td>
<td>4.04</td>
</tr>
<tr>
<td>F6</td>
<td>3.78</td>
<td>2.97</td>
<td>4.78</td>
<td>3.23</td>
</tr>
<tr>
<td>SE1</td>
<td>25.35</td>
<td>5.90</td>
<td>24.64</td>
<td>5.20</td>
</tr>
<tr>
<td>SE2</td>
<td>32.45</td>
<td>7.81</td>
<td>28.94</td>
<td>7.66</td>
</tr>
<tr>
<td>SE3</td>
<td>32.06</td>
<td>5.84</td>
<td>30.95</td>
<td>6.27</td>
</tr>
<tr>
<td>SE</td>
<td>9.52</td>
<td>4.49</td>
<td>10.73</td>
<td>5.51</td>
</tr>
</tbody>
</table>

DISCUSSION

The aim of this study was to determine the link between emotional behavioral problems and self-esteem in children with absent father. Parenting is the most important activity which impacts children’s life. Good parenting passes on good, values and norms for the survival of their children in society. Like the father’s presence, the absence of father also has greater impact on the children. The absence of fathers also effects the different areas of child’s life such as academic, social and emotional behavior. The schooling phase is of prime important as it is here that the child learns many things but also faces many problems. These problems increase with absence of their fathers in their lives. Although mother’s role significance is very essential but father gives them strength, courage and emotional power to face outer world challenges. Parent-child affiliation is significant in the personality development of a child. This affiliation has both short as well as long-term effects on children mental and physical and also on their education achievement. Positive parenting is linked with the high child self-esteem, social and academic competence, and shields alongside antisocial behavior and substance misuse.

The existing literature also revealed that the children with absent fathers are more likely to experience health related & emotional behavioral problems. Another study told about the consequences of absence of fathers: as they experience behavioral problems of poor attention span and defiance behavior in school. Without fathers, boys are experience externalizing problems and are more unhappy, sad, depressed, dependent, and hyperactive whereas the girls are more likely to become overly dependent and have internalizing problems such as anxiety and depression. The current research findings also prove that both categories of children with absent fathers face behavioral problems and lower self-esteem. It means that higher the emotional behavioral problems lower the self-esteem. It is also evident from the previous researches the children with absent father show more
problems in emotional and psychosocial adjustment and exhibit a variety of internalizing and externalizing behaviors.

No gender difference was found in manifestation of emotional behavioral problems and self-esteem in children with absent father from current findings. So, the findings of the current research is constant with the existing literature. In one study it was found that the gender difference typically is not statistically significant boys and girls appear to respond similarly or no difference was found in both genders. The main focus of research was the absence of father affects the children’s mental health functioning rather than gender differences. There could be different factors in the selection of participants or that could be the non-serious attitude of participants toward the questionnaire. As the research sample was taken from government schools of Lahore.

Children with single parent have experienced emotional behavioral problems as compared to children living with both parents. Though the upbringing in a single-parent family is often viewed as a risk factor for a child, it was observed that children with single-parent families are now quite common. There are important problems in studying the impact of family on outcomes for children. In one study researchers found that parental absence due to death effect children’s education outcomes more as compare to parental absence due to divorce. So, the findings of the current research revealed the children with absent father/single parents experience emotional behavioral problems and lower self-esteem and it is consistent with the existing literature however there was no significant relationship between emotional behavioral problems and self-esteem with demographics.

The current findings show that the older children face more somatic complaints than younger ones. These findings were not consistent with the literature which declared that the younger children experienced more emotional behavioral problems than older children.

Low social self-esteem is commonly found in said older children. A recent study explored the effects of father’s absence on self-esteem and self-reported sexual activity in rural population (adolescents) and noted that children with absent father have lower self-esteem and increased sexual activity in adolescents.

Same results were found in both working and non-working mothers and family system and as such no difference was found with emotional behavioral problems and absent father. There could be multiple factors which are contributing about these hypotheses. One reason could be the collectivistic culture as in our society which provides a greater support system for each other. Because in this culture, if mother is a working woman, than other caregivers from the family can provide emotional support to the children, thus fulfilling their needs for care. Not any related research was found with reference to absence of fathers and findings of the current study are also novel as no previous researches are available. So, this serves to be a new finding.

Analysis show that children with deceased fathers experience more somatic complaints than children with emigrant fathers. There could be many reasons of this phenomenon as they know their father can’t come back and they feel un-protective or insecure and sometime they are unable to express their emotions which manifested in form of physical problems.

In second category, children with emigrant fathers have more aggression as compared to children with deceased fathers. Self-confidence was also found to be a positive predictor with reference to absent father. This condition could be due to sense of insecurity which leads to aggression and it could be due to burden of responsibility they have to take from an early age. The reason of this particular behavior is that they feel lack of love and care of father in their lives. Secondly, they know that their father is unable to stand besides them at the time of need so, they are more confident in taking any decisions for themselves.
In more than 6 months category, aggression was found as negative predictor and self-confidence was a positive predictor in children. Aggression could be due to missing of their father, now they have to adjust without them, in such scenario children may face adjustment problems. Continuous pampering, morale building from sibling and family could lead to high self confidence. In second category of duration which was more than 1 year category, they scored higher on SCPS factor 6 (somatic complaints). In some cases children fail to adjust after their father’s absence, non cooperative behavior of sibling or high affection with father making them physically sick. These findings are purely new in reference to absence of father and will be beneficial for others in field of research.

In some respect, the results provided clear and unequivocal evidence. The children experience emotional behavioral problems and self-esteem issues due to absence of father. But secondary hypotheses could be unclear as because no difference could be found between emotional behavioral problems with age, class, gender, mother’s occupation and family system. In essence, the current study is valuable and contributes significantly in the limited reservoir research that is available with reference to Pakistan’s setup.

REFERENCES

Emotional Behavioral Problems and Self-Esteem in Children with Absent Fathers


RED CELL ALLOIMMUNIZATION IN POLYTRANSFUSED THALASSEMIC CHILDREN

Muhammad Asif Naveed, Romaisa Naem, Saad Zafar, Rafeeda Maab, Ammarah Sharif, Mehak Khalid

Abstract

Objective: The objective of the study was to determine the prevalence and the type of various alloantibodies in multiple transfused thalassemic patients.

Study design: Cross Sectional Study

Place and Duration of the Study: The Study was conducted at Al-Khidmat Lab, Blood Bank and Thalassemia Care Centre, Surrayya Azeem Hospital Lahore. The Study was conducted from January 2018 to December 2018

Material and Methods: We enrolled 673 patients from both genders. Age, gender and history of transfusion was recorded. Arrangement were made to take informed consent from parents of children and data was collected. Screening for antibodies was done using screening cells. Positive results were further proceed with 11 cell Antibody identification panel.

Results: A total of 673 patients were included in the study. Male to female ratio was 1.6:1. Mean age of the patients was 7.3 years. Alloantibodies identified were Anti D, E, e, C, c, Cw, K, Fya, Fyb, Jka, Jkb, S, s and Lua. Anti D, anti K and anti E were found to be the most frequent antibodies. The average interval of transfusion requirement for patients having antibodies is 16 ±7.5 and for patients not having antibodies is 28±9.61.

Conclusion: After alloimmunization transfusion requirement is increased and inter-transfusion interval is decreased in long term transfusion dependent thalassemic patients. Long term transfusion dependent patient suffer due to alloimmunization. Phenotyping the newly diagnosed thalassemic patients and provision of antigen matched blood can prevent the alloimmunization.

Keywords: Alloimmunization, Antibodies, thalassemia, Rh blood group, transfusion.

Thalassemia is commonest among the disorders occurring in one gene. Cooley and Lee recognized Thalassemia as separate entity in 1925 when they encountered with a child having severe anemia, splenomegaly and effects one bones. In some countries like Pakistan beta thalassemias are relatively common so they are becoming an important public health problem.¹

The beta thalassemia major is quite common in certain regions of the world including Indian sub-continent and Pakistan. The carriers of β-thalassemia in these areas are so much that their frequencies range in these areas ranging from 1 to 20%, but rarely this may even be higher in few areas. A total of 270 million carriers having abnormal haemoglobins including thalassemia have been estimated. Out of these Eighty (80) million are the carriers of β-thalassemia.²
The molecular pathology behind Beta Thalassaemia cause reduction in β chain synthesis, this reduction in synthesis may partial or complete. It is noteworthy that α chain synthesis usually remains unaffected. As the α chain are synthesized in normal quantity so there are excess α chains.³

Clinical features of the disease appears during the later half of the first year of life when fetal hemoglobin is to be replaced by adult hemoglobin. Anemia due to ineffective erythropoiesis, extramedullary haematopoiesis and hepatosplenomegaly are the main clinical features. Blood transfusion remains the main treatment which is lifesaving in these patients. Red cell transfusion carries a number of risks the delayed ones are transmission of infection, iron overload and development of red cell antibodies (alloimmunization).¹

Alloimmunization against the transfused donor or foreign red cells is one of the most serious adverse effects of red cell transfusion in thalassemic and other patients with red cells disorders.⁴ This alloimmunization against red cells hinders the transfusion by complicating cross-matching, shortening of the survival of transfused cells in vivo thus delaying the provision of safe transfusions. Alloimmunization rates reported from various centers around the world ranges from 4%- 50 % in thalassemia.⁵

We conducted this study for the prevalence of alloimmunization and frequency of the various types of alloantibodies among thalassemic patients who are on regular red cell transfusions.

METHODS

The study was conducted at Al-Khidmat Lab, Blood Bank and Thalassemia Care Centre, Surrayya Azeem Hospital Lahore. The Study was conducted from December 2017 to June 2019. Those patients of thalassemia major were included in the study who had received at least 08 transfusions. Patients with known alloantibodies, autoimmune disease, renal disease, liver disease and viral infections were excluded from the study. An informed consent was taken and after that a total of 3 ml venous blood was collected in purple top EDTA vial and 3 ml venous blood was collected in yellow top vial (Serum). Blood group (ABO, Rh) DAT and IAT were performed manually by tube method.

Antibody screening was done using three cell panel on serum samples of the patients. The technique for antibody screening included 100µl serum and 50µl of screening red cells. An immediate spin was given and agglutination/no agglutination was recorded. After immediate spin LISS was added and it was incubated for 15 min. After LISS phase agglutination/no agglutination was again recorded. Washing was given three times and after dispensing all the water one drop of Coomb’s reagent was added, agglutination was again noted. Antibody identification was carried out for the samples with positive screening results using commercially prepared 11 cell identification panel with same method as described above for Antibody Screening. Check cells were added in each tube to see if the procedure was alright. The results were graded as 0, +1, +2, +3 and +4. All the results were recorded and specificity of alloantibodies was determined using Anti-gram provided by manufacturer.

RESULTS

The enrollment in this study consisted of 673 children. There were 415 males and 258 females. Male to female ratio was 1.6:1. Mean age of the patients was 7.3 years ± SD 3.68. Age range was 2.3-20.5 years. Mean age of alloimmunized range from 2.9-19.2 and non alloimmunized age range 2.3-20.5. Antibodies were found in 79 patients (11.7%). 74 (11%) patients had single antibodies while 5 (0.74%) patients had multiple antibodies. The frequency of various antibodies identified in order of prevalence was as follows Anti D 15 patients (2.08%), anti K 13 patients (2.08%), anti E 8 patients (1.2%), anti C patients 7 (1.04%), anti e 7 patients (1.04%), anti C patients 6 (0.74%), anti Fya 6 patients (0.74%), anti Fyb 5 patients (0.74%), anti Jka 3 patients (0.74%), anti Jkb 1 patient (0.14%), anti Lua 4 (0.6%)
patients, anti S 4 (0.65%), anti Cw 3 patients (0.44%), and anti s 2 (0.3%). Figure 1

Multiple antibodies were found in 5 patients in following combinations anti D and Fyb (0.14%), anti e and S (0.14%), anti Fyb and E (0.14%), anti E and K (0.3%), anti C and Lua(0.14%). Anti D and anti K were found to be the most prevalent antibodies.

Figure 1: Prevalence of different Antibodies in Polytransfused Thalassemic Children having Single Antibody

The average interval of transfusion requirement for patients having antibodies is 16 ±7.5 and for patients not having antibodies is 28±9.61.

Figure 2: Prevalence of Antibodies in Patients having more than one Antibodies

DISCUSSION

Thalassemic children in Pakistan suffers a lot due to alloimmunization and absence of adequate transfusion services. We calculated the overall prevalence of red cell antibodies in this study. A higher prevalence of alloantibodies was found in males as compared to females with male to female ratio M:F 1:6:1. A study conducted by Roberto de Oliveria showed male prevalence as well. In a study conducted in India there was also male prevalence.

Mean age was 7.3 years with range of 2.3-20.5 years. In a study conducted in Pakistan by Rehan M showed the age range was from 2 years to 22 years with the mean age of 8.1 year. This was comparable with our study. In a study conducted in Iran showed mean age of the patients as 14.97 years with the range of 2-33 years. This mean age as well as range was higher as compared to our result.

The frequencies of prevalence of red cell alloantibodies have been reported from many countries around the world. The data from various centers shows low rate of incidence of alloantibodies. The prevalence of alloantibodies in the current study was 11.7%. In a study conducted in Pakistan in 2015 showed antibody prevalence as 8.6%. In a study conducted by Jain R in India showed the prevalence of 5.21%. These results were comparable with our result. In a study conducted by Ali Davoudi the prevalence of red cell alloantibodies was 24.7%. This frequency of alloimmunization was higher as compared to our result as well as the from the results reported in other studies.

Anti D and Anti K were found to be the most prevalent antibodies in this study. In a study by Roberto anti E was the most prevalent antibody followed by Anti D and Anti K. This was comparable with our study. Sadeghian MH revealed that all antibodies in his study belong to Rh group.

In a study conducted in Iran, anti D and anti K were the most frequent antibodies found. Our results were in concordance with this study. In another study conducted in Iran anti Kell was the most prevalent antibody followed by Anti D and Anti E. This was comparable with our results. A study conducted by Dhawan showed that majority of
Red cell alloantibodies belonged to Rh and Kell blood group system. The Rh and K system antibodies are notorious in causing hemolytic transfusion reaction.\(^{18-20}\)

**CONCLUSION**

Red cell antibodies formation is not uncommon phenomenon especially in poly-transfused patients. Antibodies against Rh and Kell blood group system are a frequent occurrence. Phenotyping the newly diagnosed thalassemic patients and provision of antigen matched blood is required to stop this phenomenon.

**REFERENCES**

Abstract

Aim: To determine the prevalence of hypertensive retinopathy in eclampsia and pre-eclampsia and its association with severity of disease and status of gravida.

Material and Method: This was a cross sectional observation study conducted in Jinnah hospital Lahore over a period of sixteen months. Fifty patients who fulfilled the diagnostic criteria of PIH (≥ 24 weeks of pregnancy, high arterial blood pressure and proteinuria) in obstetric ward were included in the study. Patients' age, number of pregnancies, gestational period in weeks, blood pressure and proteinuria were noted from the clinical record. The pupils were dilated with Tropicamide eye drops 1% and retina was examined with help of direct ophthalmoscope. Any pathological changes were noted and Keith- Wagner classification was used to grade the hypertensive retinopathy.

Results: A total 50 patients were examined. Age range was from 20 to 37 years (Mean age 26.9±4.83). The gestational period ranged between 25 and 41 weeks. 13 patients (26%) were primi gravida,17 (34%) multigravida and 20 patients (40%) were grand multi gravida. Out of fifty cases, 14 cases (28%) had mild pre-eclampsia,10 cases (20%) had severe pre-eclampsia and twenty-six cases (52%) had eclampsia. Hypertensive changes were recorded in 31 cases (62%) of PIH, nineteen patients (38%) did not show any retinal pathology. 44% had grade 1 retinopathy, 10% patients had grade 2 while 4% patients each with grade 3 and grade 4 retinopathy. Ocular fundus changes were observed more in eclampsia patients (84.6%), followed by severe pre-eclampsia (50%) and least in mild pre-eclampsia (28.5%).

This study showed that the severity of hypertensive retinopathy is directly associated with the severity of Pregnancy induced hypertension and status of gravida.

Conclusion: Hypertensive retinopathy is a valid and reliable prognostic factor in determining the severity of PIH, thus retinal examination is a valuable procedure in the management of patients with PIH.

Key words: Eclampsia, Pre-eclampsia, Pregnancy induced hypertension, Gravida.
of these cases.\textsuperscript{2,4,5}

High blood pressure during pregnancy can affect the development of the placenta, causing limitation in the nutrient and oxygen supply to the baby. This can lead to premature delivery, low birth weight, placental separation (abruption) and other complications both to the mother and the baby if left untreated.\textsuperscript{6}

Pregnancy induced hypertension (PIH) is a condition that develops in the absence of other causes of hypertension. According to National high blood pressure educative program (NHBPEP 2000) and American college of obstetricians and gynecologists (ACOG 2002), PIH is directly related to the gravid state of mother and placenta is the main cause. PIH includes gestational hypertension, pre-eclampsia and eclampsia. Pre-eclampsia is best described as multisystem disorder of unknown etiology characterized by development of hypertension ≥ 160/110 mmHg with proteinuria after the 20th week of pregnancy in the previously normotensive and non-proteinuria patients. Pre-eclampsia is classified as mild or severe according to its severity. Blood pressure less than 160/110 mm Hg and proteinuria less than 3 gram/24 hours or less than + 3 is defined as mild and blood pressure ≥ 160/110 mm Hg and proteinuria ≥ 3 gram/24 hours or ≥ + 3 is defined as severe pre-eclampsia. If convulsions are associated with pre-eclampsia, it is termed as eclampsia.\textsuperscript{7}

Pathological changes of this disease are directly related to vascular endothelial dysfunction.\textsuperscript{8} Due to this phenomenon, vasospasm and increase in capillary permeability results. Pre-eclampsia/eclampsia associated retinopathy is characterized by retinal arteriolar narrowing due to systemic ischemia that causes damage to the retinal and choroidal vasculature and to the retinal pigment epithelium. This ischemic state can manifest as reduced arteriolar caliber and arteriovenous ratio, retinal hemorrhages, edema and cotton wool spots, choroidal dysfunction with secondary RPE damage creating serous retinal detachment, retinal pigment epitheliopathy and vitreous hemorrhage.\textsuperscript{4,8,10,11} These vascular changes are reversible and resultant sign and symptoms usually resolve after pregnancy.

As eye is the only organ in the body where we can directly visualize the blood vessels in retina. So with the assessment of retinal vasculature we can predict the vascular status of the mother as well as fetal circulation.\textsuperscript{12} Hypertensive retinopathy is a well-known predictor of increase cardiovascular risk. Women affected with pre-eclampsia and eclampsia are twice at the risk of cardiovascular accidents as compare with healthy women.\textsuperscript{13,14}

This study was conducted to determine the prevalence of retinopathy in PIH, and its association with severity of disease and status of gravida. This study also determined the association of blood pressure with severity of disease.

**METHODS**

This cross sectional observation study, was conducted from January 2015 to MAY 2016 in obstetric ward in Jinnah hospital Lahore. All patients who fulfilled the diagnostic criteria of PIH (≥ 24 weeks of pregnancy, high arterial blood pressure and proteinuria) were included in the study. Patients with diabetes, pre-existing hypertension, renal disorders, hazy ocular media, hematological disorders and Human immunodeficiency virus infection were excluded from the study.

Patients age, number of pregnancies, gestational period in weeks, blood pressure and proteinuria were noted from the clinical record. The pupil was dilated with Tropicamide eye drops 1% and retina was examined with help of direct ophthalmoscope by an ophthalmologist. Any pathological changes were noted and Keith-Wagner classification was used to grade the hypertensive retinopathy. According to this classification, grade 1 includes mild generalized arterial attenuation particularly of small arterioles. Grade 2 includes more severe grade 1 with focal arteriolar attenuation, grade 3 includes grade 2 with hemorrhages, hard exudates, cotton wool spots. Grade 4 includes grade 3 with optic disc swelling.

The data were recorded in a predesigned
performa and analyzed using Statistical Package for Social Sciences (SPSS, IBM Statistics, Chicago, IL, USA version 23.0). Chi-square test was used to determine the association between retinal changes, severity of PIH and status of gravida. A p-value ≤ 0.05 was taken as statistically significant.

RESULTS

A total 50 patients were examined. Highest number of patients were observed in the age group of 20 to 25 years 22 (44 %), while 16 patients (32%) were in age group of 26 to 30 years. Only 12 patients (24%) were in the age range of 31-37. The gestational period ranged between 25 and 41 weeks. 13 patients (26%) were primi gravida, 17 (34%) multigravida and 20 patients (40%) were grand multi. 27 patients(54%) had blood pressure below 160/110 mmHg, while in 23 patients(46%) blood pressure was above 160/110 mmHg.

Out of fifty cases, 14 cases (28%), 7 cases (20%) and 29 cases (52%) had mild pre-eclampsia, severe pre-eclampsia and eclampsia respectively. Hypertensive retinopathy was recorded in 31 cases (62%) of PIH, whereas, nineteen patients (38%) did not show any retinopathy. In our study, 44%, 10%, 4% and 4% had grade 1, grade 2, grade 3 and grade 4 retinopathy respectively (Fig 1). Ocular fundus changes were observed more in eclampsia patients (84.6%), followed by severe pre-eclampsia (50%) and least in mild pre-eclampsia (28.5%) (p-value: 0.001) (Table 1). Statistically significant association was also noted between status of gravida and degree of hypertensive retinopathy (p-value: 0.041) (Table 2).

One patient each was enrolled with serous macular detachment, exudative retinal detachment in both eyes and occipital infarction. Both cases of serous macular detachment and exudative retinal detachment were associated with severe eclampsia and had grade 3 hypertensive retinal changes. The patient with occipital infarction had eclampsia with grade 4 hypertensive changes.

Fig 1: Grade of hypertensive retinopathy in pregnancy induced hypertension (n=50)

Table 1: Association of Hypertensive Retinopathy with Severity of PIH. p-value 0.001

<table>
<thead>
<tr>
<th>Severity of PIH</th>
<th>Nil</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild pre-eclampsia</td>
<td>10</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14 (28.5%)</td>
</tr>
<tr>
<td>Severe pre-eclampsia</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>4</td>
<td>14</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>26 (84.6%)</td>
</tr>
</tbody>
</table>

DISCUSSION

PIH is a common cause of morbidity and mortality worldwide. Like other developing countries, incidence of this disease is higher in Pakistan as compared to the developed countries. According to literature, 10-20% of Pakistani female suffered from PIH2, whereas in US, only 4% female have chance to develop PIH.18 This study included fifty women who were diagnosed with pregnancy induced hypertension. The mean age was 26.9 ± 4.83 years.

Out of 50 cases enrolled in this study, 19 patients (38%) did not show any retinopathy, 31 patients (62%) showed different grade of hyper-
tensive retinopathy. Our results are comparable with Reddy9 from Malaysia. He reported prevalence of 59%. Similarly in a study from Crotia, by Tadin et al14 have reported retinal changes in 45% patients of PIH. Reddy and Tadin found a statistical correlation between proteinuria, blood pressure and hypertensive retinopathy. Degree of retinopathy was directly proportional to severity of PIH. Our results demonstrated the same correlation. So hypertensive retinopathy is a valid and reliable prognostic factor in determining the severity of PIH, thus retinal examination is a valuable and necessary diagnostic procedure in patients with PIH.

Karki et al from Nepal have reported retinal changes in 13.7% in their study.19 They assessed fetal outcome in patients with PIH and concluded that retinal and optic nerve head changes were associated with low birth weight of babies. He also reported that choroidal and optic nerve head changes were associated with low Apgar score. So retinal examination is essential both for maternal health and neonatal health.

Most of previous studies recorded high number of cases with grade 1 and 2 hypertensive changes3,14,28. Our results demonstrated 44% of grade 1 and 10% of grade 2 changes, while 4% each for grade 3 and grade 4. These results are consistent with Akshay et al16 who noted 29%, 5%, 3% and 2% respectively for grade 1, grade 2, grade 3 and grade 4. Thirteen (26%), seventeen (34%) and twenty (40%) patients were primigravida, multigravida and grand multigravida and hypertensive retinopathy was observed in 3 (23.07%), 12 (70.58%) and 16 (80%) cases. Hence, results show a significant correlation between number of pregnancies and severity of retinopathy (p-value 0.041). Similar correlation was seen in results reported by Muhammad IJ et al17.

One patients each of severe pre-eclampsia and eclampsia had exudative retinal detachment. Our observations regarding retinal detachment in eclampsia group match with Akshay16 and Fry W17 and Policiano18. Reddy Sc et al2, in their study did not find any case of retinal detachment12.

**CONCLUSION**

This study showed that the severity of retinopathy is directly associated with the severity of Pregnancy induced hypertension and status of gravida. Thus, hypertensive retinopathy is a valid and reliable prognostic factor in determining the severity of PIH. The retinal examination is a valuable procedure in the management of patients with PIH.

**REFERENCES:**


Chronic obstructive pulmonary disease (COPD) is rapidly emerging as a growing cause of mortality worldwide. In a World Health Organization (WHO) survey, it was estimated that 8% of the world population is suffering from COPD. Approximately 16 million American adults are affected by COPD and it becomes the 4th leading cause of death. There is evidence that exacerbations of COPD are increasing in number and severity. There are many causes of such exacerbations ranging from common pollutants, viruses, bacteria and noncompliance to treatment. These account for more than 2.4% of all hospital admissions through emergency department, and put substantial burden on health care costs. In USA, the approximate hospital admission cost per COPD patient is $7100.

Since the reasons for exacerbations are multifactorial, it is logical that multiple modalities of management including antibiotics, bronchodilators, & corticosteroids may have a significant role in treating exacerbations of COPD.
ROLE OF PROCALCITONIN IN DETERMINING ANTIBIOTIC THERAPY IN ACUTE EXACERBATION

in the treatment of these exacerbations.

It has been reported that 85% of patients presenting with exacerbations of COPD (ECOPD) received antibiotics although other studies have shown that antibiotics have marginal efficacy. It is clear that not all patients who present with ECOPD need antibiotics. Patients who have a high pneumonia severity index tend to benefit more than those with a lower index. It is, therefore, of great importance to objectively identify those patients who need antibiotics. This will have a good impact on health-care cost and minimize the side effects of medications.

Antibiotics are frequently used in ECOPD without any clear cut objective evidence of infection. In a recent study, antibiotics were prescribed in about 85% of hospital admitted cases for exacerbation of COPD. However, the frequency of bacterial detection in the sputum of COPD patients at a stable state and at exacerbation contrasts with the marginal effects of antibiotics therapy suggesting that suppression of inflammation may be more important than antibacterials for symptomatic and functional improvement that has been associated with ECOPD.

The rationale for the rampant use of antibiotics in ECOPD has been further been questioned by the recent available data that viral infection is the most common cause of ECOPD.

Previous studies have been demonstrated that procalcitonin reduced antibiotics prescription (42% vs 72%; p<0.0001) compared to standard therapy. Keeping in view of all above facts, the present study is therefore conducted to test the hypothesis that procalcitonin guidance would help stratify the patients presenting with ECOPD into those who require antibiotics and those who do not.

The result of this study may help in reducing the health care costs resulting from hospitalization, unnecessary antibiotics usage and further help in the prevention of emergence of resistant species.

METHODS

Ethical Statement

The present study was carried out in accordance with the Declaration of Helsinki and local regulations. It was ethically approved by the College of Medicine Ethical Committee, King Saud University, Riyadh, Saudi Arabia.

Single centre case series study was carried out during 6 months time period from April 2013 to September 2103. One hundred and sixteen patients were included in this study (p = 42%; d = 9%; n=116). Patients were collected by consecutive non-probability sampling technique.

Inclusion Criteria

Patients who were known cases of COPD and presented to the emergency department with acute exacerbation (defined in the operational definition) and who had a procalcitonin level in the range of 0.1-0.25mcg/l were included in the study.

Exclusion Criteria

1. Immunosuppression e.g. patients known to have HIV and malignancy or on immunosuppression drugs.
2. Asthma.
3. Cystic fibrosis and bronchiectasis.
4. Patients with underlying psychiatric illness e.g. schizophrenia.
5. Patients with alternate explanation for physical signs & symptoms e.g. heart failure.
6. Recent use of antibiotics prior to initiation of current exacerbation (in the last 4-6 weeks)

Data Collection Procedure

Patients who fulfilled the inclusion criteria, were admitted, a written informed consent was taken, their clinical status was assessed (for worsening of symptoms if any) and a follow up procalcitonin level was monitored daily till discharge after 24-28 hours.

Data Analysis

Data analysis was done by the statistical
software SPSS 15 to explore the mean age of patients, frequency and percentage of the patients who required antibiotics in the treatment of exacerbation of COPD guided by the procalcitonin level.

**Experiment Method**

During the study duration, one hundred and eighty patients with suspected COPD exacerbations were admitted to the emergency department. Out of 188, 126 patients were randomly selected, 10 were removed because they failed to meet spirometric criteria for the presence of COPD. No patient dropped out thereafter, and no patient lost his/her follow-up.

The mean ± SD age of our population was 58.18 ± 6.207 years and mean duration of COPD was 13.67 ± 4.452 years. On the analysis of gender distribution of study population, we found that 70 (60.34%) were male patients and 46 (39.66%) were females.

Overall, cultures from sputum yielded pathogenic bacteria in 40 (34.5%) patients. Gram-negative bacteria accounted for 27 (67.5%) of all microorganisms recovered (53 organisms), and Gram-positive organisms accounted for 13 (32.5%) of all microorganisms recovered (24 organisms. The most frequently isolated organisms were Enterobacteriaceae spp (18 organisms) and Streptococcus pneumoniae (14 organisms).

Seventy patients (60.3%) had severe or very severe COPD. During the previous 30-day period, antibiotic or oral steroid therapy for exacerbations of COPD was reported by 17 (14.7%) and 28 (24.1%) patients, respectively. 21 (18.1%) patients had received antibiotics within the 24 hours preceding ICU admission. 70 (60.3%) patients required ventilator support, non invasive ventilation (NIV) in 50 (71.4%) patients and invasive mechanical ventilation in 20 (28.6%) patients. All those patients having severe or very severe pneumonia (70 (60.3%) received antibiotics and 70 (60.3%) received inhaled steroids and 40 (34.5%) received systemic steroids. The mean length of ICU stay was 29±7.2 days. The mean length of non-invasive ventilation, invasive mechanical ventilation, and ventilation-free days during the ICU stay were 2.8±5.1 days, 17.8±5.32 days, and 2.56±2.34 days, respectively. 14 (12%) patients developed septic shock, nine during the first hours following ICU admission and five during their ICU stay.

The median [25%-75% IQR] Procalcitonin (PCT) levels were as follows:

Procalcitonin level at admission (PCT-H0) was 0.493 μg/L [0.131-1.471], Procalcitonin level after 6 hours (PCT-H6) was 0.724 μg/L [0.167-2.646], and Procalcitonin level after 24 hours (PCT-H24) was 0.557 μg/L [0.123-3.4].

**RESULTS**

PCT levels were not different in patients who had received antibiotics prior to ICU admission, compared to antibiotic-naive patients (PCT-H0 0.695 μg/L [0.202-1.139] vs 0.470 μg/L [0.088-1.471], p = 0.73 and PCT-H0 0.942 μg/L [0.202-1.110] vs 0.438 μg/L [0.088-0.902], p = 0.22, respectively) (Table 1). In addition, steroids prior to ICU admission did not influence PCT levels (p = 0.76). PCT-H0 was significantly higher when abnormal breath sounds or rales were present (PCT-H0 1.661 μg/L [0.745-26.83] vs 0.207 μg/L [0.086-0.470], p = 0.0005) and when fever > 38°C was present; PCT-H0 1.495 μg/L [0.828-56.48] vs 0.272 μg/L [0.087-0.902], p = 0.005) (Table 2). No association was found between PCT-H0 levels and the presence or absence of sputum and cough.

The PCTmax was < 0.1 μg/L in 12/116 (10.3%) patients, from 0.1 - 0.25 μg/L in 26/116 (22.4%) patients, and > 0.25 μg/L in 78/116 (67.3%) patients, including 20 patients with PCTmax > 0.5 μg/L (Table 3). There were no associations between PCTmax levels > 0.25 μg/L and severity of COPD (p = 0.21).

**DISCUSSION**

An ECOPD is defined as “a sustained worsening of the patient’s condition, from the stable state
ROLE OF PROCALCITONIN IN DETERMINING ANTIBIOTIC THERAPY IN ACUTE EXACERBATION

Table 1: Comparison of Procalcitonin Level in Patients having Antibiotics Pre-admission with Antibiotic-Naive Patients

<table>
<thead>
<tr>
<th>Procalcitonin Level</th>
<th>Median</th>
<th>Range</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-admission</td>
<td>PCT-H0</td>
<td>0.695 μg/L</td>
<td>0.202-1.139 μg/L</td>
</tr>
<tr>
<td></td>
<td>PCT-H24</td>
<td>0.470 μg/L</td>
<td>0.088-1.471 μg/L</td>
</tr>
<tr>
<td>Antibiotic Naive patients</td>
<td>PCT-H0</td>
<td>0.942 μg/L</td>
<td>0.202-1.110 μg/L</td>
</tr>
<tr>
<td></td>
<td>PCT-H24</td>
<td>0.438 μg/L</td>
<td>0.088-0.902 μg/L</td>
</tr>
</tbody>
</table>

PCT-H0 = Procalcitonin level at admission  
PCT-H24 = Procalcitonin level after 24 hours

Table 2: Comparison of Procalcitonin Level in Patients having Abnormal Breath Sounds & Fever

<table>
<thead>
<tr>
<th>Procalcitonin Level</th>
<th>Median</th>
<th>Range</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal breath sounds</td>
<td>PCT-H0</td>
<td>1.661 μg/L</td>
<td>0.745-26.83 μg/L</td>
</tr>
<tr>
<td></td>
<td>PCT-H24</td>
<td>0.207 μg/L</td>
<td>0.086-0.470 μg/L</td>
</tr>
<tr>
<td>Fever &gt; 38°C</td>
<td>PCT-H0</td>
<td>1.495 μg/L</td>
<td>0.828-56.48 μg/L</td>
</tr>
<tr>
<td></td>
<td>PCT-H24</td>
<td>0.272 μg/L</td>
<td>0.087-0.902 μg/L</td>
</tr>
</tbody>
</table>

PCT-H0 = Procalcitonin level at admission  
PCT-H24 = Procalcitonin level after 24 hours

Table 3: Procalcitonin Level

<table>
<thead>
<tr>
<th>Procalcitonin levels</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT max &lt; 0.1 μg/L</td>
<td>12</td>
<td>10.3%</td>
</tr>
<tr>
<td>PCT max 0.1-0.25 μg/L</td>
<td>26</td>
<td>22.4%</td>
</tr>
<tr>
<td>PCT max &gt;0.25 μg/L</td>
<td>78</td>
<td>67.3%</td>
</tr>
<tr>
<td>Total</td>
<td>116</td>
<td>100%</td>
</tr>
</tbody>
</table>

and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD.17

In the United States, COPD affects approximately 16 million adults, and is one of the fastest growing causes of morbidity and mortality.18 Exacerbations of COPD are responsible for > 2.4% of all acute medical hospital admissions and constitute the most important direct health-care costs associated with COPD.19 In the United States, the mean cost of hospital admission for COPD in a cohort of patients with severe COPD was estimated to be 7,100 (in US dollars).20

Exacerbations of COPD can be triggered by a variety of factors, such as viruses, bacteria, and common pollutants.21 Thus, corticosteroids,22 antioxidants,23 and antibiotics24 may all have beneficial effects in treating or preventing some episodes.

Antibiotics have demonstrated a marginal efficacy in the treatment of exacerbations of COPD.25 Nevertheless, a recent survey26 including 69,820 patients who had been hospitalized for exacerbations of COPD in 360 hospitals throughout the United States showed that 85% of all patients were given antibiotics. Not all patients will equally experience benefit from antibiotics. Subgroups of patients selected by evidence of bacterial infection or by severity of illness are more likely to benefit than those patients who are less ill.27 Therefore, the definition of a biomarker, which potentially detects such episodes or is specific to one subtype of exacerbation would be of great interest.

Serum levels of procalcitonin increase rapidly in the presence of infection.28 The ubiquitous release of procalcitonin during infections is induced either directly by microbial toxins (eg., endotoxin) and/or indirectly by humoral factors or the cell-mediated host response.29 This induction is rather attenuated by cytokines released during viral infections.30 Therefore, circulating levels of procalcitonin are markedly elevated in patients with bacterial infections compared to those with viral infections or other inflammatory conditions.31

In previous studies,32,33 procalcitonin guidance markedly and safely reduced antibiotic prescriptions and the duration of antibiotic therapy in patients with lower respiratory tract infections.

Our findings indicate that guidance with the measurement of procalcitonin levels reduces the exposure of patients to antibiotics after presentation to the emergency department for exacerbations of COPD. This initial difference in antibiotic exposure is not followed by increased antimicrobial usage after hospitalization for up to 6 months. Thereby, the clinical outcome, including exacerbation rate and time to the next exacerbation, was not compromised. The absolute risk reduction in antibiotic exposure implies that for one in every four patients who were...
admitted to the hospital due to an ECOPD, one course of antibiotic therapy can be prevented.

Given the prevalence of COPD and the duration of illness, a reduction in antibiotic prescriptions for the treatment of exacerbations could have a tremendous impact on the overall economic burden of the disease under current budget constraints. In addition, the controlled prescription of antibiotics decreases selective pressure for the emergence of bacterial resistance.

A meta analysis of placebo-controlled trials concluded that there was a small but significant benefit from the treatment of exacerbations of COPD with antibiotics in terms of overall recovery. A more recent extensive review of the literature suggested that antibiotic therapy significantly decreased mortality and lack of response to treatment in patients experiencing exacerbations of COPD. Moreover, it has been proposed that antibiotic therapy may reduce further antibiotic prescriptions following the presenting exacerbation and may increase the time until the next exacerbation in a selected population of patients. Several characteristics have been suggested to identify patients who are at a greater risk for severe exacerbation, including the presence or severity of underlying obstructive disease, comorbid conditions, frequency of exacerbations, and severity of symptoms at presentation. Most of these proposed criteria have been analyzed in different retrospective study designs. However, none has been validated by a prospective randomized trial.

Similarly, a wide variety of surrogate markers of the inflammatory process have been measured in patients in the stable state and during an episode of ECOPD. Most of them provide laboratory confirmation supporting the diagnosis of exacerbation. Unfortunately, their role in patient management is far from certain, as prospective studies under long-term follow-up are not available.

In this prospective, interventional study, we randomized unselected, consecutive COPD patients to receive antibiotics based on serum procalcitonin levels at hospital admission. The vast majority of admitted patients took part in the study, assuring the applicability of the proposed approach under “real-life” conditions.

Although procalcitonin guidance reduced antibiotic prescription, its use did not result in decrease in the relapse of COPD, a decrease in the length time before the next exacerbation, or a more rapid decline in lung function. Thus, it is tempting to speculate that measuring procalcitonin levels at hospital admission identifies the patients who present with more severe or tissue-invasive bacterial infection and hence would most likely to benefit from antibiotic therapy.

Sputum microbiology is considered to be of limited value in investigating exacerbations of COPD. Conversely, the acquisition of new strains of microorganisms might indicate an impending bacterial exacerbation.

This study might have a potential limitation in regard to its generalization. As previous experience with procalcitonin was available at the study site, physicians’ adherence to the study protocol was facilitated. Furthermore, only patients with an ECOPD requiring hospitalization were included in the study. Thereby, procalcitonin measurement results were available within 1 h after hospital admission, allowing an immediate treatment decision. Thus, the applicability of these findings to mild exacerbations treated in the outpatient setting still has to be confirmed in multi-institutional and international studies. Furthermore, we cannot exclude that some of the patients who received antibiotics because of elevated circulating procalcitonin levels, would have recovered without antibiotic therapy.

CONCLUSION

Our results support that of patients admitted to ICU for ECOPD have a low likelihood of bacterial infection and correlates with a PCT less than 0.1 µg/L suggesting a possible inappropriate use of antibiotics. However, further studies are necessary to assess the short-term effect of a procalcitonin-
ROLE OF PROCALCITONIN IN DETERMINING ANTIBIOTIC THERAPY IN ACUTE EXACERBATION

based therapeutic strategy in critically ill COPD patients in ICU and secondly, to address the role of antimicrobial agents in COPD patients in the long-term, particularly in patients with low PCT levels and bacteria-positive sputum.

REFERENCES


ASSESSMENT OF DIETARY HABITS, PHYSICAL ACTIVITY PATTERNS AND BONE HEALTH OF FEMALES IN REPRODUCTIVE YEARS (18 – 40)

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Abstract

Strong bones are crucial to good health, and good nutrition is crucial to strong bones. This research was conducted to assess the dietary habits, physical activity patterns and bone health of females in their reproductive years (18 – 40). A cross-sectional survey was conducted to collect a sample of 138 females from the gynaec outpatient department (OPD) of two hospitals of Lahore i.e. Saira Memorial Hospital and Ch. Rehmat Ali Memorial Trust Hospital. A structured interview schedule was used to collect relevant data. Data obtained from the survey was then analyzed by conducting various statistical tests in SPSS software. A p-value less than 0.05 (p< 0.05) was considered statistically significant for all the tests. Results revealed that majority of the females had a normal BMD (T-score = ≥ -1), however their serum calcium (< 8mg/dl) and vitamin D3 (<30ng/ml) levels were low. Most of the females had a normal BMI. Majority were consuming almost 1200-1400kcal per day and had an insufficient intake of milk and dairy products. Most of the females used to consume 1-2 cups of tea / coffee daily. Most of the females had the habit of working out in the evening, though 1-3 days a week for less than an hour. Since females are more prone to osteoporosis, the same study must be conducted on a large and diverse scale in order to procure results of the whole population of reproductively aged females.

Decreased density or thinning of the bone leads to a condition called osteoporosis. Imbalances in bone resorption and bone formation result in decreased bone density. Women are at higher risk of osteoporosis than are men, primarily as a result of differences in bone mass and density. Commonly, osteoporosis develops as a consequence of aging. Secondary osteoporosis is used to define reduced bone mass that develops from reasons other than aging. Young women who have had their ovaries surgically removed have the same risk as do post-menopausal women. Various nutrients and dietary components affect bone health of an individual. These dietary factors range from inorganic minerals like calcium, magnesium, phosphorus, sodium, potassium & various trace elements and vitamins including A, D, E, K, C and certain B vitamins to macronutrients like protein and fats. Most women don’t consume adequate calcium in their early years of life to achieve peak bone mass. Women who drink soft drinks and more than a few cups of coffee with caffeine daily increase their risk to develop osteoporosis as a result of calcium loss. Main dietary items that interfere with calcium absorption include fibre, sodium, protein, iron, caffeine and oxalates.

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Physical activity is extremely important for bone health and has the potential to affect bone density at different time periods during a lifetime. Many longitudinal intervention studies have proved that bone density may be increased to about 1% to 3% in active young adults compared with controls. In later adult life, physical activity slows the rate of decline in bone mass as much as 1% per year. Because of the hormonal changes associated with menopause and their relation to bone health, post-menopausal women are a high-risk population with an accelerated risk of osteoporosis. Higher levels of physical activity are associated with lower rates of fracture particularly of the proximal femur.

The purpose of this research is to study the effect of diet and exercise on bone health of an individual. The aim of this study is to evaluate the bone health of females during their reproductive years, to assess the dietary habits of reproductively aged females, to inspect their physical activity patterns, and to find out the impact of dietary habits and physical activity patterns on bone health.

The significance of this study is the high prevalence of osteoporosis in Pakistan, a public-health concern. This study was an attempt to provide objective data on the status of bones in females during the reproductive years of their lives. The study aimed to assess whether their dietary practices were healthy, particularly with respect to their bones. It investigated the importance of a healthy and active lifestyle to prevent bone loss. Exploration of females’ level of awareness and their understanding of a balanced and bone healthy diet might help future researchers generate material to educate the ones who were less aware of the requirements during reproductive years to prevent early bone loss. Since females of modern age influence the course of change in society, dietary counseling of females with poor bone health would not only benefit them but would eventually benefit the entire society.

**Research questions included**

- Were the dietary habits of females healthy?
- What was the physical activity level of females?
- Was there any impact of the dietary habits and physical activity patterns of females on their bone health?

The present study aims to provide clear knowledge about bones and how one can acquire osteoporosis. Bone is a composite material whose extracellular matrix consists of mineral, collagen, water, non-collagenous proteins, and lipids in decreasing proportion depending upon age, species and site. Nutrients required for optimal bone health include adequate calcium during growing years to achieve optimal peak bone mass. Unfortunately, very few females meet calcium requirements during bone-forming years. Consequently, most girls start their adult years with less-than-optimal bone density. As adults, women rarely meet their recommended intakes of calcium (1000 – 1200mg) from food. Besides calcium, many other nutrients support bone health too. Adequate protein protects bone and reduces the likelihood of hip fractures. Lately, there has been a fair bit of speculation about a correlation between protein intake and bone density. Some studies seemed to show that increased protein intake leads to unwanted calcium loss through urine. However, the research shows that increased protein is positive for bone health as long as there is enough calcium in circulation and enough stored in the bone.

A research was conducted to examine cross-sectional and longitudinal associations between baseline dietary protein and bone mineral density among females between the ages of 14 to 40 years. Data from this longitudinal study suggested that a higher protein intake does not have an adverse effect on bone in premenopausal women. Cross-sectional analyses suggested that low vegetable protein intake is associated with lower bone mineral density.

Caffeine and caffeine-containing beverages such as coffee increase urinary calcium excretion although the effect of caffeine on bone health is unknown. Excessive caffeine intake may increase...
the risk of osteoporosis via increased calcium excretion. A lifetime ingestion of caffeine has been shown to decrease BMD in postmenopausal women. In a study conducted in postmenopausal women, BMD was decreased in the hip and lumbar spine as demonstrated by dual-energy X-ray absorptiometry. Women who ingested an equivalent of two cups of coffee daily throughout their adult lives were found to be at an increased risk for decreased BMD. On the other hand, results of another research carried out to study the long-term coffee consumption in relation to fracture risk and bone mineral density in women showed that high coffee consumption was associated with a small reduction in bone density that did not translate into an increased risk of fracture.

Another cross-sectional study was conducted to find out the prevalence of soda drinking, which is one of the dietary sources of caffeine, among adolescent girls and to discover its effects on health. Prevalence of soda drinking was 81.8%. Drinkers were associated with higher risk of increased calcium and phosphorus excretion in urine. Researchers concluded that soda drinking was associated with higher risk of obesity and decreasing level of blood calcium and increasing urinary calcium excretion, which may lead to osteoporosis later in life though it did not have any effect on renal function tests in the study group.

Vitamin D is needed to maintain calcium metabolism and optimal bone health. Research suggests that a combination of calcium and vitamin D supplements is the best option for the prevention or treatment of osteoporosis. Daily supplementation with a low dose of vitamin D may reduce bone loss and the risk of fractures, but a single high dose seems to increase the risk of falls and fractures. Vitamin D increases the absorption of calcium in the intestine by increasing the permeability of intestinal membrane, leading to higher levels of calcium in the blood, which signals the body to slow down breakdown. Without the presence of vitamin D, only about 10% of the calcium one eats gets absorbed.

Results of a research conducted to study 25(OH)D status and bone mineral density (BMD) in reproductive and post-menopausal aged women concluded that vitamin D deficiency coexisted with low BMD in the study group.

A research was carried out on female competitive distance runners with an objective to identify the nutrients, foods, and dietary patterns associated with stress fracture risk and changes in bone density among them. The researchers concluded that low-fat dairy products and the major nutrients in milk i.e. calcium, vitamin D, and protein were associated with greater bone gains and a lower stress fracture rate in young female runners whereas potassium intake was also associated with greater gains in hip and whole-body BMD.

Phosphorus combines with calcium to make hydroxyapatite (calcium phosphate), the principal player in bone density. So it is essential to bone health – 85% of a body’s phosphorus is stored in bones. When phosphorus levels are in balance that means in the ideal ratios for life, calcium and phosphorus naturally form calcium phosphate when it is needed and balanced levels of both minerals in the body leave calcium in the bone where it is needed. A phosphorus overload in the circulation, however, triggers the release of PTH which in turn triggers bone breakdown to release calcium. Meat, poultry, processed foods and carbonated sodas contain very high levels of phosphorus. Soda has 10-20 times more phosphorus than calcium, so drinking one serving of soda can trigger the body to breakdown bone.

Intake of foods with a ratio of calcium to phosphorus close to that found in dairy products led to positive effects on bone health.

A study was conducted for a cross-sectional examination of the influence of habitual phosphorus and calcium intake and the calcium / phosphorus intake ratio on the bone mineral density in young Japanese women aged 18 – 22 years whose calcium / phosphorus intake ratio was assumed to be lower than young Western women. The results indicated that phosphorus intake did not have a significantly
negative effect on bone mineral density, and calcium intake and calcium/phosphorus intake ratio had a small but significant association only in a site-specific manner with BMD.\textsuperscript{13}

Clearly, a well-balanced diet that depends on all the food groups to supply a full array of nutrients is central to bone health.\textsuperscript{14}

For bone health assessment the most frequently used clinical measure is bone mineral density assessed by dual-energy X-ray absorptiometry (DEXA). This technique measures only the mineral content of bone which is composed of organic matrix \textit{i.e.} collagen and multiple non-collagenous proteins. Since the level of bone mineral density is reasonably predictive of fracture rates, this simple noninvasive test provides the handiest tool to track bone health in the general population, with a minimal radiation dose.\textsuperscript{15}

During the prepubertal and adolescent growth years, bone mineral density / bone mass increases in healthy individuals. Once people cross the age of 40, though, small amounts of bone mass are lost each year. In women, this bone loss accelerates during a 3 – 5 year period after menopause. Women typically have lower bone mass than men and because of the accelerated decline following menopause, they tend to be more prone to osteoporosis.

Osteoporosis can be defined as a pathological condition associated with increased loss of bone mass caused by increased bone resorption.\textsuperscript{16} Imbalances in bone resorption and bone formation result in decreased bone density.\textsuperscript{17} Osteopenia is a less severe form of the disease in which bone mass has declined below normal levels but not to the extent seen in osteoporosis\textsuperscript{18}. It is a very common state in middle-aged women and in certain population of young women particularly those who resist their dietary energy intake for prolonged periods.\textsuperscript{19}

Osteoporosis has often been referred to as a ‘silent condition’ because it has no signs and symptoms until a fracture occurs. It is estimated that 200 million people worldwide are affected by osteoporosis. The most devastating clinical consequence of osteoporosis is fracture. It is estimated that up to 90% of all fractures can be attributed to osteoporosis. Current estimates indicate that about 30-50% of women and 15-30% men will suffer a fracture related to osteoporosis in their lifetime. The most common osteoporotic fracture sites are the hip, spine and distal forearm.\textsuperscript{20}

There are many modifiable and non-modifiable risk factors for osteoporosis which are given as follows. Non-modifiable risk factors include;\textit{Aging} in which several mechanisms associated with it lead to a negative calcium balance and predispose to osteoporosis, including reduced physical activity and impaired gastrointestinal absorption of calcium and vitamin D\textsuperscript{21}, \textit{Gender} as in all ethnic groups, women tend to have smaller skeletons than men and are therefore more likely to develop osteoporosis, \textit{Ethnicity} as Caucasians tend to have the lowest bone mass, and hip fractures are far more common among whites than nonwhites. Age-adjusted hip fracture incidence rates are higher among Scandinavian residents than other comparable populations. Afro-Americans tend to have the highest bone density and lose bone less rapidly as they age\textsuperscript{22}, a \textit{positive family history} of osteoporosis increases the risk of fracture. Several factors predisposing to osteoporosis are not inherited but are acquired and influenced by the patient’s family such as lifestyle choices, a \textit{low body weight} is an independent predictor of low bone mass and osteoporosis. Women who weigh less than they did when they were 25 years old are more at risk of sustaining fractures\textsuperscript{23}, \textit{Menarche & menopause} has wide range of effects on the skeleton. Estrogen exerts a protective effect. It stimulates bone formation and reduces bone resorption. Patients who have periods of amenorrhea or irregular menstrual cycles are more at risk of low bone mass, \textit{Previous history of fractures} has a positive effect even if the cause is unknown, the risk of sustaining another fracture is doubled when one has already occurred. Possibly individuals with one fracture tend to fall and develop subsequent fractures at a greater rate than indivi-
duals with no history of fractures, **Loss of height** greater than 1.5cm is suggestive of vertebral compression fractures. In the absence of significant trauma, these represent fragility fractures, are diagnostic of osteoporosis, and increase the subsequent risk of fractures. Pregnancy & lactation can lead to osteoporosis. A woman nursing a baby secretes about 500mg calcium daily into the milk. After nursing five babies, she will have secreted some 300g of calcium – about a third of the amount of bound calcium incorporated into skeleton. To some extent the high levels of sex hormones during pregnancy stimulate a greater absorption of calcium from the gastrointestinal tract and a greater uptake by the bones. However, there are additional risks for osteoporosis when several weeks’ bed rest is required and also if muscle relaxants and sedation are administered. In some cases, corticosteroids are also given. In these circumstances, a massive excretion of calcium and loss of bone is the inevitable result, then there are number of diseases & medications which lead to bone fragility and fracture risk e.g. loop diuretics lead to increased renal calcium excretion and thyroid supplements cause increased bone turnover etc. malabsorption syndromes cause negative calcium balance and several nutritional deficiencies etc.

Research shows that genetic factors determine 46% to 62% of bone mineral density, 38% to 54% is determined by lifestyle and environmental factors. Hence, **modifiable risk factors** include; **improper diet** as nutrition is an important factor in the maintenance of bone health. We frequently under-consume most of the key bone building nutrients. Especially when insufficient calcium is absorbed from food, it is mobilized from the bones by parathyroid hormones, causing a negative bone balance i.e., more resorption than formation. **Sedentary lifestyle** which includes insufficient physical movement is an important risk factor for osteoporosis. This applies also to younger, bedridden patients who may lose up to 30% of their bone mass in a few months but may require years to regain their original bone density, **Cigarette smoking** doubles the risk of osteoporosis. Women who smoke one pack a day during adulthood have 5-10% less BMD at the age of menopause than do nonsmokers.

Fortunately, osteoporosis can be prevented ideally by the establishment of an optimal peak bone mass, postponement of the onset of bone loss and reduction of the subsequent rate of bone loss. The extent to which peak bone mass can be modified is uncertain, and whilst the effects of race, sex and other hereditary factors on bone mass cannot be altered, exercise, dietary calcium intake and hormonal factors may potentially modify the deposition of bone during growth and consolidation.

Osteoporosis can be treated by prevention strategies and treatment strategies for those who documented osteopenia or osteoporosis. For all osteoporotic patients, a comprehensive program is needed that includes patient education, appropriate exercise and appropriate nutrition coupled with psychosocial support.

The amount of calcium intake is generally recommended to be 1000mg for premenopausal women and 1500mg for postmenopausal women. For the elderly or homebound patient, it is recommended to consider the need for vitamin D supplementation. The recommended daily allowance is between 400 and 800IU. Medical options for postmenopausal women include drug options like hormone replacement therapy, biphosphonates, selective estrogen receptor modulators and calcitomin.

Exercise increases bone mass which is mild to modest in the order of 1% to 3%. However it must be kept in mind that simply preventing further bone loss is a major goal of an exercise prescription. The general rule of thumb for causing bone mass response is that the exercise must provide mechanical loading either through pull of muscle on bone or with weight bearing. Literature shows that walking does not seem to provide enough stimulation for increased bone mass; it must be combined with resistance exercise. Non-weight bearing exer-
cises including swimming and cycling are relatively ineffective approaches. Resistance exercise must exceed that provided by daily activities. The effects of exercise are site specific e.g. running does not provide stimulation for bone in the upper extremities. Impact activities that apply relatively large loads on bone quickly are the most osteogenic and are the most risky; therefore, a progression of exercise up to the level of these types of activities is the final goal.

**Menstrual cycle** has important effects on the acquisition of peak bone mass. Peak bone mass is generally reached at approximately age 25 to 30. Adults who do not achieve their predicted peak bone mass are at risk of developing osteoporosis at an earlier age. When the rate of bone resorption exceeds that of new bone formation, the overall increased rate of bone turnover leads to a net loss of bone mass.\(^{27}\)

A regular well-functioning monthly cycle is of paramount importance in bone deposition during the adolescent growth spurt and then in prevention of bone loss after peak bone mass is achieved in the second decade of life. The main hormone involved in bone regulation is estrogen. If menarche is delayed or if menstrual dysfunction occurs or menses disappears entirely, then the protective mechanism of estrogen on bone is lost. If this menstrual disturbance is not corrected fairly promptly, it will eventually result in osteopenia or frank osteoporosis, ultimately increasing one’s susceptibility to fractures. In fact, osteoporotic prevention starts as early as the initial onset of menarche during adolescence.\(^{28}\)

**Physical activity** is defined as any bodily movement produced by skeletal muscles that results in energy expenditure. Regular physical activity is essential for bone health. It has been shown that weight-bearing activities such as jumping, dancing and aerobics, gymnastics, volleyball and football etc are particularly good for increasing bone mineral density. In general, the amount of physical activity that is needed for any kind of benefit appears to be achieved after only a few repetitions of an activity done on regular basis.\(^{29}\) Physical activity is an important modifiable risk factor for both bone mineral density and body mass index (BMI). However, BMI is itself strongly predictive of bone mineral density. A study was conducted to determine the association between physical activity and bone mineral density, with consideration of BMI as a potential mediating factor. Physical activity was inversely associated with BMI at baseline, and an increase in physical activity between baseline and Year 5 was associated with a decrease in BMI in both men and women. BMI was strongly associated with bone mineral density, both cross-sectionally and longitudinally. Results of the study proved that increased physical activity was associated with an increase in bone mineral density and a concomitant decrease in BMI.\(^{30}\)

Recommended levels of physical activity for both male and female adults aged 18 – 64 years suggest that they should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week or do at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity. Aerobic activity should be performed in bouts of at least 10 minutes duration. For additional health benefits, adults should increase their moderate-intensity aerobic physical activity to 300 minutes per week or engage in 150 minutes of vigorous-intensity aerobic physical activity per week or an equivalent combination of moderate- and vigorous-intensity activity. Muscle-strengthening activities should be done involving major muscle groups on 2 or more days a week.

**RESEARCH METHODOLOGY**

A cross-sectional survey was conducted to carry out this research. The main purpose of conducting this study was to assess the dietary habits, physical activity patterns and bone health of reproductive aged females. It also aimed to know their understanding of a balanced diet and its impact on bone health.
1. **Population**

The population of the study consisted of reproductive aged females (18 – 40 years) coming to the outpatient department (OPD) of both the hospitals.

2. **Sample**

The sample of the study consisted of 138 reproductive aged females (18 – 40 years) coming to the gynae outpatient department (OPD) of two hospitals of Lahore i.e. Saira Memorial Hospital and Ch. Rehmat Ali Memorial Trust Hospital. The sample size was calculated by using G-Power.

3. **Sample Collection**

The sample was collected from the gynae outpatient department (OPD) of the selected hospitals from 1st February, 2017 to 15th March, 2017. Prior to data collection, permission was taken from both hospitals. Convenience sampling technique was used to reach the targeted sample size of 138 reproductive aged females who visited the outpatient department (OPD) of the selected hospitals during data collection period and agreed to participate in the study.

4. **Tool of Data Collection**

A structured interview schedule was used to collect relevant data. For that purpose, a questionnaire was formulated for the interviewer which covered the following areas:

- Demographic information
- BMI, BMD & certain blood parameters of the respondents for which fresh samples were collected and test were performed in the same laboratory.
- Dietary habits of the respondents
- Physical activity patterns of the respondents

5. **Pilot Study**

A pilot study was conducted before actual data collection for the study. The sample for pilot study included 15 reproductive aged females (18 – 40 years) coming to the gynae outpatient department (OPD) of the selected hospitals. The data collected for pilot study was quickly analyzed to judge if the tool and methods selected for data collection were suitable enough to provide desired data from the actual sample of 138 respondents.

6. **Method of Data Collection**

- Height and weight of the respondents were noted to calculate their BMI with the help of height-measuring scale and weighing machine and then BMI was calculated by using the following formula:
  \[
  \text{BMI} = \frac{\text{Weight in KG}}{(\text{Height in meter})^2}
  \]
- Bone mineral density of the respondents was assessed by using a bone mineral densitometer.
- Biochemical tests that were done included serum calcium and vitamin D3 levels.
- Dietary assessment was done by taking dietary history of the respondents, 24 hour dietary recall and food frequency checklist. The respondents were asked a few questions regarding their dietary routine and daily food intake. The researcher then asked the respondents to recall all the foods and beverages that were consumed in the last 24 hours, including their quantities. To identify daily, weekly and monthly consumption of certain foods, the respondents were asked to report the usual frequency of each food item mentioned in the food frequency checklist.

7. **Data Analysis**

Data analysis was done by using SPSS software.

8. **Data Presentation**

The data was presented in MS Word 2007. Tables and figures were formed for the presentation of data.

Data Analysis and Interpretation

Data obtained from the survey was analyzed by using SPSS software and Microsoft Office Excel 2007. All the data obtained was entered into the grid sheets of SPSS. While analyzing the data, objectives of the study and research questions were kept in mind. Categories were made for those variables which had multiple values. Codes were given to each category. Descriptive statistics (mainly frequency, percentage, mean & standard deviation) and
### Table 1: Demographic Information of Females

<table>
<thead>
<tr>
<th>Variables</th>
<th>Levels</th>
<th>Frequency</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
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<td></td>
<td></td>
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<tr>
<td>18-23</td>
<td>73</td>
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<td>24-29</td>
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<td>25</td>
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<td>30-35</td>
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<td>36-40</td>
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### Table 2: Impact of BMI on Bone Health of Females

<table>
<thead>
<tr>
<th>BMI</th>
<th>Serum Calcium Level</th>
<th>Vitamin D3 Level</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Underweight</td>
<td>7.57</td>
<td>0.53</td>
<td>23.10</td>
</tr>
<tr>
<td>Normal</td>
<td>7.66</td>
<td>0.68</td>
<td>24.85</td>
</tr>
<tr>
<td>Overweight</td>
<td>7.60</td>
<td>0.70</td>
<td>21.59</td>
</tr>
<tr>
<td>Obese</td>
<td>7.48</td>
<td>0.79</td>
<td>21.24</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F</td>
<td>0.426</td>
<td>1.05</td>
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<tr>
<td>p</td>
<td>0.735</td>
<td>0.373</td>
<td>0.663</td>
</tr>
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</table>

### Table 3: Dietary Supplements Intake, Meal Skipping & Dining Out Practices of Females

<table>
<thead>
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<th>Variables</th>
<th>Levels</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake of Dietary Supplement</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
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<td>24</td>
<td></td>
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<tr>
<td>No</td>
<td>93</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Don’t remember</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Type of Supplement</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Calcium &amp; Vitamin D</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>6</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Folic Acid</td>
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<td>6</td>
<td></td>
</tr>
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<td>Hikmat (Kushta)</td>
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<td>3</td>
<td></td>
</tr>
<tr>
<td>Powdered Supplements (e.g. Ensure)</td>
<td>7</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Multivitamins</td>
<td>9</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Meal Skipping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skip occasionally</td>
<td>65</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Skip regularly</td>
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<td>12</td>
<td></td>
</tr>
<tr>
<td>Never skip</td>
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<td>41</td>
<td></td>
</tr>
<tr>
<td>Dining Out</td>
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</tr>
<tr>
<td>On daily basis</td>
<td>10</td>
<td>7</td>
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<tr>
<td>On weekly basis</td>
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<td>35</td>
<td></td>
</tr>
<tr>
<td>On fortnightly basis</td>
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<tr>
<td>On monthly basis</td>
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<td>44</td>
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### Table 4: Impact of Daily Caloric Intake, Dietary Supplements Intake, Meal Skipping & Dining Out Practices of Females on Their Bones

<table>
<thead>
<tr>
<th>Variables</th>
<th>Levels</th>
<th>Serum Calcium Level</th>
<th>Vitamin D3 Level</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Daily Caloric Intake</td>
<td>&lt; 1200kcal</td>
<td>7.39</td>
<td>0.88</td>
<td>19.00</td>
</tr>
<tr>
<td></td>
<td>1200-1400kcal</td>
<td>7.55</td>
<td>0.70</td>
<td>22.31</td>
</tr>
<tr>
<td></td>
<td>&gt;1400kcal</td>
<td>7.79</td>
<td>0.57</td>
<td>26.13</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F</td>
<td>2.46</td>
<td>2.918</td>
<td>1.580</td>
</tr>
<tr>
<td>p</td>
<td>0.089</td>
<td>0.057</td>
<td>0.210</td>
<td></td>
</tr>
<tr>
<td>Intake of Dietary Supplements</td>
<td>Yes</td>
<td>7.65</td>
<td>0.72</td>
<td>24.97</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7.58</td>
<td>0.69</td>
<td>21.99</td>
</tr>
<tr>
<td></td>
<td>Don’t Remember</td>
<td>7.51</td>
<td>0.58</td>
<td>19.91</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F</td>
<td>0.22</td>
<td>1.80</td>
<td>1.870</td>
</tr>
<tr>
<td>p</td>
<td>0.80</td>
<td>0.17</td>
<td>0.158</td>
<td></td>
</tr>
<tr>
<td>Meal Skipping</td>
<td>Skip occasionally</td>
<td>7.7</td>
<td>0.7</td>
<td>24.4</td>
</tr>
<tr>
<td></td>
<td>Skip regularly</td>
<td>7.4</td>
<td>0.8</td>
<td>20.4</td>
</tr>
<tr>
<td></td>
<td>Never skip</td>
<td>7.6</td>
<td>0.7</td>
<td>22.3</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F</td>
<td>0.973</td>
<td>1.141</td>
<td>0.284</td>
</tr>
<tr>
<td>p</td>
<td>0.381</td>
<td>0.323</td>
<td>0.753</td>
<td></td>
</tr>
<tr>
<td>Dining Out</td>
<td>On daily basis</td>
<td>7.39</td>
<td>1.02</td>
<td>18.90</td>
</tr>
<tr>
<td></td>
<td>On weekly basis</td>
<td>7.67</td>
<td>0.70</td>
<td>24.44</td>
</tr>
<tr>
<td></td>
<td>On fortnightly basis</td>
<td>7.85</td>
<td>0.57</td>
<td>23.63</td>
</tr>
<tr>
<td></td>
<td>On monthly basis</td>
<td>7.50</td>
<td>0.64</td>
<td>22.41</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F</td>
<td>1.7392</td>
<td>0.8437</td>
<td>0.559</td>
</tr>
<tr>
<td>p</td>
<td>0.1620</td>
<td>0.4722</td>
<td>0.643</td>
<td></td>
</tr>
</tbody>
</table>
Table 5: Impact of Daily Intake of Milk, Fizzy Drinks & Tea / Coffee and Related Practices of Females on Their Bones

<table>
<thead>
<tr>
<th>Variables</th>
<th>Levels</th>
<th>Serum Calcium Level</th>
<th>Vitamin D3 Level</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Milk Intake (Per day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No intake</td>
<td>7.31</td>
<td>0.63</td>
<td>19.41</td>
<td>9.43</td>
</tr>
<tr>
<td>1 cup</td>
<td>7.96</td>
<td>0.53</td>
<td>25.54</td>
<td>5.85</td>
</tr>
<tr>
<td>1-2 cups</td>
<td>8.11</td>
<td>0.60</td>
<td>33.60</td>
<td>15.74</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F</td>
<td>16.803</td>
<td>15.024</td>
<td>1.108</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.348</td>
</tr>
<tr>
<td>Fizzy Drinks Intake</td>
<td>Yes</td>
<td>7.52</td>
<td>0.71</td>
<td>21.89</td>
</tr>
<tr>
<td>No</td>
<td>7.76</td>
<td>0.64</td>
<td>25.30</td>
<td>10.73</td>
</tr>
<tr>
<td>Independent samples t-test</td>
<td>T</td>
<td>-1.905</td>
<td>0.059</td>
<td>-1.16</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.059</td>
<td>0.80</td>
<td>0.250</td>
</tr>
<tr>
<td>Mixing of Fizzy Drinks with Milk or Milk Products</td>
<td>Yes</td>
<td>7.7</td>
<td>0.5</td>
<td>24.9</td>
</tr>
<tr>
<td>No</td>
<td>7.6</td>
<td>0.8</td>
<td>22.2</td>
<td>7.8</td>
</tr>
<tr>
<td>Don’t take milk and/or fizzy drinks</td>
<td>7.5</td>
<td>0.6</td>
<td>23.7</td>
<td>13.5</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F</td>
<td>0.385</td>
<td>0.718</td>
<td>1.339</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.681</td>
<td>0.490</td>
<td>0.266</td>
</tr>
<tr>
<td>Amount of Tea Coffee Intake (Per Day)</td>
<td>No intake</td>
<td>7.75</td>
<td>0.71</td>
<td>25.60</td>
</tr>
<tr>
<td>1-2 cup</td>
<td>7.53</td>
<td>0.65</td>
<td>21.62</td>
<td>9.68</td>
</tr>
<tr>
<td>&gt;3 cup</td>
<td>7.60</td>
<td>0.76</td>
<td>23.47</td>
<td>14.13</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F</td>
<td>0.73</td>
<td>1.81</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.53</td>
<td>0.15</td>
<td>0.90</td>
</tr>
<tr>
<td>Timing of Tea / Coffee Intake Following a Meal</td>
<td>Immediately after meal</td>
<td>7.75</td>
<td>0.71</td>
<td>25.60</td>
</tr>
<tr>
<td>Within an hour</td>
<td>7.53</td>
<td>0.65</td>
<td>21.62</td>
<td>9.68</td>
</tr>
<tr>
<td>More than an hour</td>
<td>7.60</td>
<td>0.76</td>
<td>23.47</td>
<td>14.13</td>
</tr>
<tr>
<td>Don’t take tea or coffee</td>
<td>7.75</td>
<td>0.71</td>
<td>25.60</td>
<td>9.46</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F</td>
<td>0.734</td>
<td>1.810</td>
<td>0.199</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.533</td>
<td>0.148</td>
<td>0.897</td>
</tr>
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</table>

Table 6: Impact of Food Frequency on Bone Health of Females: Vegetable Group

<table>
<thead>
<tr>
<th>Vegetable Group</th>
<th>Levels</th>
<th>Serum Calcium Level</th>
<th>Vitamin D3 Level</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Starchy Vegetable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>7.50</td>
<td>0.75</td>
<td>21.95</td>
<td>8.60</td>
</tr>
<tr>
<td>Weekly</td>
<td>7.70</td>
<td>0.68</td>
<td>24.65</td>
<td>13.25</td>
</tr>
<tr>
<td>Monthly</td>
<td>7.55</td>
<td>0.40</td>
<td>19.64</td>
<td>4.41</td>
</tr>
<tr>
<td>Never</td>
<td>8.00</td>
<td>0.28</td>
<td>24.00</td>
<td>2.83</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F</td>
<td>1.125</td>
<td>1.048</td>
<td>0.694</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.341</td>
<td>0.373</td>
<td>0.557</td>
</tr>
<tr>
<td>Other Vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>7.61</td>
<td>0.68</td>
<td>22.23</td>
<td>7.33</td>
</tr>
<tr>
<td>Weekly</td>
<td>7.60</td>
<td>0.71</td>
<td>23.66</td>
<td>12.61</td>
</tr>
<tr>
<td>Monthly</td>
<td>7.60</td>
<td>0.71</td>
<td>19.00</td>
<td>8.49</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F</td>
<td>0.069</td>
<td>0.304</td>
<td>2.300</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.976</td>
<td>0.822</td>
<td>0.080</td>
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</table>
## Table 7: Impact of Physical Activity Patterns of Females on Their Bone Health

<table>
<thead>
<tr>
<th>Physical Activity Patterns</th>
<th>Serum Calcium Level</th>
<th>Vitamin D3 Level</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td><strong>Workout</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7.71</td>
<td>0.65</td>
<td>23.64</td>
</tr>
<tr>
<td>No</td>
<td>7.48</td>
<td>0.73</td>
<td>22.33</td>
</tr>
<tr>
<td>Independent samples t-test</td>
<td>T 1.987</td>
<td>0.708</td>
<td>-0.316</td>
</tr>
<tr>
<td></td>
<td>P 0.049</td>
<td>0.480</td>
<td>0.752</td>
</tr>
<tr>
<td><strong>Form of Workout</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking</td>
<td>7.74</td>
<td>0.65</td>
<td>23.87</td>
</tr>
<tr>
<td>Running</td>
<td>7.84</td>
<td>0.63</td>
<td>28.00</td>
</tr>
<tr>
<td>Jogging</td>
<td>8.17</td>
<td>1.04</td>
<td>30.67</td>
</tr>
<tr>
<td>Aerobics</td>
<td>7.66</td>
<td>0.53</td>
<td>21.18</td>
</tr>
<tr>
<td>Any Other</td>
<td>7.35</td>
<td>0.65</td>
<td>20.25</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F 1.082</td>
<td>1.713</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>P 0.372</td>
<td>0.157</td>
<td>0.83</td>
</tr>
<tr>
<td><strong>Number of Workout Days</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>7.80</td>
<td>0.65</td>
<td>25.09</td>
</tr>
<tr>
<td>4-6</td>
<td>7.56</td>
<td>0.68</td>
<td>22.07</td>
</tr>
<tr>
<td>7</td>
<td>7.79</td>
<td>0.56</td>
<td>23.21</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F 1.189</td>
<td>1.132</td>
<td>1.38</td>
</tr>
<tr>
<td></td>
<td>P 0.311</td>
<td>0.157</td>
<td>0.26</td>
</tr>
<tr>
<td><strong>Average Length of Workout Time</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1hour</td>
<td>7.83</td>
<td>0.62</td>
<td>25.26</td>
</tr>
<tr>
<td>1 hour</td>
<td>7.86</td>
<td>0.58</td>
<td>24.12</td>
</tr>
<tr>
<td>&gt; 1 hour</td>
<td>7.33</td>
<td>0.64</td>
<td>19.95</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F 4.807</td>
<td>3.136</td>
<td>0.035</td>
</tr>
<tr>
<td></td>
<td>P 0.011</td>
<td>0.050</td>
<td>0.966</td>
</tr>
<tr>
<td><strong>Preferred Workout Time</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>7.64</td>
<td>0.55</td>
<td>22.08</td>
</tr>
<tr>
<td>Afternoon</td>
<td>7.44</td>
<td>0.39</td>
<td>20.71</td>
</tr>
<tr>
<td>Evening</td>
<td>7.76</td>
<td>0.69</td>
<td>24.35</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F 0.801</td>
<td>0.948</td>
<td>0.674</td>
</tr>
<tr>
<td></td>
<td>P 0.453</td>
<td>0.392</td>
<td>0.571</td>
</tr>
<tr>
<td><strong>Preferred Workout Place</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indoor</td>
<td>7.56</td>
<td>0.54</td>
<td>21.46</td>
</tr>
<tr>
<td>Outdoor</td>
<td>7.88</td>
<td>0.72</td>
<td>26.06</td>
</tr>
<tr>
<td>Independent samples t-test</td>
<td>T -2.184</td>
<td>-2.62</td>
<td>1.328</td>
</tr>
<tr>
<td></td>
<td>P 0.032</td>
<td>0.011</td>
<td>0.188</td>
</tr>
<tr>
<td><strong>Post-Workout Feeling</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tired</td>
<td>7.63</td>
<td>0.66</td>
<td>21.37</td>
</tr>
<tr>
<td>Fresh</td>
<td>7.70</td>
<td>0.65</td>
<td>24.57</td>
</tr>
<tr>
<td>On the go</td>
<td>7.84</td>
<td>0.66</td>
<td>23.92</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F 0.392</td>
<td>1.109</td>
<td>0.465</td>
</tr>
<tr>
<td></td>
<td>P 0.677</td>
<td>0.335</td>
<td>0.630</td>
</tr>
<tr>
<td><strong>Preferred Drink in Post Workout State</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td>8.10</td>
<td>0.36</td>
<td>25.50</td>
</tr>
<tr>
<td>Tea / Coffee</td>
<td>7.72</td>
<td>0.36</td>
<td>22.64</td>
</tr>
<tr>
<td>Fruit Juices</td>
<td>7.69</td>
<td>0.64</td>
<td>22.75</td>
</tr>
<tr>
<td>Plain Water</td>
<td>7.67</td>
<td>0.74</td>
<td>23.85</td>
</tr>
<tr>
<td>Any Other</td>
<td>7.73</td>
<td>0.60</td>
<td>26.67</td>
</tr>
<tr>
<td>One-way ANOVA</td>
<td>F 0.390</td>
<td>0.262</td>
<td>1.134</td>
</tr>
<tr>
<td></td>
<td>P 0.815</td>
<td>0.902</td>
<td>0.348</td>
</tr>
</tbody>
</table>
inferential statistics (mainly chi-square test for independence, one-way ANOVA & independent samples t-test) were used to analyze the data. A p-value lesser than 0.05 (p<0.05) was considered significant for all the tests. Results obtained from data analysis were presented in Microsoft Office Word 2007 in the form of tables and figures. The survey bore significant findings.

Graph 1: BMD and Biochemical Tests of Females

Graph 2: Body Mass Index (BMI) of Females

Graph 3: Daily Caloric Intake of Females Calculated on the Basis of Their 24-Hour Recall

RESULTS

Study shows that out of a total of 138 females, majority 73 (53%) of the females belonged to the age range of 18-23 years, 35 (25%) females belonged to the age range of 24-29 years, 17 (12%) participants fell into the age range of 30-35 years whereas 13 (9%) participants were from the age range of 36-40 years as given in table 1.

Graph 1 shows that BMD of 68% females was ≥ -1, 23% females had BMD level within the range -1 to -2.5 whereas 9% females had BMD ≤ -2.5. Serum calcium level of 51% females was within the range of 7 – 8mg/dl, 30% females had serum calcium level within the range of 8 – 9mg/dl whereas 19% females had their serum calcium level within the range of 6 – 7mg/dl. Vitamin D3 level of 50% females was ≤ 20ng/ml, 33% females had vitamin D3 level within the range of 20 – 29ng/ml whereas 17% females had vitamin D3 level ≥ 30ng/ml.

43% females had a normal body weight, 32% females were overweight, 18% females fell into the category of obesity whereas only 7% (10) females were underweight, according to their BMI as given in graph 2.

A one-way ANOVA was conducted to explore the difference in the impact of BMI on bone health parameter values. There was no statistically significant difference in the impact of BMI on serum calcium, vitamin D3 and BMD.

Graph 3 shows that 60.7% females were taking approximately 1200 – 1400kcal per day, 28.7% females were taking more than 1400kcal per day whereas 10.6% females were taking less than 1200kcal per day.

Table 3 shows that 93 (68%) females had not taken any dietary supplement whereas 22 (24%) females had not taken a dietary supplement in the last six months. Out of a total of 33 females who has taken a dietary supplement in the last six months, 9(28%) females had taken a multivitamin, 7(21%) females had taken powdered supplements such as Ensure and 6 (18%) females had taken a calcium supplement. Majority of the females (47%) used to skip their meals occasionally. Sixty one (44%) females used to dine out on monthly basis.

There was no statistically significant (p> 0.05) difference in the impact of daily caloric intake, dietary supplements intake, meal skipping and dining out practices on serum calcium level, vitamin
Table 5 shows that there was no statistically significant (p = 0.05) difference in the impact of fizzy drinks intake, mixing of fizzy drinks with milk or milk products, amount of tea / coffee intake per day and timing of tea / coffee intake following a meal on any of the bone health parameter values including serum calcium level, vitamin D3 level and BMD. However, there was a statistically significant difference in the impact of milk intake per day on serum calcium and vitamin D3 level. Females who were not consuming milk daily had lower vitamin D3 level. Females who were consuming 1 – 2 cups of milk per day had a better vitamin D3 level value than vitamin D3 level of females who were consuming up to 1 cup of milk per day. However, there was no statistically significant difference in the impact of milk intake per day on BMD.

Then there was no statistically significant (p> 0.05) difference in the impact of vegetables intake (both starchy and other vegetables) on any of the bone health parameter values including serum calcium level, vitamin D3 level and BMD for reference see table 6.

Result of independent samples t-test indicated a statistically significant difference in serum calcium level of the females who used to workout had a higher serum calcium level than females who were not working-out. There was no statistically significant (p> 0.05) difference in the impact of different forms of workout, number of workout days, preferred workout time, post-workout feeling and preferred drink in post workout state on serum calcium level, vitamin D3 level and BMD. However, there was a statistically significant difference in the impact of average length of workout time on serum calcium level. Females who were working out for less than an hour had better vitamin D3 level than vitamin D3 level of those females who were working out for more than an hour. However, there was no statistically significant difference in the impact of average length of workout time on BMD. Results of an independent samples t-test showed that there was a significant difference in serum calcium and vitamin D3 levels of the females who preferred indoor workout and females who preferred outdoor workout. Females who preferred outdoor workout had higher serum calcium and vitamin D3 levels than females who preferred indoor workout. However, there was no statistically significant difference on BMD of females who preferred indoor workout and females who preferred outdoor workout.

DISCUSSION

Osteoporosis is a well-known and studied term. It leads to thinning of bones which makes them prone to fractures. Women are at higher risk as estrogen is major factor in contributing bone health which increases or decreases during different time period of a women’s life. Calcium is the main mineral keeping bones healthy. Vitamin D is the next important factor as it is directly linked to calcium for its absorption. Multiple factors play a vital role in maintaining bone health. Some have direct while others have indirect relation. Calcium, vitamins, phosphorus, daily milk intake and physical activity at recommended levels have beneficial effects on bone health. Demographics of the study include modifiable risk factors i.e. improper diet, sedentary lifestyle and cigarette smoking. These factors can be modified so that osteoporosis can be prevented. Some of them are studied in detail here. Aim here is to make people aware so that they can make amendments where they can. Non-modifiable risk factors which aren’t possible to change include aging, gender, ethnicity, positive family history, menarche and menopause, previous history of fractures, pregnancy and lactation, chronic diseases and medication. They have strong impact on bone health and are
briefly given in the study. Risk factors of the disease are age around 30, women over the age of 50, positive family history, bone structure and body weight, broken bones previously, ethnicity, certain diseases and some medications.

The key finding of this study is female of reproductive years which were taken as a subject, are deficient in calcium and vitamin D3. There are multiple parameters which were used for the present study which included serum calcium, vitamin D levels and DEXA scan.

According to WHO criteria for diagnosis of osteoporosis, majority of the females were not diagnosed as osteoporotic neither osteopenic. However, blood tests revealed women to be having calcium and vitamin D below normal levels.

BMI is one of the important factors when it comes to the assessment of health. As, Body mass index (BMI) is a measure of body fat based on height and weight that applies to adult men and women and it has indirect relations to serum calcium and vitamin D3 levels. However, in this study, our results are not likely to be biased for the following reasons:

1) A previous study shows higher BMI leads to low vitamin D3 (Vimaleswaran et al. (2013)) which is in contradiction with the results of the present study.

2) Results of another study conducted by Langsetmo et al. (2012) regarding the impact of BMI on BMD also oppose the findings of the present study.

Our results are clearly in contradiction with the effects of BMI on bone health parameters; calcium, vitamin D, BMD.

Food is an important factor contributing to various outcomes depending upon how it is consumed and how much is it taken. Daily caloric requirement when isn’t met by a person, deficiencies occur. Deficiencies can be reduced by supplements prescribed by the doctors. Women having sufficient awareness regarding the importance of dietary supplements have positive effects on health. As a study conducted to determine the prevalence of vitamin and mineral supplement use in the US population, more than 11,000 respondents out of 33,905 reported taking atleast 1 vitamin or mineral supplement at any time in the past month. There is a general rule that overall health is also affected by meal skipping practices, could be any reason, i.e. low socioeconomic status where daily needs are not met, not aware of the importance of taking regular meals or society of female conscious about their weight in socially active or self conscious females etc. Multiple factors could contribute to the meal skipping practices. Our study has shown meal skipping has no direct role on serum calcium, vitamin D levels and BMD. According to a systematic literature search, meal skipping (any meal) was reported in 12 studies with prevalence ranging between 5 and 83%.

One of the world wide important factors in contributing to lower calcium and vitamin D is consumption of caffeine most importantly in the form of tea/coffee. Tea has some positive as well as negative effects but here we are concerned only with the relation to bone health. Tea has caffeine in it and many recent researches from the New England Journal of Medicine claim that too much tea could cause brittle bones and teeth. Frary, Johnsoon, & Wang (2005) concluded in their research that 87% of the sample consumed food and beverages containing caffeine.

Milk is the most important factor when it comes to providing adequate calcium to body. Trend is changing over the years in consuming lower daily milk intake. Instead milk if used in the tea/coffee is mostly a tea whitener which has no significant effect in providing calcium. Daily intake of milk has a pronounced increase effect on serum calcium and vitamin D levels. Fizzy drinks, sodas and carbonated drinks are again a common practice. By studying our results, there was no impact of fizzy drinks intake, mixing of fizzy drinks with milk or milk products, amount of tea / coffee intake per day and timing of tea / coffee intake following a meal on any of the bone health parameter values. But pronounced effects of milk intake per day on serum calcium and
vitamin D3 level are seen in our results and females who were not consuming milk daily had lower vita-
moin D3 and calcium levels.

Vegetables are important source for providing adequate minerals for body if consumed regularly. Overall consumption of vegetables is quite less and awareness isn’t common as well. It is not just common in Pakistan as study conducted in the United States in 2009 which showed that only a few American adolescents or adults were consuming the recommended amounts vegetables. As we are studying direct impact of factors contributing bone health, vegetables where possibly have positive effects on overall body health, it has shown no direct effect on bone health.

One of the major topics worldwide is how important is physical activity? Second question that arises is which type of exercise has positive effects on human body. Multiple researches in the past have show physical activity is directly proportional to the bone health unless vigorous besides which adequate intake of minerals is necessary otherwise there will be a negative effect.

In Pakistan, mostly females have a habit of going out for just a walk or working home chores in the sun which they consider working out, which actually isn’t a workout and here it shows a severe lack of awareness. A Brazilian study showed only 13% of the Brazilians performing a minimum of 30 minutes of their leisure time in physical activity in a week. For good bone health, the recommended levels of physical activity for both male and female adults aged 18 – 64 years suggest that they should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week or do at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combi-
nation of moderate- and vigorous-intensity activity. By collecting data of 138 different females, we came to know that walking is mostly preferred by females of Pakistan, second most common physical activity is aerobics. Result of the previously discussed study conducted in Brazil showed that walking / jogging was the preferred form of workout by Brazilian females. Talking to females it was assessed that they feel fresh after workout even mostly preferred indoor workout. There are some benefits of post workout drinks as well. Keeping that in mind females were asked their choices for the post workout drink majority were consuming plain water but few have the habit of drinking any fruit juice. Studies have shown that during exercise lasting approximately 1 hour in duration or small amounts of carbohydrate can result in a performance benefit.

Meticulously looking into the picture, working out has a beneficial effect on serum calcium levels as shown by previous studies. Results of a study showed that serum ionized calcium was significantly elevated by exercise at 50% of maximum aerobic capacity. Results of our study showed workout has a major role in increasing serum calcium levels but it has no significant role in BMD levels in contrast with the research study at Harvard School of Public Health (2017) showed that people who exercised vigorously had higher levels of vitamin D. Different forms of workout, number of workout days, preferred workout time, post-workout feeling and preferred drink in post workout state isn’t having any significant effect on serum calcium level, vitamin D3 level and BMD. However, average length of workout time and preferred workout place is directly proportional to the levels of serum calcium and vitamin D3 levels of females. Outdoor workout has somehow positive effect on vitaminD3 levels which might be due to an increase exposure to the sun.

CONCLUSION

Bones are a body’s foundation. Having strong, dense bones is essential to good posture, strength and balance. Results of the present study revealed that majority of the females had a normal BMD however their serum calcium and vitamin D3 levels were low. Majority of the females had a normal BMI. Majority of the females was taking almost 1200-1400kcal per day and had an insufficient intake of milk and dairy products. Consumption of fizzy drinks on daily basis
was a common practice. Majority of the females used to consume 1-2 cups of tea/coffee daily and had the habit of taking it immediately after having a meal. Most of the females never had an energy drink whereas other caffeinated foods were consumed on weekly basis. Physical activity patterns of females showed that majority had the habit of working out in the evening, though 1-3 days a week for less than an hour. Walking was the most preferred form of workout by females.

Due to time constraints, this study was conducted on a small sample size (n=138). Data was collected from the OPD of only two hospitals of Lahore. All the confounding factors that can affect bone health could not be considered in the study. The same study must be conducted on a large and diverse sample in order to procure results generalizable to the whole population of reproductively aged females.

**RECOMMENDATIONS**

To maintain optimal bone health and to minimize the risk of osteoporosis among females, some of the recommendations are as follows:

- Policies that not only improve the consumption of calcium rich foods but also influence the production, marketing, availability and affordability of such foods are essential.
- It is important to improve knowledge, skills and competence about nutrition and a bone healthy diet by focusing on food literacy.
- Awareness must be created through media regarding the interactions between nutrients and/or non-nutrient factors that might affect bones.
- Nutrition education programs must be planned for females who are at risk of developing osteoporosis.
- Non-dietary factors that can lead to poor bones or can influence the overall health of females e.g. body frame, family history, use of certain medications, hormonal disturbances, poverty, educational level of the family and family size etc must be monitored and addressed.
- Seminars can be arranged to counsel females to get enough calcium every day in their diet and the ways to increase daily calcium intake.
- Awareness campaigns can be run in the OPDs of hospitals to make the public aware of the importance of a healthy diet for strong bones.
- Females must get regular medical check-ups to track hormone function.
- A nutritionist’s consultation is of immense importance to get guidance about calcium or vitamin D supplement that can be taken if the diet does not provide enough of these nutrients.
- A comfortable environment must be provided to females at gyms and even at homes to let them workout and be physically active.

**REFERENCES**


CLINICAL PATTERNS OF POST CHOLECYSTECTOMY SYNDROME
Liaqat Ali Deokah, Fakhur-uz-Zaman, Abeera Liaqat, Shafqat Ali

Abstract

Background: Post Cholecystectomy Syndromes (PCS) represents a heterogeneous group of symptoms and signs in patients who had gone open cholecystectomy. It can be attributed to as bile duct injury, biliary leak, Retained/Recurrent CBD stones and Bile duct stricture. We aimed to know the patterns and causes of PCS and evaluate the approaches to PCS.

Objective of Study: To assess the patterns and analyze the causes and evaluate the approaches to patterns presenting with PCS.

Place & Duration: All the Patients who underwent open cholecystectomy from April 2016 to 30th March 2019 in M.Islam Medical and Dental College / Teaching Hospital, Gujranwala.

Patients and Methods: 939 Patients underwent Open Cholecystectomy. 153 patients presented with PCS.

Results: Out of 939 with Cholelithiasis and had Open Cholecystectomy, 153 Patients were diagnosed with PCS. The incidence rate of PCS was 16.3%. The male to female ratio was 1:1.94%. The most common causes were as follows, H.phlori infection in 18 (11.76%), Peptic Ulcer Diseases (PUD) without Hphlori 15(9.80%) patients, Recurrent CBD stones in 5(3.26%) Patients, Retained CBD stones in 9 (5.88%) patients, Bile leakage in 9 (5.88%) patients, stricture of Spinster of Oddi in 7(4.57%) patients and stricture of CBD in 4 (2.61%) patients. No obvious cause in 33 (%) patients. The Mortality rate was 0(%).

Conclusion: Any clinical presentation of PCS should not be under estimated and be thoroughly investigated. Multi-disciplinary collaboration is crucial for the best outcome and safe approach for all patients of PCS.

Keywords: PCS, Open Cholecystectomy, Gall stones.

Cholecystectomy is an established successful operation for symptomatic gall stones in the world which provides total relief of pre-operative symptoms in more than 90% of patients.

Postcholecystectomy Syndrome (PCS) is defined as the recurrence of complex group of heterogeneous symptoms similar to those experienced before a Cholecystectomy. They commonly manifest as upper Abdominal pain and Dyspepsia with or without jaundice. The Incidence varies widely; it has been reported in many studies between 10-15%.

The incidence of recurrent symptoms in female patients is higher as compared to male patients.1-2

The onset of symptoms may vary from 2 days to 25 years.5-6

The cause of PCS can be Biliary, Extra Biliary or intestinal in origin. The most common cause of PCS is an over looked extra biliary cause which was present pre-operatively.

The patients of PCS need symptomatic treatment and detailed work up to diagnose exact cause of symptoms.

Abdominal Ultra Sound (US) and Liver Function Tests (LFT) are initially done and further investigations are tailored accordingly.4

All the patients presenting with PCS should be thoroughly investigated and definite diagnosis should be made and treated.

METHODS

A Retrograde study was done at M.Islam Medical and Dental College / Teaching Hospital, Gujranwala for 3 years, from April 2016 to 30th March 2019.

The patients who were diagnosed as cholelithiasis and surgically treated (open cholecystectomy) for gall stone disease, were reviewed. Of
these, 153 patients were re-admitted to the surgical ward or managed in Outdoor Patient Department for PCS.

All patients who presented with PCS were initially screened with Trans Abdominal Ultra Sound and LFT. All patients who either had CBD dilation or narrow CBD were further evaluated by Endoscopic Retrograde Cholangio Pancreatography (ERCP).

Those having suspicion of malignancy, underwent Computerized Tomography Scan (CT scan). In particular cases upper GIT Endoscopy was conducted.

The patients for effective surgical procedures were admitted one day before for the surgical procedure.

The emergency cases were admitted to the surgical ward from the emergency department.

RESULTS

Out of 939 patients with gall stone disease who had cholecystectomy, 153 patients were diagnosed with PCS. The incidence rate of PCS was 16.3%. 52 were male and 101 were female. The male to female ratio was 1:1.94 as shown by figure 1. The age range was between 26-61 years.

All the patients presenting with PCS underwent Abdominal Ultra Sound (US) Abdomen and Liver Function Tests (LFT). The presenting symptoms were recorded. 10(6.53%) patients presented with pain Rt Hypochondrium, 90(58.82%) patients presented with dyspepsia. 13(8.49%) patients had diarrhea, 5(3.26%) patients presented with jaundice, 27 (17.64%) patients presented with pain Rt Hypochondrium with dyspepsia. 8(5.22%) patients presented with pain Rt Hypochondrium with jaundice. The Symptoms of PCS recorded were as table no 1.

Abdominal Ultra Sound detected CBD Retained stones in 9(5.88%) patients, Recurrent CBD stones in 5 (3.26%) patients and bile leakage in 9(5.88%) patients.

CT scan showed features of Ch pancreatitis in 11(7.18%) and 5(3.26%) patients were having carcinoma of head of pancreas on CT scan. GIT Endoscopy diagnosed Peptic Ulcer Disease in 33(21.56%) patients. 18, patients of Peptic Ulcer Disease were positive H.pylori.

15(9.80%) of PUD were not positive H pylori. ERCP diagnosed stenosis of sphincter of Oddi in 7(4.57%) patients and stricture of CBD in 4 (2.61%) patients. In 33(21.56%) patients of PCS, no organic cause was found. 20(13.07%), patients were diagnosed Bile Induced Gastritis and 17(11.11%), patients were diagnosed Bile Induced Diarrhoea. The most common causes of PCS recorded were as table no 2. The offered treatment modalities were directed depending on the particular cause.

For no obvious cause, the patient’s management included assurance, supportive treatment and then discharged. All of the H.Pylori infection Patients were referred to Gastero-Enterologist for treatment. Follow up of these patients was done in surgical Outdoor Patient Department (OPD) for 02 Months.

11 patients of pancreatitis were treated meticu-

All patients of Peptic Ulcer Disease were treated medically and follow up was done in surgical OPD. Concerning Recurrent CBD stone, the patients were treated by ERCP, Endoscopy, papilotomy, stone extraction and stenting. The patients had follow up in surgical OPD for four weeks.

The Retained CBD stones patients treated by ERCP, Endoscopy, stone extraction and stenting. The follow was done in surgical OPD for four weeks.

For bile leakage, the patients had Laparotomy for the repair of ducts. The patients were followed up in surgical OPD for Four weeks.

All the patients of stenosis of sphincter of Oddi had Endoscopic sphincterotomy and setenting. The patients had follow up in surgical OPD for four weeks.

The patients of stricture of CBD had ERCP, Endoscopy and stenting. All the patients had follow up in surgical OPD for three months. Mortality rate
was (0%).

**Table 1: Presenting Symptoms of PCS**

<table>
<thead>
<tr>
<th>S No.</th>
<th>Symptoms</th>
<th>Total</th>
<th>Percent %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pain Rt Hypochondrium</td>
<td>10</td>
<td>6.5</td>
</tr>
<tr>
<td>2</td>
<td>Dyspepsia</td>
<td>90</td>
<td>58.8</td>
</tr>
<tr>
<td>3</td>
<td>Diarrhoea</td>
<td>13</td>
<td>8.4</td>
</tr>
<tr>
<td>4</td>
<td>Jaundice</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>5</td>
<td>Pain Rt Hypochondri with Dyspepsia</td>
<td>27</td>
<td>17.6</td>
</tr>
<tr>
<td>6</td>
<td>Pain Rt Hypochondrium with Jaundice</td>
<td>8</td>
<td>5.2</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Stone formation is the most common pathology of gall bladder. Although Laproscopic Cholecystectomy is rapidly gaining popularity but still open Cholecystectomy is widely performed for definite management of symptomatic gall stones. Cholecystectomy has excellent therapeutic outcomes for symptomatic gall stones. However 10-15% Cholecystectomized patients continue to have similar symptoms experienced by the patients before Cholecystectomy. Laproscopic Cholecystectomy is a safe procedure in trained hands when the procedure converted early and there is insistence in persisting with the minimally invasive approach. The rate of bile duct injuries is slightly higher with Laproscopic Cholecystectomy than Open Cholecystectomy.

The presence of symptoms after Cholecystectomy is termed Postcholecystectomy Syndrome. PCS was described for the first time in 1947. PCS is known as the recurrence of a complex group of heterogeneous symptoms similar to those experienced before cholecystectomy.

They commonly manifest as upper abdominal pain and dyspepsia with or without Jaundice and can be early if occurring in the post-operative period and late if manifest after months or years.

The incidence of PCS is about 15-20%. The incidence of PCS is higher among female patients as compared among male patients. PCS may be caused by Organic biliary diseases, Organic Extra-biliary diseases, Functional biliary causes and functional Extra-biliary causes.

Residual or de Novo CBD stones are the most common organic biliary causes. Organic extra-biliary diseases may originate from Esophagus, Stomach, Small or large intestine present with symptoms or signs similar to those of PCS.

Functional biliary causes are rare and include Dysfunction of sphincter of Oddi and are 1-3%, Cause of PCS. Functional Extra-biliary causes may be Irritable Bowel Syndrome and may present similar to PCS.5,6,7

The patients of PCS are initially assessed by Trans Abdominal Ultra Sound and LFT followed by ERCP as gold standard. The management options of PCS are focused on the treatment of cause.

Multi-Disciplinary management approach is adopted including surgical, medical, Radiological and other Specialists. The collaboration of many.

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**Table 2: Diagnosis Data of PCS**

<table>
<thead>
<tr>
<th>S No.</th>
<th>Cause</th>
<th>No. of Patients</th>
<th>Percent %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Retained CBD Stones</td>
<td>9</td>
<td>5.8</td>
</tr>
<tr>
<td>2</td>
<td>Recurrent CBD Stones</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>3</td>
<td>Bile Leakage</td>
<td>9</td>
<td>5.8</td>
</tr>
<tr>
<td>4</td>
<td>CBD Stricture</td>
<td>4</td>
<td>2.6</td>
</tr>
<tr>
<td>5</td>
<td>Stricture Sphincter of Oddi</td>
<td>7</td>
<td>4.5</td>
</tr>
<tr>
<td>6</td>
<td>Ca Head of Pancreas</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>7</td>
<td>Chronic Pancreatitis</td>
<td>11</td>
<td>7.1</td>
</tr>
<tr>
<td>8</td>
<td>Peptic Ulcer Disease with H.Plori</td>
<td>18</td>
<td>11.7</td>
</tr>
<tr>
<td>9</td>
<td>Peptic Ulcer Disease without H.Plori</td>
<td>15</td>
<td>9.8</td>
</tr>
<tr>
<td>10</td>
<td>Bile Induced Gastritis</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>11</td>
<td>Bile Induced Diarrhoea</td>
<td>17</td>
<td>11.1</td>
</tr>
<tr>
<td>12</td>
<td>No Organic Cause</td>
<td>33</td>
<td>21.5</td>
</tr>
</tbody>
</table>
specialist as needed is done early as possible for the best outcome and safe approach for all patients.

The usual and most common cause of PCS is incorrect pre-operative diagnosis. The cause of PCS can be classified into three groups.

1. The symptoms of initial presentation i.e “Cholecystitis” were not related to gall bladder stones.
2. A surgical error i.e Leaving stone in the ducts or injuries to the ducts.
3. A new disease either of the Biliary tract or another system.

CONCLUSION

Postcholecystectomy Syndrome is distressing to a patient who even after having undergone a successful Cholecystectomy needs to be eventually investigated thoroughly once again to look for any cause of PCS. More than 90% patients undergone Open Cholecystectomy to have been resounding success to their pre-operative symptoms. However the patients should be thoroughly assessed/evaluated pre-Operatively. Multi-Disciplinary collaboration is crucial for the best outcome and safe approach for all patients of PCS.

Multi-Disciplinary management approach Leads to a pathway of success. Symptomatic gall stones patients should be admitted/counseled both of risks of surgery and risks of post-operatively persistence of symptoms.

REFERENCES


Diabetes mellitus is a very common medical condition. Diabetic foot ulcers are one of several serious complications of diabetes progression. Major contributing causes to diabetic foot ulcers are peripheral neuropathy, peripheral arterial disease, and immunosuppression. The multifactorial causative factors in diabetes need meticulous approach towards management. The lifetime risk of diabetic foot ulcers for patients with diabetes may reach up to 68 per 1,000 persons as reported by some studies. As a diabetic foot ulcer progresses, the patient's risk for amputation increases; in nearly 84% of patients who have a lower limb amputation secondary to diabetes, the amputation is preceded by a diabetic foot ulcer. Peripheral neuropathy secondary to diabetes is one of the most consistent etiologic factor of diabetic foot ulcers. The neuropathic foot, for example, does not spontaneously ulcerate. It is the combination of insensitivity and either extrinsic factors e.g. walking barefoot and stepping on a sharp object, or simply wearing ill-fitted shoes, or intrinsic factors such as diminished sensation and the development of a callosity which progresses to an ulcer on walking. Neuropathy is the most significant pathology in the pathway to ulceration.

These collective findings indicate that diabetic foot ulcers lead to serious disability, serious reduction in patient quality of life, and high financial costs for society. Multidisciplinary approach is effective way of managing diabetes from the very start. With increased vigilance on risk assessment, diagnosis, and management of diabetic foot ulcers, clinicians can improve patient outcomes and reduce healthcare costs.

METHODS
This study was conducted at Mayo Hospital Lahore from August 2014 to August 2018. 80 patients with diabetic foot lesions were admitted and managed accordingly to the lesion. Both type I and type II Diabetics having diabetic foot lesions were included in this study. Patients with pre-existing conditions e.g. Carcinoma, Chronic Eczema, varicose ulcers, were excluded from this study.

Abstract
Objective: To identify modes of presentations of diabetic foot lesions along with various surgical procedures for their management and the commonest causative organisms.

Design: This study was conducted at Mayo Hospital Lahore from August 2014 to August 2018.

Patients and Methods: 80 Patients admitted with Diabetic Foot lesions were assessed with various surgical procedures performed upon them. The patients were graded according to Wagner's Meggit classification. Complete blood picture, blood sugar level, urine for sugar and proteins, Culture and sensitivity of pus, X-Ray of foot along with serum urea and Electrolytes were performed on each patient.

Results: Out of the 80 patients, 60 were males and 20 were females. The common diabetic foot lesions seen were gangrene of the toes with underlying osteomyelitis. Incision and drainage, repeated debridements and amputation of the toes were the common surgical procedures performed. The common infecting organisms were staphylococcus (42) and Pseudomonas (28).

Conclusion: Diabetic foot lesions are avoidable complications of diabetes. Healthcare professionals must educate the society, diagnose the diabetic foot complications early, treat them effectively to preclude mortality and long term morbidity.

Key Words: Diabetic Foot, Incision and drainage, Amputation.
After the admission of patient, History was taken which included age, gender, occupation, history of present ulcers, risk factors, Insulin or non-insulin dependent diabetes, type of diabetic control, Rest pain, claudication, neuropathy, smoking and family history of diabetes. Examination of the feet was carried out for hygiene, ulcers, gangrene, presence of infection and hair loss. Neurological Examination of feet was also done. Posterior tibial and dorsalis pedis arteries were palpated for vascular integrity. Local examination of the feet of each patient was done and graded according to Meggitt Wagner's classification.

**WAGNER’S MEGGITT CLASSIFICATION**

*Grade 0:* High risk foot.

*Grade i:* Superficial ulcer skin deep

*Grade ii:* Deep ulcer involving soft tissue but no bony involvement.

*Grade iii:* Ulcer extending upto involvement of bones.

*Grade iv:* Localized gangrene (forefoot, toe or heel).

*Grade v:* Gangrene of the entire foot.

**RESULTS**

80 patients were managed having different types of diabetic foot lesions. Out of them, 60 patients were male and 20 were female (Table-1). Majority of patients were in the age range of 49 to 73 years. Most of the patients were admitted through the emergency (61) and OPD (14) while the rest were referred from the other wards.

Various procedures performed were recorded both for male and female patients (Table-2). The wounds of admitted patients were examined and classified according to Meggitt Wagner’s classification (Table-3). The culture reports of pus showed different organisms, however, the most common organism remained staphylococcus. The common surgical procedures were debridement of wounds and incision and drainage with curettage of wounds, as majority of wounds were grade III and grade IV. According to C/S common antibiotic used were benzyl penicillin 6 MU IV QID, Moxifloxacin, 400mg, IV OD followed by injection Linezolid 600mg IV BID. The duration of hospital stay of the patients ranges 5-13 days.

**Table 1:** Sex Distribution (n=80)

<table>
<thead>
<tr>
<th>Sex</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>20</td>
<td>25%</td>
</tr>
<tr>
<td>Male</td>
<td>60</td>
<td>75%</td>
</tr>
</tbody>
</table>

**Table 2:** Various applied surgical procedures

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Wash, dressing &amp; antibiotic</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Incisions drainage &amp; curettage</td>
<td>8</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Re-debridement and curettage</td>
<td>11</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Big Toe Nail extraction</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Single Toe amputation / Ray Amputation</td>
<td>8</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Multiple (&gt;2 toes) amputation</td>
<td>9</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Mid tarsal amputation</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Below knee amputation</td>
<td>7</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Above knee amputation</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>60</strong></td>
<td><strong>20</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>

**Table 3:** Grades of Wound According to Maggit Wagner Classification

<table>
<thead>
<tr>
<th>Grade</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade i</td>
<td>8</td>
<td>3</td>
<td>11</td>
<td>13.75</td>
</tr>
<tr>
<td>Grade ii</td>
<td>11</td>
<td>5</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Grade iii</td>
<td>22</td>
<td>5</td>
<td>27</td>
<td>33.75</td>
</tr>
<tr>
<td>Grade iv</td>
<td>17</td>
<td>6</td>
<td>23</td>
<td>28.75</td>
</tr>
<tr>
<td>Grade v</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>60</strong></td>
<td><strong>20</strong></td>
<td><strong>80</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

**Table 4:** Frequencies of Involved Organisms

<table>
<thead>
<tr>
<th>Infecting Agents</th>
<th>No of case</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Staphylococcus</td>
<td>42</td>
<td>56</td>
</tr>
<tr>
<td>Streptococci</td>
<td>26</td>
<td>35</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>28</td>
<td>37</td>
</tr>
<tr>
<td>Proteus</td>
<td>21</td>
<td>28</td>
</tr>
<tr>
<td>E-coli</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>Bacteroides</td>
<td>14</td>
<td>19</td>
</tr>
<tr>
<td>Klebsillae</td>
<td>10</td>
<td>13</td>
</tr>
</tbody>
</table>
DISCUSSION

Duration of Diabetes Mellitus and poor control of blood glucose levels are well known risk factors for diabetic foot. Peripheral neuropathy is considered to be a major contributor for development of foot ulcers. Most of the ulcers are on forefoot. Lack of proper control of infection in diabetic ulcers may require major amputation inspite of proper debridement. Surgical complications of diabetic foot include ulcerations, abscesses and Gangrene of foot and Osteomyelitis.

Diabetic foot lesions commonly occur in elderly male patients and those with associated diseases. Once a lesion has developed, infection plays an important role in determining its outcome, whether the primary cause is neuropathic, ischemia or both. Local examination of feet of each patient should be done and graded according to Wagner’s Meggitt classification.

The Pathophysiology of diabetic foot infection is multifactorial. The usual mode of patient’s presentation is cellulitis and ulceration with or without planter abscess formation and Osteomyelitis. Charcot’s deformity, achilles tendon contracture and sequelae of generalized atherosclerosis may further complicate the management of these patients.

Patients of diabetic foot lesions can efficiently be managed, provided the diabetic patients have knowledge about their blood sugar control and care of feet. We should diagnose the diabetic foot complications early, treat them effectively to preclude mortality and long term morbidity.

Amputation of a limb does not leave just a physical dent on an individual, but loads of psychological and emotional effects thus feeling useless because of the inability to do anything. This corroborates with the findings of De Godoy et al. who found that the quality of life was generally lower for amputees.

Diabetic foot ulcer patients are at a 12 times higher lifetime risk of amputation. Similarly, Wukich et al. have linked history of cellulitis and moderate-to-severe foot infection to amputation.

Diabetes is so debilitating disease that even in West, diabetic patients have a 10–15 times greater risk of lower extremity amputation than non-diabetic patients.

In our study Staphylococcus was the most common organism isolated followed by Streptococci Gu et al found that Staphylococcal species comprised 24.1% of all isolates recovered from diabetic foot wounds, 55% of these were S. aureus, with 16.8% isolated in pure culture. Streptococci were cultured from 41% of the patients, with S. agalactiae comprising almost half of the strains. This is a well-recognized pathogen in diabetic foot infection; but other streptococci, such as those of the S. milleri group, which have long been associated with acute and chronic suppurative infections were also present in 4.2% of the patients.

CONCLUSION

Diabetic foot lesions are very commonly found in diabetic patients and pose serious health problems. The commonest lesion is ulceration of the forefoot with Osteomyelitis. Incision and Drainage, repeated debridements and amputation of the toes are the common surgical procedures performed.

We need to educate our community about diabetes mellitus and its complications in order to manage diabetes mellitus effectively and to delay the development and harnessing the progression of these complications.

REFERENCES


The Paraumbilical hernia is a common surgical problem. This is the common acquired Ventral Hernia in the adults. It appears through a defect that is adjacent to the Umbilical scar. It does not appear through the center of umbilicus. Para Umbilical Hernia usually appears in the middle and old age. It is more common in Female Especially multiparous and obese Women. Most of Hernias have Expansible cough impulse and Reducibility, which are the cardinal signs of a hernia.

Different modalities of surgical repair of Para Umbilical Hernia are being adopted. Simple Repair, Mayo’s Repair, Mesh Repair and laparoscopic methods are done for the management of the Para-Umbilical Hernia.

METHODS

In this study, the patients were divided into two groups. Each group included 20 patients. In group I patients, Hernia defect was repaired by simple suture and Mayo's Repair using prolene No1.Wound was closed in layers, keeping the Radivac drains in all patients.

In group II patients, the defect was closed with interrupted prolene No 1 sutures and on lay Mesh having size of 15 by 15 cm was kept and sutured by prolein 2/0. Radivac drains were also used in this group. All the patients have pre-Anesthesia assessment before the surgery. All patients were given General Anesthesia for the repair of Hernia.

The duration of Hospital stay, the complications during the Hospital stay and then in follow up period were recorded.

RESULTS

This study included 40 patients, out of which 4, were male, rest were Female (Table-1). The age of these patients was from 35 to 60 years. These patients were divided in two groups. Each group was having 20 patients. The operative time for group I patients remained from 1 hour to 1 hour 30 minutes and for group II patients, the operative time was 1 hour 15 minutes to 1 hour and 45 minutes.

The most common complication in the both groups was wound infection.5, patients developed wound infection (Table-2). The patients of wound infection were managed by removal of skin stitches with antibiotic cover after having C/S reports. In one patient, the wound infection was only settled after removal of the mesh. Anesthetist and Medical specialist were consulted for the treatment of Respiratory Complications. 3, patients of group I developed Recurrence (Table-2). Recurrence was more in group I patients as compared to group II patients. Hospital stay was longer in group II patients (7-18 days) as compared to group i (5-10 days).

Objective: To know and Compare the different methods of repair of Para umbilical Hernia. Duration 4 Years, from March 2013 to March 2017. Place This study was conducted at Avicenna Medical College and Teaching Hospital Lahore.

Patients and Methods: This study included 40 patients, 4 were male, rest were Female. The patients were divided in two groups. Group I consisted 20 patients who had simple repair and Mayo's Repair. Group II consisted 20 patients who had Mesh repair. Recurrence rate was high in group I patients.

Results: In both groups of 40 patients, the most common complication was wound infection. The Recurrence was high in group I patients.

Conclusion: Mesh Repair is superior as compared to simple and Mayo's Repair.

Key Words: Simple Repair, Mesh Repair Paraumbilical Hernia.
DISCUSSION

Paraumbilical Hernia is one of the Ventral Hernia which protrudes through a defect besides the umbilicus. The main bulge of Hernia is adjacent to the umbilicus which is pushed to one side and stretched into crescent shape. The patients are usually overweight Female, between 35 to 60 years of age. Obesity and repeated pregnancies are main causative factors. The patients usually present a lump which is just above or below the umbilicus.

Expansile cough impulse and Reducibility are present in most of the patients.

The narrow neck of the Hernia enhances the risk of strangulation. Small, asymptomatic Hernias can be left as such. A Paraumbilical Hernia has a tendency to be associated with high morbidity and mortality in comparison with Inguinal Hernia because of the high risk of Incarceration and Strangulation that require an emergency repair. Surgery is usually advised for larger defects in the form of open or Laparoscopic surgery. Recurrent Paraumbilical Hernia often tends to enlarge faster than Primary ones. Large Seroma and surgical site infection are classical complications that may result in recurrence. Obesity and excessive weight gain following repair are obviously potential risk factors. Defect more than 2cm have been reported as possible factor for surgical failure. Moreover, smoking may create a risk for Recurrence.

Mesh Repair of Hernia has better results and less complications as compared to simple and Mayo’s Repair.

CONCLUSION

This study has revealed that Mesh Repair of Paraumbilical Hernia has superior results and less chance of Recurrence as compared to simple and Mayo’s Repair.

It is concluded by this study that Mesh repairs are superior to Non-Mesh and Tissue-Suture repairs.

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Chronic pilonidal sinus is a common disease and is usually found in the midline of the sacrum of hairy young men. It is an acquired condition with high morbidity and discomfort for the patient. The name pilonidal means Latin "nest of hairs". The predictable occurrence is 27 out of 1,26,000 people. It is usually seen as a cyst with or without secretions, an abscess or sinuses. Before puberty and after 40 years, men are more often affected than women.

The pilonidal sinus aetiology is controversial. Initially, it was suggested that the innate origin was secondary to the epithelial lined residue of vestigial scent cells or post coccygeal epidermal cell rests. Now the vision has changed significantly in relation to the acquired theory and is grounded on the interpretations that the innate pathways are hairless and the cuboid epithelium covers the tract. Karydakis recommended 3 chief reasons instigating the ailment, explicitly large amounts of hair, excessive strength and susceptibility to infection. The presence of hair in the gluteal cleft plays an important role in the pathogenesis of this disease. Deep natal cleft are suitable for sweating, bacterial contamination, maceration and hair penetration. Other risk factors include local trauma, obesity or irritation, a sedentary lifestyle, family history, excessive hair growth and poor hygiene. It is widely acknowledged that pilonidal sinus is the result of...
infiltration of shed hair shafts into the skin, which primes to a chronically or an acute infected area and this can be effectively treated with the help of an appropriate surgical procedure. However, with a large number of pilonidal openings, branched paths and obvious symptoms, extensive disease may require significant excision of the affected area.6

The diagnosis is usually clinical and the patient may have chronic inflammation or a sinus with persistent discharge; abscess or multiple subcutaneous tracts. Although pilonidal sinus can be treated with a variety of conservative and surgical methods, the relapse rate is high. Complete pilonidal sinus removal and proper reconstruction can lead to successful recovery7. Various techniques have been described for the sacroccocygeal sinus; which includes hair cutting with better cleanliness of that area, packing and extensive excision and primary closure, marsupialization, rotation advancement fasciocutaneous flap, and flap techniques like elliptical rotation flap, modified Limberg transposition flap, and Limberg flap. Of the various surgical methods in the treatment of the sacroccocygeal sinus, flap reconstruction techniques eliminate the aetiology of the disease by levelling the inter gluteal sulcus with less hairy fascial and cutaneous flap and less perspiration. Among them, the most commonly used method for limberg flap is rhomboid excision8. With this flattening technique, tension-free repair is performed with a wide and well vascularized flap. It is reported to be one of the best treatments with a relapse rate of 0-15% and surgical complications of 0-6%.

METHODS

This Prospective study was held in the In the Department of Surgery, Allama Iqbal Medical College, Jinnah Hospital Lahore for two year duration from 1st January 2017 to 31st December 2018. Sixty two consecutive patients who underwent reconstruction with the Limberg flap were included in the study after informed consent. Patients with simple, complex and recurrent pilonidal sinuses were evaluated. Patients with acute abscess were excluded from the study. Patients were followed for at least one year to determine the recurrence of the disease. There were 40 men and 22 women. All surgical interventions were accomplished under spinal anaesthesia. The average duration of symptoms was 3.5 years. All patients underwent a full medical history and routine laboratory tests and clinical or local evaluation. After explaining the procedure, written informed consent was attained from all subjects. Patient data was of pre-operative and post-operative observation was recorded on Performa for each patient. Patients with other local pathologies, such as eczema, fungal or other deforming pathologies, were excluded from the study. All patients underwent surgical refurbishment with a Limberg flap. The patient’s average age was 21 years. Seven patients (23%) had abscess drainage in the past due to pilonidal sinus. The main result of this study was the assessment of the surgical procedure in terms of surgical complications and relapse rate.

Surgical Method

One day before the surgery; the natal cleft was clean-shaven. Before the incision, 1 gram of cefazoline and 500 mg metronidazole were given intravenously prophylactically. The selectees were positioned in prone situation and the buttocks strapped apart by adhesive tapes. Using a sterile pen to mark the rhomboid area of the skin on the pilonidal sinus, if containing any lateral extensions and midline pits were marked. Onto the skin, flap design was mapped (Fig. 1).

Figure 1: Marking with Letters
The rhomboid long axis in midline was manifest as A-C, C being nearby to perianal skin, A positioned in the way that all contaminated tissues can be encompassed for expurgation. The B-D line crosses the A-C centre at right angles and is sixty percent of its size. D-E was a straightforward B-D line continuation and was the same size as the B-A incision and was stitched subsequently on rotation. E-F was analogous to DC and of same span. When rotated, it was stitched to AD. A rhombic-designed skin excision having subcutaneous tissue and sinus up to the pre-sacral fascia was achieved by electrocautery (Figure 2) (Figure 3).

Figure 2: Placing Skin Incision

Figure 3: Excision of Pilonidal Sinus Complex till Deep Fascia

Then perforator-based Limberg flap elevation (Figure 4) (grounded on the sacral or superior gluteal perforators conferring to the Koshimaetal study on post-mortem dissection) in the similar way and the dissection level was pre muscular fascia, better haemostasis was attained and the sticky tape which withdrew the buttocks were unconfined to permit flap stitching deprived of tension.

Figure 4: Raising of Inferior Limberg Flap

A fasciocutaneous Limberg transposition flap on right or left side, integrating the gluteal fascia, was completely militarised on its lower edge and was medially transposed to seal the Limberg defect (Fig. 5).

Figure 5: Rotation of Flap Over Defect

Figure 6: Final Outcome after Suturing

Thus, defect created was sealed in a linear manner (FIG. 6). Interrupted Vicryl 2-0 sutures containing fat and fascia were positioned over vacuum drain, and stitched finally with a skin stapler. As a result of this process, a tension-free flap of unscarred skin covers the midline (Figure 6). Antibiotics were first administered intravenously for 1 week, and then orally, suction drainage detached
after 2 days, and staples removed about the tenth day. The subjects were counselled not to press the flap for minimum 21 days. All patients were evaluated for flap healing, serous and oedema formation, necrosis of flap, surgical site infection, and pain and hospital stay duration. The objective pain grading was performed using a visual analogue scale. Patients were followed 1 and 6 months after surgery.

RESULTS

Sixty two consecutive patients who underwent reconstruction with the Limberg flap were operated successfully, with very little postoperative pain, hospital stay for an average of 5 days, returned to the daily routine after 19 days, 6 were having seroma, 3 flap necrosis, hematoma in 3 and two patient have infected wounds and recurrence developed in 1 patient. Patients with complications were treated conservatively. The average duration of the operation was 50 minutes (range: 30 to 80 minutes). All patients were initially monitored for 2 weeks, followed by 1 month and 6 months later.

The reconstruction by Limberg flap for defect has many benefits, because it is calm to make and design, and it straighten the natal cleft with great vascularized pedicle, stitched deprived of tension. Thus, provides better hygiene, reduces resistance, prevents maceration and prevents the formation of marks on the midline. This procedure of flap recovery is improved than other flap procedures, such as simple excision and closure, combination. Bescom and Karydakis. Iesalnieks examined the long-term results after primary midline closure and pilonidal sinus resection compared to open surgery in 71 patients. 41% of high relapse proportion was noted after pilonidal sinus excision and primary closure of the midline. This study shows that there is lower relapse in this procedure. In this study, the flap has a lower base with better aesthetic appearance and more anatomical recovery. In 2014, El-Khatiband Al-Basti stated 8 case series of pilonidal sinuses rebuilt by a two-piece perforator flap, with an average surgery time of 90 minutes, so it's a long time with extensive mark of scar. In the analysis, we accomplished inferior based flap, the average time of surgery was 50 minutes with full treatment of the disease, and the frequency of postoperative complications was very low compared to previous studies.

Table 1: Shows Complications of Limberg Flap for Pilonidal Sinus

<table>
<thead>
<tr>
<th>Complications</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seroma Formation</td>
<td>9.7%</td>
</tr>
<tr>
<td>Flap necrosis</td>
<td>4.8%</td>
</tr>
<tr>
<td>Wound infection</td>
<td>3.2%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>1.62%</td>
</tr>
<tr>
<td>Hematoma</td>
<td>4.8%</td>
</tr>
</tbody>
</table>

Resolving of the seroma took about 8 days and infection of the surgical site lasted three weeks. The patient with flap necrosis underwent multiple dressings and debridement, and recovery took 8 weeks to reconcile by secondary intention. The range of pain ratings was 2 to 8 and the average rating was 4.5. The average hospital stay was 5 days (from 2 to 14 days). All other patients recovered mainly with minimal scarring and less postoperative pain, so far without recurrence. The average time to return to work was 19.6 days (from -10 to 30 days).

DISCUSSION

Sacrococcygeal pilonidal sinus is known for long-term morbidity and relapses, and ideal treatment must guarantees low pain, short hospitalization, low risk of complications, and fast return to normal activity, better aesthetics, and low relapse rate. Understanding the importance of avoiding midline natal cleft suture because of recurrence. To minimize recurrence, emphasis should be placed not only on the flattening of the natal cleft, but also on closure beyond the midline of the defect that occurs to minimize complications and recurrence of the wound. Flap reconstructions with midline lower edge or suture line on intergluteal sulcus are supposed to rise relapse rates, wound infection and wound dehiscence risk. Limberg valve reconstruction ensures closure outside the midline and flattens natal cleft.

The reconstruction by Limberg flap for defect has many benefits, because it is calm to make and design, and it straighten the natal cleft with great vascularized pedicle, stitched deprived of tension. Thus, provides better hygiene, reduces resistance, prevents maceration and prevents the formation of marks on the midline. This procedure of flap recovery is improved than other flap procedures, such as simple excision and closure, combination. Bescom and Karydakis. Iesalnieks examined the long-term results after primary midline closure and pilonidal sinus resection compared to open surgery in 71 patients. 41% of high relapse proportion was noted after pilonidal sinus excision and primary closure of the midline. This study shows that there is lower relapse in this procedure. In this study, the flap has a lower base with better aesthetic appearance and more anatomical recovery. In 2014, El-Khatiband Al-Basti stated 8 case series of pilonidal sinuses rebuilt by a two-piece perforator flap, with an average surgery time of 90 minutes, so it's a long time with extensive mark of scar. In the analysis, we accomplished inferior based flap, the average time of surgery was 50 minutes with full treatment of the disease, and the frequency of postoperative complications was very low compared to previous studies.
CONCLUSION

Limberg flap for the defect closure after sacrococcygeal pilonidal sinus excision is an effective and reliable technique with high patient satisfaction, related with comprehensive recovery and have low incidence of postoperative complications.

REFERENCES

Obesity has struck the world in the form of an epidemic, affecting all ethnicities, ages, and genders. Obesity is rising in both developed and developing countries of the world. Obesity is associated with complications like Diabetes Mellitus, hypertension, OSA, polycystic ovarian syndrome, arthritis, etc. Gastric bypass was the most common procedure but associated with many complications. Then sleeve was started as a two-stage procedure, but due to its comparable five-years results with RYGB and less complications, it has become the most commonly performed bariatric procedure. Most surgeons practice 4 or 5 ports sleeve, using subxiphoid incision for lifting hypertrophied left lobe. Three ports sleeve gastrectomy involves special liver retraction technique without any use of extra port but with the help of sutures. In this procedure a sleeve of stomach starting from antrum to fundus is cut, leaving behind a tube of stomach with a smaller reservoir as compared to the original. The sleeve gastrectomy was done in standard way using 38 FR gastric tube. Sleeve is anchored with prepancreatic fat to prevent torsion. Technically it requires a lot of skills but better cosmesis. Many surgeons are now opting for single incision sleeve gastrectomy that is associated with even more better cosmesis, less demand for analgesia and more patient satisfaction.

METHODS

About 40 patients admitted in Jinnah hospital Lahore fulfilling the inclusion criteria were included in the study. An informed consent was taken about the procedure and sleeve gastrectomy was chosen as a modality for metabolic surgery. Patients were informed about the details of three ports technique. They were briefed about the special liver retraction system which is safe and effective. The outcome was measured in terms of reduction in mean postoperative BMI at 6 months and the mean duration of surgery. The data was statistically analysed with the help of paired sample t test and significance value p was taken as significant if ≤ 0.05.

Abstract

Objective: To evaluate the mean BMI after 6 months of surgery and the mean total duration of surgery for sleeve gastrectomy.

Methods: About 40 patients requiring metabolic surgery admitted in Jinnah hospital Lahore from June 2015 to March 2019, fulfilling the selection criteria were operated.

Results: Females: 32, males 8; mean Age: 37.5 years. The paired sample test for mean preoperative BMI was 50.51 ±8.66, whereas the mean postoperative BMI was 34.06 ±3.42 and the p value was 0.00. The mean total duration of study was 161.12±40.08 min with minimum 90 min and 240 maximum minutes.

Conclusion: From the results it was concluded that three ports sleeve gastrectomy is a safe procedure for obesity. The initial duration of surgery which was high, after experience and practice was gradually reduced thus avoiding major long anaesthesia complications. The reduction in BMI after six months was also comparable with international standards.

Clinical Trial Number: [nil]

Keywords: obesity, sleeve gastrectomy, BMI after 6 months
RESULTS

Total females were 32, total males were 8; minimum age was 21 years and maximum age was 65 years. The paired sample test for mean preoperative BMI was 50.51±8.66, whereas the mean postoperative BMI at 6th month was 34.06±3.42 and the p value was significant as 0.00. The mean total duration of study was 161.12±40.08 min with minimum 90 min and 240 maximum minutes.

DISCUSSION

It not only results in reduction of excess weight of an individual, but also treats the co-conditions like diabetes mellitus, hypertension and sleep apnoea. Our present study showed a significant reduction in the BMI of the patients at sixth month postoperatively, along with reduction in procedure time.

Over the years sleeve gastrectomy has proved to be a definite and novel procedure. Its five years are comparable with RYGB in terms of weight loss and metabolic control. Three ports sleeve gastrectomy has proved to be a safe procedure, but technically demanding. In experienced and skillful hands, the learning curve is reduces and results are the same or that of four or five ports procedure with better cosmesis. Time duration of procedure and reduction in BMI also comparable with five ports and international standards.

Table 1: Mean Preoperative and Postoperative BMI

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>mean±S.D</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative BMI</td>
<td>40</td>
<td>50.51±8.66</td>
<td></td>
</tr>
<tr>
<td>Postoperative BMI at 6 month</td>
<td>40</td>
<td>34.06±3.42</td>
<td>P=0.00</td>
</tr>
</tbody>
</table>

Table 2: Mean duration of surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Min.</th>
<th>Max.</th>
<th>mean±S.D</th>
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<tr>
<td>Duration of surgery</td>
<td>40</td>
<td>90</td>
<td>240</td>
<td>161.12±40.08</td>
</tr>
</tbody>
</table>

CONCLUSION:

Although six months post operative results are conclusive in our study but a large number of data is required to prove the long term efficacy of three ports sleeve gastrectomy in terms of patient safety and BMI reduction.

Conflict of interest: none

REFERENCES

Breast cancer is the commonest cancer in females though rare in males but cases are often seen. Breast cancer is categorized as stage 1,2,3,4 based on TNM staging. The prognosis of the disease also depends on degree of differentiation of tumor and lymph node status. Sentinel lymph node biopsy avoids the need of axillary lymph node dissection, if sentinel lymph node is negative for cancer. Many patients can benefit from unnecessary dissection of axilla and its complications subsequently.

SLNB is the current paradigm in the management of regional basin in breast cancer.

SLNB predicts the status of the other lymph nodes and has a bearing on prognosis of breast cancer. Everyone has a unique number of sentinel lymph nodes; you may have one or more. To determine SLN has cancer it must be removed and examined. Axillary lymph node dissection has been a gold standard for many years, though now the paradigm shift is towards SLNB.

METHODS

This study was carried out in tertiary care hospital from 1st January 2013 to 1st January 2019, including 100 patients, divided equally into group A and group B of ALND & SLNB respectively. Either mastectomy or breast conservation surgery was combined with ALND or SLNB. All patients were operated in general anesthesia with informed consent and ethical considerations taken into account. All patients were females from 20 to 70 years of age with peak in forties. Clinical Stage 1, 2, 3 were included in study with metastatic carcinomas excluded from the study. Sentinel lymph node was identified by using methylene blue as well as gamma camera. 1-3 lymph nodes identified as sentinel were removed and sent for examination by fresh frozen section and/or imprint cytology. The accuracy of SLN diagnosis using fresh frozen section (FFS) as well as imprint cytology improved with an increase in number of sections could obtain a sensitivity as that of routine histological examinations of permanent sections.

ALND involves the level 2/3 axillary lymph node dissection and sent for histological examination along with excised breast tissue.
RESULTS

Total 100 female patients were included in the study. With age range 20-70. Most of the patients were in the age range of 40-50 (Table 1)

Patients were staged as 1, 2, 3 based on TNM staging. Stage wise distribution of patients is as follows

Out of 50 patients in group A, 35(%) had tumor positive lymph nodes and 15 (%) had tumor negative lymph nodes. In group B, 30 (%) patients had tumor positive lymph nodes and 20 had tumor negative lymph nodes.

Table 1: Age Distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of patients</th>
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<tbody>
<tr>
<td>20</td>
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<tr>
<td>25-30</td>
<td>10</td>
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<tr>
<td>30-40</td>
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<td>40-45</td>
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<tr>
<td>45-50</td>
<td>10</td>
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<tr>
<td>50-60</td>
<td>10</td>
</tr>
<tr>
<td>60-70</td>
<td>5</td>
</tr>
</tbody>
</table>

DISCUSSION

Though ALND was a gold standard for axilla now the trend is towards SLNB, preventing undue dissections of axilla and its unwanted consequences like seroma and lymphedema.

We in our study found out that women without SLN metastasis should not receive ALND. There are hardly any contraindications for sentinel lymph node biopsy.

SLNB is highly accurate to level 1, level 2 axillary clearance in vast majority of patients with early breast cancer. We also found out that a significant number of patients would be at risk for the morbidity of ALND without benefitting from the procedure.

CONCLUSION

It is highlighted that SLNB where negative lifts the need for unnecessary ALND therby benefiting the patients.

REFERENCES

COMPARISON OF THE MEAN DURATION OF SENSORY BLOCKADE WITH BUPIVACAINE AND BUPIVACAINE PLUS DEXAMETHASONE COMBINATION IN PATIENTS UNDERGOING ORTHOPEDIC PROCEDURES UNDER SPINAL ANESTHESIA.

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Abstract

Introduction: Regional anesthesia is preferred for any type of surgery whenever possible over general anesthesia. Among neuraxial blocks, Spinal anesthesia is widely used for orthopedic surgeries. Regional techniques can even control pain from several hours to several days, depending upon the type of local anesthetic agent, adjuvant and technique used. Dexamethasone prolongs the duration of peripheral nerve blocks. Similarly, it may prolong the duration of spinal anesthesia when used as intrathecal adjuvant to local anesthetics. Rationale of this study is to find whether adding dexamethasone as adjuvant in spinal anesthesia to bupivacaine will increase the duration of sensory blockade or not. Longer sensory blockade is necessary as it will be cost effective and decrease the requirement of post-op analgesics.

Objectives: To compare the mean duration of sensory blockade with bupivacaine alone versus bupivacaine plus dexamethasone combination in patients undergoing orthopedic procedures under spinal anesthesia.

Study design: Randomized Control trial

Setting: Orthopedic operation theatre, Jinnah hospital Lahore

Duration of study: Study was carried out over a period of six months from 1-12-2016 to 30-06-2017

Methods: 60 patients fulfilling the selection criteria were selected for the study from operation theatres of Jinnah Hospital, Lahore. Patients were divided into two groups group “B” and “D” by using lottery method. Spinal anesthesia was performed in the sitting position at L3–L4 or L4-L5 level through a midline approach using a 23-25 gauge Quincke spinal needle. Patients of the group B received 15 mg (2 ml) of 0.75% hyperbaric bupivacaine diluted in preservative free normal saline (2 ml) and patients of the group D received 15 mg (2 ml) of 0.75% hyperbaric bupivacaine and 8 mg preservative free dexamethasone 4 ml intrathecally. The duration was noted at which VAS score exceeded 3, it was labelled as the sensory blockade duration and noted.

Results: All the enrolled 60 patients completed the study from 1st December 2016 to 30th June, 2017 making the study period more than 6 months. Patients were divided into two group i.e.” B” and “D” and there was no statistical significant difference in age, weight, height, BMI, and gender in between the two groups. The duration of sensory blockade in bupivacaine and dexamethasone group was 123.30±12.30 minutes while in bupivacaine alone group it's 113.50±14.29 minutes (p-value 0.006).

Conclusions: This study proves that there is significant difference present in sensory blockade of bupivacaine alone and bupivacaine plus dexamethasone combination when administered intrathecally for spinal anesthesia.

Keywords: Intrathecal, Bupivacaine, Dexamethasone, sensory blockade, spinal anesthesia
Regional anesthesia is preferred for any type of surgery whenever possible over general anesthesia. Among neuraxial blocks, Spinal anesthesia is widely used for orthopedic surgeries, cesarean section and even laparoscopic cholecystectomy is being done in spinal anesthesia. Regional techniques can even control pain from several hours to several days, depending upon the type of local anesthetic agent, adjuvant and technique used. Initial pain management may reduce subsequent pain in the days to weeks following surgery. Regional anesthesia is associated with lesser morbidity and has decreased chances of deep vein thrombosis. Greater reduction in pain makes the possibility of earlier hospital discharge and may improve the patient's ability to tolerate physical therapy. Different adjuvant like opioids, steroid, ketamine, dexmedetomidine have been used to improve the quality and prolong the effect of the local anesthetic action in different peripheral nerves and regional block techniques. Dexamethasone is the most commonly prescribed corticosteroid for pain. Dexamethasone has also been used as an adjuvant for spinal anesthesia. Dexamethasone has been shown to possess anti-inflammatory action in addition to increasing the duration of local anesthetics action. It also decreases the need of post-operative opioid requirement when used as adjuvant with local anesthetics in peripheral neural blocks. Nadia Bani-hashem and at al conducted a study showing that the addition of dexamethasone to bupivacaine increases the duration of sensory blockade in spinal anesthesia without complications. The duration of the sensory blockade was 119.1±10.6 minutes in the case group and 89.4±8.3 minutes in the control group with a P value less than 0.001; also pain-free period in the case group was more than that in the control group (P<0.001).

Rational of my study is to find the effect of addition of dexamethasone to bupivacaine in spinal anesthesia for orthopedic procedures. There are very few studies which tried to discover the outcome of stated combination. There are no local studies available. It will be cost effective and decrease the requirement of post-op analgesics if the treatment with better sensory blockade is used.

METHODS

STUDY DESIGN: Randomized Control trial

STUDY SETTING: Orthopedic operation theatre, Jinnah hospital Lahore

DURATION OF STUDY: Six months after approval of synopsis i.e. from 01-12-2016 to 30-06-2017

SAMPLING TECHNIQUE: Non probability purposive sampling.

SAMPLE SIZE: Sample size of 60 cases, 30 in each group is calculated with 99% confidence level and 95% power of test and taking duration of sensory blockade 119±10.69(8) minutes with bupivacaine dexamethasone combination and 89.44±8.37 (8) minutes in bupivacaine alone.

SAMPLE SELECTION:

INCLUSION CRITERIA:
1. Patients with status ASA I & II
2. Age 18-70 years
3. Patients going for elective orthopedic procedures on pelvis, lower limb.

EXCLUSION CRITERIA:
1. Refusal of patient to give informed consent
2. Pre-existing coagulation disorder: INR more than 1.5
3. Morbid obesity: BMI more than 30
4. Local infection: Any sign of inflammation, pus, pain at required site.
5. Diabetes Mellitus: Diagnosed case taking medications or undiagnosed case whose BSR > 200mg/dl

DATA COLLECTION PROCEDURE

After taking approval from ethical committee and taking informed consent, 60 patients fulfilling the selection criteria were selected for the study from operation theatres of Jinnah Hospital, Lahore. After taking informed consent, demographic information...
like name, age, sex, height, weight and contact were obtained. Then patients were divided into two groups by using lottery method. After IV line preparation, a 10 ml per kg lactated ringer’s solution was given to all patients as preload. Patients did not receive any premedication, and once patients after reached to the operating room, they were monitored with ECG, peripheral oxygen saturation (SPO2), and noninvasive arterial blood pressure (NIBP) and all was recorded at 5-minute intervals until the end of surgery and vital signs were recorded every 15 minutes in the Post Anesthesia Care Unit (PACU). Spinal anesthesia was performed in the sitting position either at L3–L4 or L4-L5 level through a midline approach using a 23-25 gauge Quincke spinal needle. Patients of the group B received 15 mg (2 ml) of 0.75% hyperbaric bupivacaine diluted in preservative free normal saline (2 ml) and patients of the group D received 15 mg (2 ml) of 0.75% hyperbaric bupivacaine and 8 mg preservative free dexamethasone 4 ml intrathecally. After performance of the spinal anesthesia patients were kept in supine position and oxygen 3-5 L per min was given through a face mask. The sensory block level was assessed by pin prick test with a short bevel needle along the mid-axillary line bilaterally. The sensory block level was evaluated every 5 minutes after one hour until a 4 sensory level regression from highest level or to the end of the surgery. Hypotension, a 30% decrease in systolic blood pressure from baseline or systolic blood pressure <90 mm Hg and bradycardia, HR<50 beats/min were treated by IV adrenaline 5-10 microgram plus crystalloid fluids; and IV atropine 0.5 mg respectively. Nausea and vomiting were evaluated and was treated with 0.15 mg/kg IV metoclopramide. After 4 dermatome block regression, pain assessment intraoperatively or in PACU was done using the visual analogue pain scale (VAS) between 0-10 (0 = no pain, 10 = the most severe pain) every 1 hour. When the postoperative VAS was higher than 6, it was treated by nalbuphine 2 mg IV. Patients were observed at time of discharge from hospital and 1 month later all were questioned about any neurologic deficit. The primary outcome was duration of sensory blockade of spinal anesthesia, as evaluated by VAS for pain scoring at interval of 5 minutes starting one hour after giving spinal anesthesia. The patients were instructed preoperatively about the use of the VAS for pain assessment on a 10-cm line (VAS; 0=no pain, 10=worst pain imaginable).

DATA ANALYSIS:

The data was entered and analyzed in SPSS version 20.0. Quantitative variables like duration of sensory blockade, age and BMI were measured in the form of mean ± SD. Qualitative variables like gender and BMI (≥30kg/m², <30kg/m²) were measured in the form of frequency and percentages. Both groups were compared by using independent sample t-test taking p-value < 0.01 as significant. Data was stratified for BMI, age and gender to address the effect modifiers. Post stratification an independent sample t-test was applied to check the significance with p-value ≤ 0.05 as significant.

RESULTS:

All the enrolled 60 patients completed the study from 1st December 2016 to 30th June, 2017 making the study period more than 6 months. Patients were divided into two group i.e.” B” and “D” and there was no statistical significant difference in age, weight, height, BMI, and gender in between the two groups. The mean age in group “B” was 38.87 ± 14.13 years and in group “D” was 42.20 ± 17.7 years (p-value 0.42). The independent t-test was applied and p-value resulted in 0.42 proving that there was no difference in mean age between two groups. Mean BMI in group B was 26.40 ± 4.16 and in group D was 25.08 ± 3.57 and p-value 0.195 hence no difference in mean BMI as well. The main result of the study i.e. mean duration of sensory blockade in bupivacaine and dexamethasone group was 123.30 ± 12.30 minutes while in bupivacaine alone group it’s 113.50± 14.29 minutes (p-value 0.006). The calculated p-value was 0.006 proving that there is a significant difference in adding dexamethasone to bupiva-
caine compared to bupivacaine alone for spinal anesthesia.

Tables 1, 2 & 3 show the stratification and comparison of age gender and BMI in between the two groups. Post-stratification independent t-test was applied to see any significant difference after stratification.

Independent student's t-test was applied taking p-value above 0.05 as significant and it can be seen that there is no significant difference in 18-39 age group but significant difference is there in 40+ age group.

Independent student's t-test was applied taking p-value above 0.05 as significant and it showed that there is no significant difference in duration of sensory blockade in males but there is significant difference in females.

Independent student's t-test was applied taking p-value above 0.05 as significant and it showed that only in overweight patients there was no significant difference for sensory blockade. Only 1 case in each group in underweight category, therefore, t-test can't be applied.

**DISCUSSION**

Spinal anesthesia is the easiest regional anesthesia which can be given to patients undergoing orthopedic procedures with very less and mostly manageable complications. Many surgeries such as arthroscopy, dynamic hip screw, dynamic compression plates for fractures and fractures of ankle joint are done in spinal anesthesia. A single study even concluded that spinal anesthesia is superior than general anesthesia for total hip arthroplasty. Some of these procedures are lengthy and difficult to manage for post-operative pain. Spinal anesthesia provides not only excellent peroperative time for completion of surgery but also leads to better post-operative analgesia than general anesthesia. In order to increase the duration of blockade and increase the effect of post-operative analgesia, many adjuncts have been tried in spinal anesthesia. Brian D, Michael, Russell B and et al concluded that knee arthroplasty can be conducted in spinal anesthesia with using morphine and clonidine as adjuvants and also the 24 hours post-operative opioid was significantly lower in group given intrathecal clonidine and morphine along with bupivacaine. But both these adjuvants are not complication free. Clonidine is related to hypotension and morphine is related to nausea, vomiting and respiratory depression. An adjuvant with minimal side effects is required to produce not only deep sensory blockade but also have prolonged post-operative analgesic window. Shaheena Parveen, Masrat Jan, Arshi Taj, Arif A. Bhat proved in their study that adding dexamethasone in bupivacaine significantly increase sensory blockade duration. Their result showed that duration of sensory block in dexamethasone and bupivacaine group was 1085.73 ± 234.23 minutes and in bupivacaine alone group it was 322.37 ± 138.37 minutes (p value <0.0001). Dexamethasone is a widely used corticosteroid, it exerts its analgesic effect by slowing down the conduction in C fibers. Like many corticosteroids, dexamethasone also has local anesthetic properties. It is considered that all corticosteroids may reduce the sensiti-
zation in the dorsal horn neurons. In addition, they may have a direct effect on the CNS by effecting the production of neurotransmitters in spinal cord.

Nadia Bani-hashem, Bahman Hassan-nasab, Ebrahim Alijan Pour and et al found in their study that adding dexamethasone with bupivacaine for spinal anesthesia increases sensory blockade when compared to bupivacaine alone i.e. 119 ± 10.69 minutes and 89.44±8.37 minutes respectively (p value 0.001)(8). But in our study although we found that there is significant difference in sensory blockade of bupivacaine and dexamethasone vs bupivacaine alone but our significance p-value is lower than found above. The mean duration of sensory blockade in bupivacaine and dexamethasone was 123.30±12.30 minutes while in bupivacaine alone it’s 113.50 ± 14.29 minutes (p-value 0.006). The difference in both studies could be due to the difference in operational definition of sensory blockade and due to the difference concentration of bupivacaine used in both studies i.e. we used bupivacaine 0.75% and total volume was 4ml while in parent study they used 0.5% bupivacaine and 5ml volume. Although clinically there is benefit of 10 minutes only, but it better to give dexamethasone in combination with local anesthetic rather giving local anesthetic alone. After stratification of demographic data, it is observed that there is no significant difference in males and overweight patients. More studies are needed to evaluate its post-operative analgesia and post-operative analgesic consumption in 24 hours to deem this combination worthy to grant it as a standard

CONCLUSION
This study proves that there is significant difference present in sensory blockade of bupivacaine alone and bupivacaine plus dexamethasone combination when administered intrathecally for spinal anesthesia.

REFERENCES
Abstract

Introduction: Regional anesthesia has advantages over general anesthesia such as leaving the airways open, keeping airway reflexes intact, reducing the risk of aspiration, decreasing the post-operative recovery time and early mobilization. Among regional techniques, Intravenous regional anesthesia (IVRA) is a reliable, simple, and cost-effective technique in trauma patients that is used for performing short surgical procedures in the extremities. This anesthesia technique is considered easy with fast anesthesia induction, fast recovery, fast muscle relaxation, and with better ability to control anesthetized region. An ideal combination of agents for IVRA should have rapid analgesic effect to reduce tourniquet pain and its effects should last longer enough after deflating tourniquet. Many adjuvants have been tried. In our study we have compared the additive effect of ondansetron to local anesthesia for IVRA. This will help in revising guidelines for intravenous regional anesthesia in Pakistani surgical patients. In addition, there is no research carried out in local population. If we successfully validate this point, then we will decrease post-operative analgesics requirement and thus decreasing costs along with improving patient outcome.

Objective: To compare mean duration of the sensory blockade of lidocaine alone versus lidocaine and ondansetron in bier’s block for forearm, hand and wrist surgery

Study design: Randomized Control trial

Study setting: Orthopedic operation theatre, Jinnah hospital Lahore

Duration of study: Six months after approval of synopsis i.e. 23rd June, 2017 till 31st December, 2017

Methods: 80 patients fulfilling the selection criteria were recruited for the study. After taking informed consent and demographic information, patients were randomly recruited to two groups using a computer generated random number list. Group L was injected with mixture of 40 ml dilution of 2% lidocaine (3mg/kg) and 2ml normal saline and Group L+O was injected with mixture of 40 ml dilution of 2% lidocaine (3mg/kg) and 2ml (8mg) ondansetron. After doing Esmarch on operative hand, a tourniquet was placed around the upper arm and proximal cuff was inflated to 250 mmHg. The drugs was administered in operative hand in respective groups. Sensory blockade was monitored with pin prick test, a small, clean, sharp object such as a pin was gently applied to the skin and the patient was asked to describe if he/she feels it or not. Loss of feeling of pin prick marked the loss of sensation while feeling the pin prick marked the return of sensation.

Results: The mean age in group “L” was 36.20 ± 13.03 and in group “L+O” was 35.00 ± 13.43 (p-value 0.73) proving that there was no difference in mean age between two groups. Mean BMI in group L was 23.93 ± 2.69 and in group L+O was 23.01 ± 2.74 and p-value 0.13 hence no difference in mean BMI as well. The main result of the study i.e. mean duration of sensory blockade in group L and group L+O found to be 107.13 ± 32.74 & 114.38 ± 24.67 respectively. The calculated p-value was 0.27 proving that there is no significant difference of adding ondansetron in lidocaine for intravenous regional block.

Conclusion: There is no significant difference in mean duration of the sensory blockade of lidocaine alone versus lidocaine and ondansetron in bier’s block for forearm, hand and wrist surgery.

Keywords: Ondansetron, lidocaine, Bier’s block, intravenous regional anesthesia, post-operative analgesia, sensory blockade, Adjuvants
Regional anesthesia applications gradually became more up-to-date and preferred methods. It has advantages such as leaving the airways open, keeping airway reflexes intact, and reducing the risk of aspiration risk in emergency patients when compared to general anesthesia. Among regional techniques, Intravenous regional anesthesia (IVRA) is a reliable, simple, and cost-effective technique in trauma patients that is used for performing short surgical procedures in the extremities. It leads to short durations of the perioperative morbidity and postoperative hospital stay. This anesthesia technique is considered easy with fast anesthesia induction, fast recovery, fast muscle relaxation, and with better ability to control anesthesia region. An ideal anesthetic agent for IVRA should have rapid analgesic effect to reduce tourniquet pain and its effects should last long enough after deflating tourniquet. Researches were carried out to reduce the side effects and improve the anesthetic quality and several adjuvant substances were added to local anesthetics. Such substances include opioid analgesics (morphine, meperidine, fentanyl, sufentanil), antihistaminics, midazolam, alpha-2 mimetics (clonidine, dexmedetomidine), nonsteroid anti-inflammatory agents (ketorolac, tenoxicam, acetyl salicylate, paracetamol), ketamine, and magnesium combinations which are thought to potentiate the effects of local anesthetics. Ondansetron is a specific 5-Hydroxy tryptamine-3 (5-HT3) antagonist, which is used as an antiemetic drug while has no significant side effect. It has analgesic effect.

Honarmand A, Safavi M and Adineh-Mehr L. found that adding ondansetron to lidocaine in bier’s block leads longer for post-operative pain to appear i.e. 252 ± 50.2 when compared to lidocaine alone i.e. 105.3 ± 38.6 minutes.

This study is being carried out to validate the improvement seen in sensory blockade time after addition of Ondansetron with Lidocaine. This will help in revising guidelines for intravenous regional anesthesia in Pakistani surgical patients. In addition, there is no research carried out in local population. If we successfully validate this point, then we will decrease post-operative analgesics requirement and thus decreasing costs along with improving patient outcome.

METHODS
STUDY DESIGN: Randomized Control trial
STUDY SETTING: Orthopedic operation theatre, Jinnah hospital Lahore
DURATION OF STUDY: Six months after approval of synopsis i.e. 23rd June, 2017 till 31st December, 2017
SAMPLING TECHNIQUE: Non probability purposive sampling.
SAMPLE SIZE: Sample size of 80 cases, 40 in each group was calculated with 95% confidence level and 80% power of test and taking sensory blockade time 252 ± 50.2 minutes with odansetron with lidocaine when compared to lidocaine alone 105.3 ± 38.6 minutes

SAMPLE SELECTION
INCLUSION CRITERIA
1. Patients with status ASA I & II (Annexure II)
2. Age 18-70 years
3. Both genders
4. Patients going for elective orthopedic procedures on wrist hand and forearm e.g. wrist or hand ganglionectomy, carpal tunnel release, Dupuytren contractures, reduction of fractures etc.

EXCLUSION CRITERIA
1. Refusal of patient to give informed consent
2. Pre-existing coagulation disorder. INR more than 1.5
3. Morbid obesity. BMI more than 30
4. Local infection e.g. Cellulitis, skin infection etc.
5. Known Diabetes Mellitus BSR more than 180mg/dl

DATA COLLECTION PROCEDURE
After taking approval from ethical committee
and taking informed consent, 80 patients fulfilling the selection criteria were recruited for the study from orthopedic operation theatres of Jinnah Hospital, Lahore. After taking informed consent, demographic information like name, age, sex, height, weight and contact, was obtained. Then patients were randomly recruited to two groups using a computer generated random number list. In both groups, lidocaine will be given to maximum dose of 3mg/kg and diluted with normal saline to 40ml. Group L was injected with mixture of 40 ml dilution of 2% lidocaine (3mg/kg) and 2ml normal saline and Group L+O was injected with mixture of 40 ml dilution of 2% lidocaine (3mg/kg) and 2ml (8mg) ondansetron. Two 18 gauge intravenous cannula were inserted; one in a dorsal vein of the operative hand and the other in the opposite hand for infusion of crystalloid before beginning the anesthetic block. After doing Esmarch on operative hand, a 10cm pneumatic padded double-tourniquet were placed around the upper arm and proximal cuff was inflated to 250 mmHg. The drugs was administered in operative hand in respective groups along with recording data of blood pressure, heart rate and oxygen saturation. After loss of sensations in all dermatomes operative site, distill cuff was inflated to 250 mm Hg and after that proximal cuff was deflated. Any complications were noted and documented. Sensory blockade was monitored with pin prick test, a small, clean, sharp object such as a pin was gently applied to the skin and the patient was asked to describe if he/she feels it or not. Loss of feeling of pin prick marked the loss of sensation while feeling the pin prick marked the return of pain and sensation. Continuous monitoring of sensory block was checked at interval of 5 minutes and noted in proforma attached (Annexure III).

**DATA ANALYSIS**

The data was entered and analyzed in SPSS version 20.0. Quantitive variables like age, mean time of sensory blockade and BMI were measured in the form of mean ± SD. Qualitative variables like gender and status were measured in the form of frequency and percentages. Both groups were compared for mean time of sensory blockade by using independent sample t-test taking p-value <0.05 as significant. Stratification was done with respect to age, gender and BMI. Post-stratification independent t-test was applied taking p-value ≥ 0.05 as significant.

**RESULTS**

All the enrolled 60 patients completed the study from 23rd June 2017 to 31st December, 2017 making the study period more than 6 months.

Patients were divided into two group i.e.” L” and “L+O”. The mean age in group “L” was 36.20 ± 13.03 and in group “L+O” was 35.00 ± 13.43. The independent t-test was applied and p-value resulted in 0.73 proving that there was no difference in mean age between two groups. Mean BMI in group L was 23.93 ± 2.69 and in group L+O was 23.01 ± 2.74 and p-value 0.13 hence no difference in mean BMI as well.

The main result of the study i.e. mean duration of sensory blockade in group L and group L+O found to be 107.13 ± 32.74 & 114.38 ± 24.67 respectively. The calculated p-value was 0.27 proving that there is no significant difference of adding ondansetron in lidocaine for intravenous regional block.

Tables 1, 2 & 3 show the stratification and comparison of age gender and BMI in between the two groups. Post-stratification independent t-test was applied to see any significant difference after stratification.

After applying independent student's t-test, it was found that there was no significant difference in mean sensory block time even in stratified age groups.

After applying independent student's t-test, it was found that there was no significant difference in mean sensory block time in both groups even after gender stratification. Group L+O has 1 female patient so therefore, t-test can't be applied.

After applying independent student's t-test, it was found that there was no significant difference in
mean sensory block time in both groups even after stratification of body mass index.

**DISCUSSION**

Giving general anesthesia for short procedures such as Dupuytren contracture, k-wiring of metacarpals or removal of k wires from forearm bones is time taking and will only increase cost due to prolonged post-operative recovery period. Regional anesthesia is the preferred method for such type of short procedures. Intravenous regional anesthesia has gained popularity again and being practiced for its easiness when compared to peripheral nerve blocks especially in upper limb, forearm surgeries. Even their combination have been also successfully used for reduction of forearm fractures. The ideal IVRA should include rapid onset of sensory and motor block, reduced LA dose, reduced intraoperative and tourniquet pain, prolonged postoperative analgesia, and minimal side effects. Adjuncts to LA can help to achieve nearly ideal IVRA. That is why we selected ondansetron as adjuvant due to its additive effect of controlling post-operative analgesia. Considering it’s local anesthetic like effect, it should increase the effect of lidocaine in IVRA.

In our study, we found very varying results in both groups due to understanding and compliance of patient. It may due to the fact that in our study we checked the sensory blockade in terms of pinprick in dermatomes that were anesthetized and pin prick is subjectively different from patient to patient as initial return of touch feeling can be confused with pin prick pain.

We found that the mean duration of sensory blockade in L and L+O groups 107.13 ± 32.74 & 114.38 ± 24.67 respectively. But the parent study done by Azim Honarmand, Mohammadreza Safavi, and Leili Adineh-Mehr resulted in first time of operated pain at 105.3 ± 38.6 & 252 ± 50.2 minutes in lidocaine alone and lidocaine with ondansetron groups respectively. Lidocaine group have almost same result but there is huge difference in ondansetron group. The difference may be due to the comparison that we checked the sensory blockade in terms of pinprick. The underlying difference may be due to studying different sensations conducted by different types of nerve fibers. Nociception is conducted by A-δ while Type A-a are the fibers from muscle spindle endings and the Golgi tendon, Type A-β, and type A-γ, are afferent fibers from stretch receptors. Pinprick can produce sensation at spindle endings and stretch receptors as well. Our study was limited by the fact that we did not gather data regarding operative pain felt in terms of visual analog system that could have given us better understanding of difference after adding ondansetron in lidocaine for intravenous regional block.

**CONCLUSION**

There is no significant difference in mean dura-
tion of the sensory blockade of lidocaine alone versus lidocaine and ondansetron in Bier’s block for forearm, hand and wrist surgery.

REFERENCES

**Diffuse large B-cell lymphoma (DLBCL)** is the most common type of non-Hodgkin lymphoma (NHL) in the world, and accounts for 30%–40% of all adult NHLs. The clinicopathologic and molecular genetic diversity of DLBCL is reflected in the 2008 WHO classification of lymphomas that describes more than 15 DLBCL subgroups based on distinct morphologic, biologic, immunophenotypic, and clinical parameters. Although potentially curable, 40% of patients with DLBCL will die of relapsed or refractory disease. In Europe and USA, the current annual incidence of NHL is estimated to be 15–20 cases/100,000. DLBCL accounts for approximately 30–40% of all newly diagnosed B-cell NHL cases in Western countries, and for an even higher percentage in developing countries.

Over the past decade there have been significant improvements in long-term disease control and survival in patients with DLBCL, with over half of patients maintaining remissions beyond 5 years. This is largely due to the routine incorporation of rituximab into the standard anthracycline-based chemotherapy regimen of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). Based on literature, rituximab-CHOP (R-CHOP) has become the standard of care therapy for patients with newly diagnosed DLBCL.

It is noteworthy that Gene expression profiling (GEP) has been incorporated in WHO 2016 to

**Abstract**

**Purpose:** The aim of this study was to determine the responses of therapy with six cycles of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone in newly diagnosed untreated Germinal Centre B cell (GCB) and Activated B cell (ABC) subtypes of diffuse large B cell lymphoma.

**Patients and methods:** The design of this study was retrospective case series. 63 patients having untreated GCB/ABC subtypes of DLBCL were included. All the patients were administered and assessed for response after six cycles of rituximab 375mg/m², cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², vincristine 1.4 mg/m² (capped at 2 mg), all on day 1; prednisone 100 mg/m² per day from day 1-5. The quantitative variables like age, subtypes and various stages of disease were calculated by taking mean and standard deviation. The response was assessed in percentage and frequencies and compared by applying and chi square test.

**Results:** Out of 43 patients, mean age was 58.89±12.64 years. Male patients 34(54%) were more common than females. There were 37(58.7%) patients had GCB and 26(41.3%) patients had ABC subtype of DLBCL. In GCB vs ABC, complete and partial responses were observed in 42(66.7%) and 19(30.2%) patients respectively.

**Conclusion:** R-CHOP is a valuable treatment for newly diagnosed untreated patients of DLBCL. Molecular subtype of DLBCL should be evaluated for prognosis determination and planning of therapy. Further studies are warranted to explore appropriate therapy in local population for various subtypes of DLBCL patients.

**Key words:** Non- Hodgkin Lymphoma, Chemo-immunotherapy, R-CHOP, GCB vs ABC Diffuse Large B cell Lymphoma,
classify DLBCL. Gene expression profiling is the measurement of the activity (the expression) of thousands of genes at once, to create a global picture of cellular function. It can identify at least 3 molecularly distinct DLBCL subtypes based on differential expression of genes involved in B-cell development, including activated B-cell-like (ABC), germinal center B-cell-like (GCB), and unclassified subtypes. GCB and non-GCB DLBCL subtypes can also be distinguished using immunohistochemistry based on expression of markers including CD10, BCL6, and MUM-1.\(^9\) As GEP profiling is not widely available we would be using (HANS Algorithm) to classify the subtypes according to immunohistochemistry. This is important clinically for treatment and prognosis of patients with Diffuse Large B cell Lymphoma.

**METHOD**

After taking approval from hospital ethical committee, 63 patients coming through OPD were enrolled. Informed consent was taken from patients having age ranges from 20-80 years and included both males as well females. All were newly diagnosed untreated patients of GCB or ABC subtypes of diffuse large B cell lymphoma. Pregnant/nursing women and those patients having CNS involvement (on history / examination) were excluded as were those having post-transplantation lymphoproliferative disorder or history of cardiac disease.

**METHOD**

The design of the study was retrospective case series. It was carried out in department of Medical Oncology, Hameed Latif Hospital, Lahore. The study was carried out between 1st December, 2017 to 31st May, 2018. Sample size of 63 cases taken by 95% confidence level, 11% margin of error and expected percentage of partial response 27%8. Non-probability, consecutive sampling was done.

All the patients were advised six cycles of rituximab 375mg/m\(^2\), cyclophosphamide 750 mg/m\(^2\), doxorubicin 50 mg/m\(^2\), vincristine 1.4 mg/m\(^2\) (capped at 2 mg), all on day 1; prednisone 100 mg/m\(^2\) per day from day 1-5. For assessment of complete response and progression free survival PET/CT scan were performed. Complete and partial response after 6 cycles was recorded as per operational definition. All the information was recorded on Proforma. The data was entered and analyzed by using SPSS version 20. Mean and standard deviation was calculated for all quantitative variables like age. Frequency and percentage was calculated for all qualitative variables like gender, type of DLBCL, complete response and partial response. Effect modifiers like age, gender and type of DLBCL were controlled by stratification. Post-stratification chi-square test was applied. P-value ≤ 0.05 will be taken as significant.

**RESULT**

Out of 63 patients, mean age of the patients was 58.89±12.64 years Range: 29 -79 years. 34 (54%) patients were male. GCB subtype of DLBCL was present in 37 (58.7%) patients had and 26 (41.3%) patients had ABC subtype of DLBCL. When the response was assessed and compared using chi square, 42 (66.7%) patients had complete response and 21 (33.3%) patients had either partial responses or stable disease.

In 34 male patients, 23 (67.6%) patients had complete response. Out of 29 female patients, 19 (65.5%) patients had complete response. In 37 patients with GCB patients, 26 (70.3%) patients had complete response while in 26 patients with ABC subtype of DLBCL, only 16 (61.5%) patients had complete response. Partial response was present in 10 (27%) patients with GCB as compared to 9 (34.6%) patients with ABC subtype.

**Figure 1:** Complete Response ABC vs. GCB after Completion of Planned 6 Cycles of R-CHOP

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[The image contains a bar chart comparing complete response rates between ABC and GCB subtypes after completion of 6 cycles of R-CHOP.]
DISCUSSION

Diffuse large B cell lymphoma (DLBCL) is the most common lymphoid malignancy in adults and the most frequent subtype of non-Hodgkin lymphoma (NHL) in all countries around the world and every age group. That is why treatment directed at patients of DLBCL has a special importance and needs continuous refinements.

As for the results of my study, mean age of the patients was 58.89±12.64 years. Majority of the patients (52.4%) had age between 61.80 years, 54% patients were male and 58.7% patients had GCB. Complete and partial responses were observed in 66.7% and 30.2% patients respectively.

This result is similar to the ones mentioned in multiple international publications. Wilson et al performed a phase III randomized study of R-CHOP versus DA-EPOCH-R and molecular analysis of untreated diffuse large B-cell lymphoma: in a large study done by CALGB/Alliance 50303, they found 62% complete response and 27% partial response in patients of DLBCL. It suggests R-CHOP as the standard of care for treatment of DLBCL which is keeping in with the results of my study. In another study Huang et al also investigated outcome of R-CHOP or CHOP regimen for germinal center and non-germinal center subtypes of Diffuse Large B-Cell lymphoma of Chinese patients. Complete response was observed in 72.7% patients after 6 cycles of R-CHOP in GCB patients which favors my results as well. It is worth mentioning here that as in these studies the results and responses were similar throughout sub groups, marking R CHOP as an effective treatment in DLBCL and highlighting the decreased response observed in ABC subtype.

With relevance to above statement is this by Nowakowski et al conducted their study on lenalidomide combined with R-CHOP overcomes negative prognostic impact of non-germinal center B-cell phenotype in newly diagnosed diffuse large B-cell lymphoma: a phase II study. They noted 80% and 18% complete and partial response respectively. This study denotes that further drugs or a different regime may be needed to improve outcome in some subtypes of DLBCL.

CONCLUSION

R-CHOP is a valid treatment for newly diagnosed untreated patients of diffuse large B-cell lymphoma. The results of our study show efficacy in terms of complete and partial response after 6 cycles of R-CHOP in both GCB and ABC subtypes of DLBCL. However the results seem better for the

**Figure 2**: Partial Response ABC vs GCB after Completion of Planned 6 Cycles of R-CHOP

**Table 1**: Demographic Data of Patients Included in Study

<table>
<thead>
<tr>
<th></th>
<th>Frequency(n)</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patients</strong>:</td>
<td>63</td>
<td>100</td>
</tr>
<tr>
<td>Male</td>
<td>34</td>
<td>54</td>
</tr>
<tr>
<td>female</td>
<td>22</td>
<td>36</td>
</tr>
<tr>
<td>Age (Median ± standard deviation)</td>
<td>58.89±12.64 years</td>
<td></td>
</tr>
<tr>
<td>20-40 years</td>
<td>8</td>
<td>12.7</td>
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<tr>
<td>41-60 years</td>
<td>22</td>
<td>34.9</td>
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<tr>
<td>61-80 years</td>
<td>33</td>
<td>52.4</td>
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<td><strong>Disease characteristics</strong></td>
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<td><strong>Histological subtype</strong>:</td>
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<td></td>
</tr>
<tr>
<td>ABC</td>
<td>26</td>
<td>41.3</td>
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<tr>
<td>GCB</td>
<td>37</td>
<td>58.7</td>
</tr>
<tr>
<td><strong>Stage of disease</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>3</td>
<td>4.7</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>6</td>
<td>9.5</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>7</td>
<td>11.1</td>
</tr>
<tr>
<td>Stage III B</td>
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<td>4.7</td>
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<tr>
<td>Stage IV A</td>
<td>25</td>
<td>39.68</td>
</tr>
<tr>
<td>Stage IV B</td>
<td>6</td>
<td>9.52</td>
</tr>
</tbody>
</table>
RESPONSE OF CHEMO-IMMUNOTHERAPY IN GERMINAL CENTER B CELL VERSUS ACTIVATED B CELL

GCB sub group than the ABC sub group warranting a need for further research in optimizing treatment in ABC type of DLBCL.

REFERENCES

Ematological malignancies are the cancers that arise in blood forming tissues of body like bone marrow or cells that are part of our immune system. These are broadly classified into leukemia,

**Abstract**

**Background:** Ophthalmic examination is a way of early detection of vessels and nerves involvement in the body by a systemic disease and also it may be the only site of disease relapse in diseases like leukemia. Association of these changes is well established in acute leukemia. This study is designed to look for spectrum of ophthalmic changes in patients of chronic myeloid leukemia (CML) presenting at Mayo Hospital Lahore.

**Methodology:** A cross sectional study to look for presence of any ophthalmic changes in patients of CML. Diagnosed patients with chronic myeloid leukemia were enrolled and after informed consent in the department of medical Oncology Mayo Hospital, Lahore. Their eyes were examined for retinal corneal, anterior and posterior chamber as well as visual acuity. Parameters related to their disease of CML like percentages of blast cells, philadelphia chromosomes (Ph+ cells), peripheral smear, as well as Sokal score was calculated and compared with the eyes manifestations determined by the ophthalmologist. The quantitative variables like age was calculated by taking mean and standard deviation. The ophthalmic changes were assessed in percentage and frequencies and compared with CML disease parameters by applying chi square test using the Statistical Package for Social Sciences for Windows software, version 23.

**Results:** The study subjects (n = 66) comprised 34 (52%) females. Mean age of the study population was 38.44, ±13.03 (Range: 13 - 86 years. 7 patients (10.6%) had diabetes, 7(10.6%) had hypertension and 1 patient(1.5%) had ischemic heart disease. All the patients were Ph +, with the range of Ph+ positive cells from 8 to 100% (mean 84.98±26.54) determined by FISH on peripheral blood. 13 (20%) patients were categorized having low risk disease, 37 (56.1%) intermediate risk and 16 (24.2%) had high risk disease calculated according to Sokal score. 45(68.2%) patients were taking Imatinib while 21(31.8%) were taking Nilotinib.

On detailed ophthalmic examination 37(56%) patients had visual acuity (VA) of 6/6, 13 (19.7%) had VA 6/9, and rest of the patients 13 (20.1%) with VA of 6/12 or less. Anterior chamber was found to be normal in 61(92.4%) patient while 5(7.6%) patients had cataract. Posterior chamber only one (1.5%) patient had choroidal detachment on posterior chamber examination. Majority of the patients but retinovascular changes were observed in 12 (18.2%) patients which include sub-hyaloid hemorrhages(4.5%). Macula of 2 patient (3%) showed scarring only. Data was analyzed for association with other variables like gender, comorbid illness, Ph+ cell, Tyrosin Kinase inhibitors (TKIs) received ,presenting Hemoglobin (Hb), total leukocyte count (TLC), platelet counts,%age of blast cells in marrow and spleen size at diagnosis but none of these was found significant.

**Conclusions:** Eye is an important organ of body and wide spectrum of systemic diseases including leukemias have their manifestation in eyes. These changes are more often seen in association with acute leukemias, however, their importance in chronic leukemias cannot be denied. This is imperative to get ophthalmic examination initially and then periodically in CML patients to assess and prevent any eye related complications related to disease or therapy.
lymphomas and multiple myeloma, a disorder of plasma cells.\(^1\) According to WHO leukemia account for 3.5% of all cancer in Pakistan and are responsible for 4.1% of cancer mortalities.\(^2-5\) Leukemia are broadly classified into acute and chronic leukemia.\(^1\) Chronic leukemia are categorized into chronic myelogenous leukemia (CML) and chronic lymphocytic leukemia (CLL)\(^6\). chronic myelogenous leukemia (CML) accounts for 20% of leukemia with an incidence of 10 in 1,000,000 people.\(^7\)

Ocular involvement in leukemias result due to increased viscosity of blood, thrombocytopenia, anemia, decreased immunity of the patient, side effects of treatment modalities, and direct leukemic cells infiltration into various structures of eyeball.\(^8\) It includes, Subconjunctival haemorrhages, Leopard spot pattern of fundus, acute iridocyclitis, hyphema, endophthalmitis, vitirits, optic neuropathy due to leukemic infiltration of optic nerve,\(^9\) leukemic retinopathy, retinal and pre-retinal haemorrhages, vitreous haemorrhage, papilloedema, anterior segment uveitis, toxoplasmosis, fungal infections, keratoconjunctivitis sicca, corneal ulceration, predisposition to ocular granulocytic sarcoma\(^10,11\) Ocular involvement is more common in adults with myeloid leukemia.\(^12\) Retina is affected more than any other ocular tissue due to increased viscosity of blood, microaneurysms are formed, which burst and lead to vitreous haemorrhage ending up in serous retinal detachment.\(^13,14\) Extraocular involvement of leukemias such as lacrimal punctum, lids and orbit is very rare.\(^15\)

Ophthalmic changes are seen most commonly in acute leukemia than in chronic leukemia.\(^16\) there is limited data available on ophthalmic manifestation in chronic leukemia especially from resource limited countries like Pakistan. Therefore, a cross sectional stud was designed to look for spectrum of ophthalmic changes if present in patients of chronic myelogenous leukemia. Aim of study is to determine spectrum of ophthalmic changes in patients with chronic myelogenous leukemia.

**METHODS**

All diagnosed patients of chronic myelogenous leukemia (CML) presenting to indoor and outdoor department of Mayo Hospital Lahore were included in the study after getting informed consent. Diagnosis of CML was confirmed on history, physical examination, bone marrow biopsy, t (9;22) detected by FISH on peripheral blood. Ultrasound abdomen for spleen size and complete blood count was done at baseline and sokal score was determined at baseline to risk stratify the patients. Co-morbid conditions of the patients were also taken into consideration so we could differentiate between ophthalmic changes due to comorbid conditions and CML.

Visual acuity was determined by using Snellen chart, rest of ophthalmic examination was done by using indirect fundoscopy and slit lamp examination after dilating pupils with 1% tropicamide eye drops.

The collected data were entered to and analyzed using the Statistical Package for Social Sciences for Windows software, version 23. An initial frequency count and percentages were obtained for all the data. Descriptive statistics were reported as means, frequencies, percentages, and proportions. Inter-group comparisons were performed using the Chi-square test. All P < 0.05 were accepted as statistically significant.

**RESULTS**

The study subjects (n = 66) comprised 32 males and 34 females whose age ranged from 13 years to 86 years (mean = 38.44, ±13.03). 51(77.3%) patients had no co-morbid illness while 7 patients(10.6%) had diabetes,7(10.6%) had hypertension and 1 patient(1.5%) had ischemic heart disease as comorbid illness. Ph+, with percentage of Ph+ positive cells ranged from 8 to 100% (mean 84.98 ± 26.54) determined by FISH on peripheral blood at start of therapy. 20(30%) patients were categorized having low risk disease, 37(56.1%) intermediate risk and 9 (13.6%) had high risk disease according to Sokal score calculated at presentation.
45(68.2%) patients were started on Imatinib while 21(31.8%) were taking Nilotinib. At baseline mean hemoglobin was 10.31g/dl±1.99, mean TLC count 58.86×109/L ±77.75 and mean platelet count 332.61×109/L±231.7. mean percentage of blast cells in bone marrow was 5.61±11.03. mean spleen size at diagnosis was 18.07cm±3.83.

**Table 1: Demographic Data of Patients Included in the Study**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Count</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Patient</td>
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<td>100</td>
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<tr>
<td>Male</td>
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<td>48.5</td>
</tr>
<tr>
<td>Female</td>
<td>34</td>
<td>51.5</td>
</tr>
<tr>
<td>Married</td>
<td>57</td>
<td>86.3</td>
</tr>
<tr>
<td>Unmarried</td>
<td>9</td>
<td>13.7</td>
</tr>
<tr>
<td>co-morbid illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>51</td>
<td>77.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7</td>
<td>10.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7</td>
<td>10.6</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Table 2: Details of Various Retino-vascular Changes in Eyes of CML Patients**

<table>
<thead>
<tr>
<th>Retino-vascular Changes</th>
<th>Frequency (n=66)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>53</td>
<td>80.3</td>
</tr>
<tr>
<td>sub hyaloid hemorrhages</td>
<td>3</td>
<td>4.5</td>
</tr>
<tr>
<td>dot n blot hemorrhages</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>hard exudates</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>neo-vascularization</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>peri vascular sheathing</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>retinal atrophy</td>
<td>2</td>
<td>3.0</td>
</tr>
</tbody>
</table>

**Table 3: Optic Disc Changes in Eye in Eyes of CML Patients**

<table>
<thead>
<tr>
<th>Optic disc changes</th>
<th>Frequency (n=66)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>54</td>
<td>81.8</td>
</tr>
<tr>
<td>edema</td>
<td>5</td>
<td>7.6</td>
</tr>
<tr>
<td>pallor</td>
<td>6</td>
<td>9.1</td>
</tr>
</tbody>
</table>

On detailed ophthalmic examination 37(56%) patients had visual acuity (VA) of 6/6, 13 (19.7%) had VA 6/9, 7(10.6%) with VA of 6/12, 4(6.1%) with 6/18 and 1 with 6/60 while 4 patients had perception of light only. Anterior chamber was found to be normal in 61(92.4%) patient while 5(7.6%) patients had cataract. Posterior chamber examination showed no remarkable findings in 62(93.9%) patients while 1(1.5%) patient had choroidal detachment and 2 (3%) had choroidal atrophy. 53(80.3%) patients had normal retinal examination while retinovascular changes were observed in 12(18.2%) patients which include sub-hyaloid hemorrhages (4.5%), dot and blot hemorrhages (3%), hard exudates (3%), neovascularization (3%) peri-vascular sheathing (3%) and retinal atrophy (3%). CD ratio of 0.2-0.4 was found in 56(84.8%) patients. 4(6.2%) had ratio of 0.5, 3 patient (1.5%,1.5%,1.5%) had value of 0.6,0.7 and 0.8 respectively while CD ratio of three patient couldn’t be determined. Macula of only 2 patient (3%) showed scarring with 62(95.5%) having normal macula. Optic disc edema was seen in 5(7.6%) patient while 6(9.1%) patients had optic disc pallor with 54(81.8%) having absolutely normal optic disc.

Examination beyond anterior chamber was not done in one patient due to poor visibility. Considering retin-vascular and optic disc changes to be more significant, data was analyzed to find any association with various variables like gender, comorbid illness, %age of Ph+ cell in peripheral smear, TKI received, presenting Hb, TLC, Platelet counts,%age of blast cells in marrow and spleen size at diagnosis but none of these was found significant. Below given is table of p values of these changes with various variable.
Ophthalmic involvement in leukemia is not uncommon and may be the first sign of disease relapse. It is important to know about different ophthalmic manifestations of leukemia as eye is the site where we can directly see involvement of vessels and nerves by leukemia. Eye changes are seen in 9-90% of leukemia cases. Ophthalmic involvement in leukemia may occur as direct infiltration or indirect involvement. Direct or primary involvement in leukemia occurs by direct infiltration of malignant cells into various structures of eye. It manifests as orbital or uveal infiltration, optic nerve involvement leading to neuro-ophthalmic signs and symptoms, papilledema and involvement of various cranial nerves. While indirect or secondary involvement occurs secondary to various conditions associated with leukemia like retinal or choroidal hemorrhages due to thrombocytopenia, ischemia secondary to anemia, vascular occlusion secondary to hyper viscosity, infections due to immunosuppression. It can also occur as a result of treatment of leukemia or as GVHD after stem cell transplantation. Though any part of eye can be involved, retina is seen to be most commonly involved by leukemia. These changes are more common in acute and myeloid leukemia than chronic and lymphoid leukemia. Survival rates are lower in patients who develop ophthalmic involvement probably due to concomitant involvement of central nervous system.

This study was done specifically on patients of chronic myeloid leukemia who presented to oncology Ward of Mayo Hospital Lahore to look for any ophthalmic changes if present and also to correlate these changes with various patient related and disease related parameters like gender, presenting cell counts, spleen size, sokal score etc. Previously done studies have shown presence of some of these changes in patients of CML particularly in retina. An Indian study done in 2015 in 27.8%, while in in Malaysian study (2003) 39.5% and in Nigerian study (2010) 14.35% patients of CML were found to have some ophthalmic changes. In all these studies, CML patients were examined as a part of overall leukemic patients to look for ophthalmopathy, in none of the available study, chronic myeloid leukemia patients were taken alone. In current study, we examined 66 patients of CML, with wide range of age between 13-86 years. There is no significant gender difference in selected patients. Most of the patients didn’t have any co-morbid illness so it was difficult to establish if these factors had any contribution towards these findings. Patients were examined to look for presence of eye changes in different segments. Only finding found in anterior chamber was cataract observed in 7.6% patients which can be attributed to some other factors like age, co-morbid conditions or any therapy but we don’t have any significant evidence for that posterior chamber findings were found in 4.5% and macular changes in 3% of patients. CD ratio more than 0.5 was found in 10.70% of patients with 4 patients (6.2%) having CD ratio of 0.5. While only 3 patients had its value greater than 0.6 which might be indicative of glaucoma or other pathology. However, Intra-ocular pressure of these patients was not determined to know if they had glaucoma or not.18.2% patients had retino-vascular changes while 16.7% had optic disc changes which are probably due to secondary involvement of eye. When analyzed, no statistically significant correlation of these changes was found between these changes and other patient specific parameters was found some of which have prognostic significance. However, it may be due to small sample size of the study and their relationship may establish if a greater number of patients with CML are studied with use of modern investigation modalities like MRI along with clinical examination. As CML is a chronic disease and patient came on follow up for years. These patients will be followed with repeated ophthalmic examination to see any progression or changes if occur.

CONCLUSION

Eye is an important organ of body and wide spectrum of ophthalmic changes seen in patients of...
systemic disease including leukemia. These changes are more often seen in association with acute leukemias, however, their importance in chronic leukemias cannot be denied. Therefore, ophthalmic examination should be included as a mandatory part of initial evaluation and then periodically in CML patients to assess and prevent any eye related complications related to disease or therapy.

REFERENCES

Diabetes mellitus (DM) is a prevailing metabolic disease in modern world. In the year 2019 it is estimated that about 463 million adult people (20-79 years of age) worldwide are suffering from diabetes mellitus with global prevalence of diabetes 9.3%. More than half of these people are living in low to middle income countries. With 19.4 million people suffering from diabetes mellitus currently, Pakistan ranks 4th among countries with highest prevalence of adult population of diabetes mellitus1. While diabetes mellitus can be classified in various types, two most common types are type1 and type 2 diabetes mellitus.

Type 2 diabetes mellitus is a syndrome caused by relative insulin deficiency leading to hyperglycemia and its complications. Relative insulin deficiency is a result of either peripheral tissue resistance to insulin or secretary defects. One of the major risk factor of insulin resistance is obesity. Even in the individuals suffering from type 2 diabetes mellitus who are not considered obese based on their body mass index, abdominal obesity is thought to play an

Abstract

Objective: Obesity and abdominal obesity are commonly occurring medical conditions in patients with type2 diabetes mellitus and complicates its management. The purpose of this study was to determine the frequency of obesity and abdominal obesity in patients with type 2 diabetic mellitus.

Methods: This Cross sectional study was conducted at Jinnah Diabetes and Endocrinology Department, Jinnah Hospital Lahore from 15-02-2017 to 16-08-2018. A total of 392 cases of type 2 diabetes mellitus were enrolled in this study. Informed consent was taken from all subjects. Data regarding age, gender, duration of diabetes and anthropometric measurements (height, weight, waist circumference and hip circumference) was recorded on proforma. Body mass index (BMI) and waist to hip ratio (WHR) for each patient was calculated from the data and statistical analysis was performed.

Results: The mean age of the patients was 49.99 ± 9.79 years and majority was females 258(65.82%). Mean duration of disease was 9.18 ± 6.84 years. Obesity (BMI ≥ 30) was reported in 147(37.5%) of cases and abdominal obesity was noted in 114 (85.1%) males and 250 (96.9%) females when gender specific criteria was used for males (WHR >0.9) and females (WHR > 0.85). Significant linear relationship of duration of diabetes with WHR (p= 0.001) & age (0.00) was established. Strong Association of gender with BMI (p=0.00) & abdominal obesity (p=0.00) was determined.

Conclusion: A high prevalence of obesity & abdominal obesity was noted in patients with type 2 diabetes mellitus. Significant linear relationship of duration of diabetes with WHR & age was established.

Key Word: Obesity, Abdominal obesity, Diabetes Mellitus
important role in disease. Both type 2 DM and obesity are components of metabolic syndrome which also includes hypertension and dyslipidemia. Pathophysiology of insulin resistance and hyperglycemia in obesity is linked to the secretion of insulin resistance-inducing adipocytokines like resistin and leptin as well as with pro-inflammatory cytokines like tumor necrosis factor (TNF-α) and interleukin 6 (IL-6) which are released from abdominal adipocytes and associated inflammatory cells.

Even with the availability of ever growing number of effective anti-diabetic drugs life style modifications which include weight control remain important to control hyperglycemia and reduce the risk of complications of disease in patients suffering from type 2 DM. Guidelines recommend documentation of weight and body mass index (BMI) in patients with type 2 DM at each visit. Weight control is shown to significantly improve glycemic control with improved glycosylated hemoglobin level (HBA1c), delays progression of pre-diabetes to diabetes and lessens use of anti-diabetic drugs for glycemic control.

Unfortunately this part of management is less emphasized by the treating physician and less realized by most of patients. Obesity is defined using World Health Organization (WHO) criteria using BMI value of 30 kg/m² and above whereas weight to hip ratio (WHR) for measuring abdominal obesity is defined as a value above .90 in males and above .85 in females. Obesity itself is linked to various complications ranging from cardiovascular disease, obstructive sleep apnea to certain malignancies. Prevalence of obesity among patients suffering from type 2 DM varies with geographical area and ethnicity. A study in United States reported a prevalence of 57.9% for non-Hispanic whites. While a study in England describes that 90% of adults (16 to 54 years of age) with type 2 DM are either overweight or obese. A local study in Rawalpindi Pakistan established that 32.3% of patients suffering from diabetes are obese.

This study is directed to determine the frequency of obesity & abdominal obesity in patients suffering from type 2 diabetes mellitus. The result of the current study adds to the existing knowledge in our local community and considering both generalized obesity and central obesity, provides more insight to the problem. This results of the study will help to emphasize clinicians regarding the importance of evaluating patient of diabetes for obesity and central obesity routinely in order to practice this neglected part of management appropriately.

OBJECTIVES OF THE STUDY

To determine the frequency of obesity & abdominal obesity in patients with type 2 diabetes mellitus in a tertiary care hospital.

METHODS

This Cross sectional study was conducted at Jinnah Diabetes and Endocrinology Department, Jinnah Hospital Lahore from 15-02-2017 to 16-08-2018. All the patients who visited Jinnah Diabetes and Endocrinology Department in the said duration with established diagnosis of type 2 diabetes and fulfilled our subject selection criteria with informed consent were recruited in the study by consecutive sampling. Patients of both gender suffering from type 2 diabetes mellitus were included in the study while patients suffering from ascites or generalized body edema due to any cause including cirrhosis of liver, heart failure or nephrotic syndrome, patients suffering from active tuberculosis or active malignancy, Cushing syndrome, hypothyroidism and pregnant females were excluded from the study.

Pre designed proforma was used to collect all the data. Age, gender and duration of diabetes were noted. For the assessment of BMI, an anthropometric rod was used and in order to measure height every subject was made to stand erect on floor with back against vertically affixed ruler. A pre-standardized weight machine was used in order to measure weight of subjects. The formula, weight in kilogram (kg) divided by height in square of the meter (m²) was used in order to calculate BMI of study population. For measurement of the hip circumference (HC) maximum circumference around the hips was...
used and for measurement the waist circumference (WC) mid-point between lowest rib and highest point of iliac crest was used. The calculation of waist to hip ratio (WHR) was done by dividing waist circumference with the hip circumference. For obesity & abdominal obesity WHO standards were used.

**Statistical analysis:**

All the data obtained was entered and analyzed using statistical software “Statistical Packages for Social Sciences” (SPSS) 26.0. For age, weight, height, BMI, waist circumference, hip circumference, WHR and duration of diabetes mean and standard deviation were calculated. Frequency & percentages were calculated for underweight, normal weight, overweight, obesity & abdominal obesity. Association between BMI Classes (overweight, obesity), abdominal obesity and Gender was determined by applying chi square test. Correlation between WHR, BMI, Age, weight & Duration of diabetes was determined by Pearson’s correlation. Statistical significance was considered at P values < 0.05.

**RESULTS**

Mean age of the study population was 49.99 ± 9.79 years, mean weight was 72.91±14.27 kilograms (kg) and mean height was 159.37 ± 8.80 cm. Mean BMI was found to be 28.68 ± 5.26 kg/m², mean waist circumference was 101.98 ± 13.82 cm and mean WHR was .99 ± 0.09. Mean Duration of diabetes was 9.18 ± 6.84 years. Table 1

Significant linear relationship of duration of diabetes with WHR (p= 0.001) & age (p=0.00) was established. Significant correlation between duration of diabetes and BMI (0.241) as well as weight (0.113) was not established. Table 2

Out of total 392 subjects, 150 (38.3%) were overweight and 147 (37.5%) were obese as per BMI criteria. Among 147 total obese patients, 104 (70.7%) were in obesity class I, 31 (21.1%) were in obesity class II, and 12 (8.2%) were in obesity class III. In our study population 134 (34.2%) subjects were male and 258 (65.8%) subjects were females. When BMI criteria is used out of 134 total male subjects 50 (37.31%) were overweight and 34 (25.37%) were obese, while out of 258 total female subjects 100 (38.76%) were overweight and 113 (43.80%) were obese. Gender specific WHR criteria was used for abdominal obesity for males (WHR >0.9) and females (WHR > 0.85). According to WHR criteria 114 (85.1%) males and 250 (96.9%) females were found obese as depicted in figure 1 and

2. Strong Association of gender with BMI (p=0.00) & abdominal obesity (p=0.00) was determined. Table 3

---

**Table 1: Characteristics of Study Population (n=392)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>Std. Deviation</th>
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<td>Age</td>
<td>30</td>
<td>80</td>
<td>49.99</td>
<td>9.79</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>33</td>
<td>128</td>
<td>72.91</td>
<td>14.27</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>126</td>
<td>181</td>
<td>159.37</td>
<td>8.80</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>14.1</td>
<td>47.0</td>
<td>28.69</td>
<td>5.26</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>55</td>
<td>189</td>
<td>101.95</td>
<td>13.82</td>
</tr>
<tr>
<td>Hip Circumference(cm)</td>
<td>39</td>
<td>192</td>
<td>102.16</td>
<td>13.72</td>
</tr>
<tr>
<td>Waist/Hip Ratio</td>
<td>0.70</td>
<td>1.54</td>
<td>0.99</td>
<td>0.09</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>0</td>
<td>35.00</td>
<td>9.18</td>
<td>6.84</td>
</tr>
</tbody>
</table>

**Table 2: Correlation between WHR, BMI, Age, weight & Duration of Diabetes**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pearson Correlation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of diabetes &amp; Waist/Hip Ratio</td>
<td>0.155</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of diabetes &amp; Body Mass Index</td>
<td>0.036</td>
<td>0.241</td>
</tr>
<tr>
<td>Duration of diabetes &amp; Age</td>
<td>0.280</td>
<td>0.00</td>
</tr>
<tr>
<td>Duration of diabetes &amp; weight</td>
<td>0.061</td>
<td>0.113</td>
</tr>
</tbody>
</table>
OBESITY, ABDOMINAL OBESITY AND TYPE 2 DIABETES MELLITUS: A CROSS SECTIONAL STUDY

DISCUSSION

This study clearly shows a high prevalence of obesity and abdominal obesity in patients of diabetes mellitus visiting tertiary care hospital. Significant gender differences were also observed and obesity and abdominal obesity were found more prevalent in women (43.8% and 96.9%) compared with men (25.8% and 85.1%). Similar high prevalence of obesity in diabetes is proved in many studies performed in different parts of the world with different ethnic groups in consideration. A study in Kathmandu by Basukala A et al reported an obesity prevalence of 14.4% while 37.5% were overweight when using BMI criteria and obesity was more prevalent in females than males. In this study nearly all women subjects (94.2%) were found to be obese when WHR >0.8 was used to define abdominal obesity. A strong association between BMI and WHR was also noted. Similarly a study by Damian DJ et al in Taiwan noted 44.9% suffering from type 2 DM were overweight and 40.1% were obese using BMI for classification. Obesity prevalence was again significantly higher in women. Similar results were obtained in studies performed in England, United States, Saudi Arabia and Yemen. A study in Pakistan by Shera AS et al described that in patients with type 2 DM 61% had raised BMI and 88% had raised WHR. While study by Zafar J et al described obesity prevalence of 32.3% in type 2 DM patients. All of these studies acknowledge high prevalence of obesity in patients of type 2 diabetes mellitus, however, variation in exact percentages can be attributed to difference in research methodologies, ethnicity and geographical. Results of our study are in general agreement with above cited studies.

In our study 75.8% of type 2 DM patients had BMI above normal with only 21.9% of patients had BMI in normal range clearly indicating need of weight management in most patients. Abdominal obesity was found to be even more prevalent in women and nearly all women (96.9%) had abdominal obesity. Possible explanation behind this high prevalence may include genetic or environmental factors, urbanization, lack of patient education and lack of local weight management guidelines. An even high prevalence in women may have additional physiological and cultural factors in play. As weight control in overweight and obese patients improvement in glycemic control and translates into reduced complications of diabetes this part of diabetes management should not be neglected. It highlights the fact that physicians need to give urgent attention.
to this important part of management of diabetes mellitus. A local study by Butt F et al in different hospitals of Punjab found out that only 8% of doctors are trained in obesity management. Additionally our country is currently lacking adequate no of dieticians, effective and approved pharmacological drugs and surgeons with expertise in bariatric surgery for morbidly obese individuals. Development of local therapeutic guidelines, training of doctors and local policy development in order to make availability of essential resources are keys to improve weight control in masses.

Limitations of our study are cross sectional study design & single center. Finally we suggest that further studies are required in different settings to confirm the findings of this study followed by studies to document effectiveness of locally available interventions for controlling obesity and abdominal obesity.

CONCLUSION:
High Frequency of obesity & abdominal obesity was noted in patients with type 2 diabetes mellitus. Significant linear relationship of duration of diabetes with WHR & age was established. Strong Association of gender with obesity & abdominal obesity was determined among type 2 diabetics.

REFERENCES
Abstract

Objectives: Patients with cirrhosis of liver, a prevalent disease in Pakistan, present with upper gastrointestinal bleeding which is widely considered to be from esophageal/gastric varices or portal hypertensive gastropathy. This study was conducted in these patients to establish the spectrum of non-variceal upper gastrointestinal bleeding in patients with liver cirrhosis at a tertiary care hospital.

Methods: In this descriptive case series, 312 patients were enrolled from either gender (male and female), presenting with hematemesis. After pre-procedural lab investigations (hemoglobin, viral markers, coagulation profile), these patients underwent abdominal ultrasound and upper GI endoscopy with or without conscious sedation. Findings were recorded and the source of bleeding was identified.

Results: Among 312 patients, 46-55 years was the most prevalent age range with a predominantly male population (56%). It was further observed that 80% patients were infected with hepatitis C and 2% with hepatitis B while 55 (18%) were serologically negative. Esophageal varices were noted in 151 (48%) patients, however, it is worth noting that gastritis was seen in as many as 84 (27%) patients while esophagitis was observed in 21 (7%) patients as the primary site of bleeding.

Conclusion: Non-variceal causes of upper gastrointestinal bleeding are frequent findings in liver cirrhosis patients undergoing endoscopy. Hence, the treatment protocols should be designed after due consideration for non-variceal sources of bleeding.

Keywords: Liver cirrhosis, Upper gastrointestinal bleeding, Esophageal varices, Gastric varices, Non-variceal bleeding, Upper GI endoscopy.
14%). In contrast to bleeding from esophageal varices, prevention and treatment of bleeding from portal gastropathy and gastric varices is not well evaluated in clinical studies. This study was conducted to establish non-variceal causes of upper gastrointestinal bleeding as a frequent source of bleeding in patients with liver cirrhosis presenting in tertiary care hospital.

**METHODS**

In this descriptive case series, 312 patients who fulfilled the inclusion criteria were enrolled from the department of medicine and gastroenterology in Mayo Hospital. These patients, presented with upper gastrointestinal bleeding in the form of hematemesis or melena, had an abdominal ultrasound to confirm liver cirrhosis. All the patients who had evidence of hepatic encephalopathy, bleeding disorders or pregnancy were excluded from the study. Patients who were mentally-ill or failed to co-operate during the procedure were excluded.

The patients who were included in the study underwent esophagogastroduodenoscopy using Olympus GIF-x260 endoscope either in the emergency department or as an elective procedure after securing haemostasis and stabilization and pertinent findings were recorded. Interventional procedures were introduced where necessary without having any impact on the findings. Safety outcomes included signs of hemodynamic shock, hepatic encephalopathy, aspiration of blood and stomach contents during the endoscopy.

**RESULTS**

Total patients enrolled in the study after meeting inclusion and exclusion criteria were 312. Age distribution (Table 1) showed that most of the patients were 36 or older with maximum no. of patients aged between 46-55 years with a predominantly male population (Table 2).

While analyzing the data, it was observed that 251(80%) patients were infected with hepatitis C and 6 (2%) had hepatitis B while 55 (18%) patients were serologically negative for both hepatitis B & C as shown below.

Table 4 shows the frequency of different causes of upper gastrointestinal bleeding in these patients. While esophageal varices were noted in 151 (48%) patients, it is worth noting that gastritis was seen in as many as 84 (27%) of these patients while esophagitis was observed in 21 (7%) patients. Duodenitis was the primary site of bleeding in 18 (6%) patients while esophageal ulcers were identified in 15 (5%) patients.

**DISCUSSION**

In 2015, Hadayat R conducted a series of endoscopies on patients who had liver cirrhosis and concluded that the most common endoscopic finding was esophageal varices (92.9%) followed by portal hypertensive gastropathy (38.9%) and gastric varices were found in 33.3% of patients with almost equal distribution among males and females. Among other non-variceal lesions, peptic ulcer disease was seen in 10.3% while gastric erosions were found in 3.2% of the patients. Gabr MA further supported these findings in 2016 when the results showed a similar trend. 415(75.5%) patients bled from vari-

---

**Table 1: Distribution of Age**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Age Range</th>
<th>%age of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>16-25</td>
<td>6%</td>
</tr>
<tr>
<td>2.</td>
<td>26-35</td>
<td>9%</td>
</tr>
<tr>
<td>3.</td>
<td>36-45</td>
<td>27%</td>
</tr>
<tr>
<td>4.</td>
<td>46-55</td>
<td>29%</td>
</tr>
<tr>
<td>5.</td>
<td>56-65</td>
<td>17%</td>
</tr>
<tr>
<td>6.</td>
<td>&gt;65</td>
<td>13%</td>
</tr>
</tbody>
</table>

**Table 2: Distribution of Gender**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Gender</th>
<th>%age of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Male</td>
<td>56%</td>
</tr>
<tr>
<td>2.</td>
<td>Female</td>
<td>44%</td>
</tr>
</tbody>
</table>

**Table 3: Serological Distribution of Patients**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Virological Status</th>
<th>No. of patients</th>
<th>%age of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>HCV</td>
<td>251</td>
<td>80%</td>
</tr>
<tr>
<td>2.</td>
<td>HBV</td>
<td>6</td>
<td>2%</td>
</tr>
<tr>
<td>3.</td>
<td>Normal</td>
<td>55</td>
<td>18%</td>
</tr>
</tbody>
</table>
esophageal sources (esophageal and gastric) while 135 (24.5%) of them had non-variceal sources. Among variceal sources of bleeding, esophageal varices were much more common than gastric varices while peptic ulcer was the most common non-variceal source of bleeding. 10 Ahmed A studied the prevalence of esophageal varices in patients presenting with upper gastrointestinal bleeding in a tertiary care hospital. They enrolled 120 patients and concluded that 50% of the patients had bled from esophageal varices. 11

Contrary to these results, when the results were analysed in this study, it was observed that esophageal varices were seen in 151 (48%) patients. However, this is worth noting that gastritis was seen in as many as 84 (27%) of these patients while esophagitis was observed in 21 (7%) patients. In cirrhotic patients with a possible variceal source of bleeding, esophageal varices were the most common of the findings but gastritis or esophagitis were observed in a significant number of patients. In 2016, Ugiagbe RA studied the cause of upper gastrointestinal bleeding in 311 patients. The results of their study showed peptic ulcer disease as the most common cause of bleeding in patients with liver cirrhosis as seen in other studies. This is further substantiated by Palmer KR in 2002, who found out that among the causes of acute upper gastrointestinal bleeding, peptic ulcer is the most common (35-50%) followed by gastrointestinal erosions (8-15%), esophagitis (5-15%) and varices (5-10%). 14

However, this must be taken into account that this study included patients who presented with upper gastrointestinal bleeding without considering the serological status of these patients. This is evident from the fact that 55 (18%) patients were serologically negative for both hepatitis B & C but they were diagnosed with liver cirrhosis on ultrasonography. This is a plausible explanation for a frequent finding of gastritis in the study in addition to esophageal varices being the most common cause of bleeding in patients with liver cirrhosis as seen in other studies. This is further substantiated by Palmer KR in 2002, who found out that among the causes of acute upper gastrointestinal bleeding, peptic ulcer is the most common (35-50%) followed by gastrointestinal erosions (8-15%), esophagitis (5-15%) and varices (5-10%).

A limitation of the study, however, was the fact that in a small group of patients the cause of bleeding was not identified which in turn could be due to esophageal varices that had collapsed by the time endoscopy was performed, esophageal tears or concealed ulcers in the duodenum or fundus. Moreover, the presence of multiple findings in one patient could have affected the results without conclusively proving the particular finding as the cause behind the bleeding event. This suggests that more studies should be designed to localize the source of bleeding in patients with liver cirrhosis considering the fact that upper gastrointestinal bleeding is a common cause of mortality in these patients. 15 Since, the treatment protocols differ in cases of variceal bleeding as compared to non-variceal bleeding, this is imperative that a multicentre trial should be conducted on a larger group of patients. Despite emergency endoscopy being the diagnostic procedure of choice in these patients to detect the source of bleeding, this is imperative that non-variceal causes of bleeding must be considered till the endoscopy is performed.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Findings on Endoscopy</th>
<th>No. of patients</th>
<th>%age of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Esophageal Varices</td>
<td>151</td>
<td>48%</td>
</tr>
<tr>
<td>2.</td>
<td>Gastritis</td>
<td>84</td>
<td>27%</td>
</tr>
<tr>
<td>3.</td>
<td>Esophagitis</td>
<td>21</td>
<td>7%</td>
</tr>
<tr>
<td>4.</td>
<td>Duodenitis</td>
<td>18</td>
<td>6%</td>
</tr>
<tr>
<td>5.</td>
<td>Esophageal Ulcer</td>
<td>15</td>
<td>5%</td>
</tr>
<tr>
<td>6.</td>
<td>Gastric Ulcer</td>
<td>9</td>
<td>3%</td>
</tr>
<tr>
<td>7.</td>
<td>Candidiasis</td>
<td>8</td>
<td>2.5%</td>
</tr>
<tr>
<td>8.</td>
<td>Unidentified</td>
<td>6</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 4: Findings on Endoscopy in Patients who Presented with Upper Gastrointestinal Bleeding
and the site of bleeding is identified.

**CONCLUSION**

Non-variceal sources of upper gastrointestinal bleeding are frequent findings in liver cirrhosis patients undergoing endoscopy. Hence, the treatment protocols should be designed after due consideration for non-variceal sources of bleeding. However, a large scale multicentre trial should be conducted after adjusting for all the variables including serological status of the patients to underscore the prevalence of non-variceal causes of upper gastrointestinal bleeding.

**REFERENCES**

Abstract

Objective: To determine the perinatal outcome of patients having stillbirth in preceding pregnancy

Study design: Descriptive case series study

Place and Duration of study: From January 2018 to June 2018 at Combined Military Hospital, Lahore.

Material and Methods: Sample size of 300 cases is calculated with 95% confidence level, 2.5% margin of error and taking expected percentage of fetal distress i.e. 5.1% (least among all) perinatal outcome in patients presenting with stillbirth in preceding pregnancies. The collected information was entered and analyzed through SPSS version 20.

Results: The results of the study reveal that 43.67%(n=131) were between 20-32 weeks of gestation, 56.33%(n=169) were between 33-40 weeks of gestation, while frequency of perinatal outcome of patients having stillbirth in preceding pregnancy was recorded as 8.67%(n=26) pre-eclampsia, 6.33%(n=19) had fetal distress, 18.33%(n=55) had spontaneous preterm delivery and 15.67%(n=47) had IUGR.

Conclusion: The results of the study determined that the perinatal outcome i.e. Pre-eclampsia, Fetal distress, Spontaneous preterm delivery and IUGR are significant in patients having stillbirth in preceding pregnancy

Keywords: Association, preceding pregnancy, perinatal outcome, stillbirth

Stillbirth is the birth of a dead fetus at ≥20 weeks of gestation. It is a globally health problem of public affecting millions of women worldwide. It is generally responsible for about one half of all perinatal deaths. It accounts worldwide each year of about four million. Stillbirth is most commonly occurring in developing countries of about 97%. It has been understudied and under reported due to many reasons and fewer efforts have been made to improve adverse pregnancy outcomes in developing countries. Every Newborn Action Plan (ENAP) sets the different world goal of stillbirth rate of 10 per 1000 by 2035. The recent estimation done suggest that still-birth rates of >30 per 1000 births are common among the least developed countries, especially in Sub-Saharan Africa and Southeast Asia. In 2015, 2.6 million stillbirths in third trimester occurred and most of these were in low- and middle-income countries (LMICs) with estimation of three quarters occurring in south Asia and sub-Saharan Africa. When compared, the rate of stillbirth is 3-5 per 1000 in developed countries and rate of 10-15 per 1000 deliveries in mid-level countries, such as those in South and Central America. Elizabeth M and co-workers conducted a study as part of the Global Network for Women’s and Children’s Health Research (Global Network), and reported that the...
mean stillbirth rate was 24 per 1000 deliveries, which ranged from 9 per 1000 in Argentina to 34 per 1000 deliveries in Pakistan.

The exact etiology of stillbirth is still unknown. The two important factors genetic and environmental have great role in pathogenesis of the disease. Research has identified numerous other maternal risk factors like advanced maternal age, low socioeconomic status, obesity, multiparty, smoking and alcohol use during pregnancy, inadequate prenatal care, and medical and obstetric complications.

Several studies have proven risk of recurrence in women with previous history of stillbirth in subsequent pregnancies. Getahun D and colleagues reported pre-eclampsia in 6.4% in subsequent pregnancy, fetal distress as 5.1%, spontaneous preterm delivery (<37 weeks) 20.8% and Intrauterine growth retardation 17.7%. However it is pertinent to mention that no local study exists on aforesaid subject which raises need to conduct a study in our population to determine perinatal outcome of patients having still birth in preceding pregnancy. So that special attention regarding perinatal outcome may be given for the avoidance of these complications.

METHODS

All pregnant patients of age group 18-35 years, gestational age between 20 -40 weeks based upon last menstrual period, singleton pregnancy and with preceding history of stillbirth were included in this study at Combined Military hospital, Lahore from January 2018 to June 2018. Permission from Ethical Committee of the institution was taken. Fetal demise occurring before 20 weeks of gestation, diagnosed cases of diabetes mellitus and APH (on history and medical record) and Unsure of dates (USOD) were excluded.

All the patients fulfilling inclusion/exclusion criteria from Out Patients Department of Combined Military Hospital, Lahore were included in the study. Non-probability Purposive Sampling Technique was applied. An informed consent was taken from the patients to include their data in research work. The patients were followed 4 weekly visits till 28 weeks, 2 weekly till 36 weeks and weekly thereafter till delivery to know the perinatal outcome i.e. pre-eclampsia, fetal distress and spontaneous preterm delivery with in women with preceding still births was recorded. All this information was collected on a pre-designed Proforma. The collected data was entered in computer software SPSS software (version 13.0). Mean and standard deviation was calculated for age and gestational age of the pregnant women. The frequency and percentages were calculated for perinatal outcome i.e. pre-eclampsia, fetal distress and spontaneous preterm delivery and IUGR. No test of significance was applied.

RESULTS

A total of 300 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the perinatal outcome of patients having still birth in preceding pregnancy. Age distribution of the patients was done, age range was 18-35 years, 31.33%(n=94) were between 18-25 years, 39.33%(n=118) between 26-30 years and 29.34%(n=88) were between 31-35 years, mean+sd was calculated as 27.60+4.57 years. (Table No. I)Gestational age of the patients was also calculated and recorded, which shows that 43.67% (n=131) were between 20-32 weeks of gestation, 56.33% (n=169) were between 33-40 weeks of gestation, mean+sd of gestational age was calculated as 32.64+5.72 weeks. (Table No. II).Frequency of perinatal outcome of patients having still birth in preceding pregnancy revealed as 8.67% (n=26) having pre-eclampsia, 6.33% (n = 19) had fetal distress, 18.33%(n=55) had spontaneous preterm delivery and 15.67%(n=47) had IUGR. (Table No. III)

DISCUSSION

Stillbirth refers to the delivery of a fetus showing no signs of life. Despite technological advances in obstetric and neonatal care, it remains one of the major causes of perinatal mortality in developed countries and even more so in developing
countries.\textsuperscript{16-17} Several case series and meta-analysis risk of stillbirth in women with previous fetal demise compared to general population.\textsuperscript{18} In developing nations, preterm births and stillbirths are grossly underreported, even in developed nations, there is considerable variability in the threshold for reporting stillbirth. The World Health Organization (WHO) classification of stillbirth is defined as fetal loss beyond 20 weeks of gestation, or, if the gestational age is not known then can be defined at birth weight of 500 g or more, which corresponds to 22 weeks of gestation in a normally developing fetus.\textsuperscript{19}

Stillbirth represents an important cause of fetal loss in the fetal distress infant.\textsuperscript{20} Although more than 90\% of fetal deaths occur in the first 20 weeks of gestation. The rate of stillbirth is about 3 per 1000 live births after 28 weeks gestation. The risk of stillbirth if observed from 36 weeks increases substantially with increasing gestation.\textsuperscript{21} Studies have proven that women with previous history of stillbirth is at increased risk of fetal demise in subsequent pregnancies.\textsuperscript{22-23} However, few data exist on the relationship between stillbirth and ischemic placental diseases (IPDs) (defined as small-for-gestational age [SGA] birth/ intrauterine growth restriction, medical problems like preeclampsia, and placental abruption) and with other adverse perinatal and neonatal outcomes in pregnancies such as fetal distress, chorioamnionitis, spontaneous preterm birth (SPTB), and neonatal mortality in subsequent pregnancies.

The reason behind this study is that no local study exists on aforesaid subject which raises need to conduct a study in our population to determine perinatal outcome of patients having still birth in preceding pregnancy. So that special attention regarding perinatal outcome may be given for the avoidance of these complications.

The results of the study reveal that 43.67\% (n=131) were between 20-32 weeks of gestation, 56.33\% (n=169) were between 33-40 weeks of gestation, while frequency of perinatal outcome of patients having still birth in preceding pregnancy was recorded as 8.67\% (n=26) pre-eclampsia, 6.33\% (n=19) had fetal distress, 18.33\% (n=55) had spontaneous preterm delivery and 15.67\% (n=47) had IUGR.

The findings of the current study are in consistent with other studies who reported that women with a history of stillbirth are at increased risk of stillbirth in subsequent pregnancies.\textsuperscript{9} Getahun D and colleagues\textsuperscript{6} reported pre-eclampsia 6.4\% in subsequent pregnancy, fetal distress as 5.1\%, spontaneous preterm delivery (<37 weeks) 20.8\% and Intrauterine growth retardation 17.7\%.

Sharma et al in 2007\textsuperscript{24} reported that the risk of stillbirth in the subsequent pregnancy is to be almost six times higher in women with a stillbirth in their first pregnancy when compared with women with history of live birth in first pregnancy. Their cohorts only included low risk women (age <35 years, absence of smoking) and included stillbirth occurring with most of the causes (apart from those due to congenital anomalies), including those where maternal medical problems like diabetes and pre-

\textbf{Table 1: Age Distribution (n=300)}

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-25</td>
<td>94</td>
<td>31.33</td>
</tr>
<tr>
<td>26-30</td>
<td>118</td>
<td>39.33</td>
</tr>
<tr>
<td>31-35</td>
<td>88</td>
<td>29.34</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean±sd: 27.60 ± 4.57

\textbf{Table 2: Gestational Age of the Patients (n=300)}

<table>
<thead>
<tr>
<th>Gestational Age (in weeks)</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-32</td>
<td>131</td>
<td>43.67</td>
</tr>
<tr>
<td>33-40</td>
<td>169</td>
<td>56.33</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean±sd: 32.64 ± 5.72

\textbf{Table 3: Frequency of Perinatal Outcome of Patients Having Still Birth in Preceding Pregnancy (n=300)}

<table>
<thead>
<tr>
<th>Perinatal outcome</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia</td>
<td>26</td>
<td>8.67</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>19</td>
<td>6.33</td>
</tr>
<tr>
<td>Spontaneous preterm delivery</td>
<td>55</td>
<td>18.33</td>
</tr>
<tr>
<td>IUGR</td>
<td>47</td>
<td>15.67</td>
</tr>
</tbody>
</table>

Mean±sd: 27.60 ± 4.57

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<table>
<thead>
<tr>
<th>Gestational Age (in weeks)</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-32</td>
<td>131</td>
<td>43.67</td>
</tr>
<tr>
<td>33-40</td>
<td>169</td>
<td>56.33</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean±sd: 32.64 ± 5.72

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<thead>
<tr>
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<tbody>
<tr>
<td>Pre-eclampsia</td>
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</tr>
<tr>
<td>Spontaneous preterm delivery</td>
<td>55</td>
<td>18.33</td>
</tr>
<tr>
<td>IUGR</td>
<td>47</td>
<td>15.67</td>
</tr>
</tbody>
</table>
DETERMINATION OF PERINATAL OUTCOME OF PATIENTS HAVING STILLBIRTH IN PRECEDING PREGNANCY

eclampsia might have contribution to the adverse outcome similar to our study as we also included the low-risk women i.e. age up to 35 years and absence of smoking.

There are many studies proving the maternal depletion hypothesis suggest a short interpregnancy interval also contribute to it due to insufficient time to recover from the nutritional burden and maternal stress attributable to the pregnancy loss. Basically, couples will try to replace a lost child within short period after miscarriage.

We did not record the interpregnancy intervals being the limitations of the study. Future studies determining outcomes of successive pregnancies need to be considered on the interpregnancy intervals and their association with Ischemic Placental Diseases and spontaneous preterm birth.

Though it is proven that patients having stillbirth in preceding pregnancy are at increased risk of Pre-eclampsia, fetal distress, spontaneous preterm delivery and IUGR, however, the data of this study is primary in our country, some other trials including interpregnancy intervals should be done to strengthen the current findings.

CONCLUSION

The results of the study determined that the perinatal outcome i.e. pre-eclampsia, fetal distress, spontaneous preterm delivery and IUGR are significant in patients having still birth in preceding pregnancy.

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**FREQUENCY OF HEPATITIS C AND ITS RELATION WITH PREVIOUS SURGICAL AND NON-SURGICAL INTERVENTIONS IN UNBOOKED PREGNANT PATIENTS**

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**Abstract**

**Objectives:** To determine frequency of Anti-HCV and its relation with previous surgical and non-surgical interventions in unbooked pregnant patients visiting Obstetrics and Gynaecology emergency department.

**Design:** Descriptive cross sectional study.

**Place and Duration of study:** Conducted at Department of Obstetrics and Gynaecology Jinnah Hospital Lahore from January 2018 to June 2018.

**Material and Methods:** One hundred and ninety eight pregnant patients fulfilling the inclusion criteria were selected. Permission from Ethical Committee of the institution was taken. After taking history, individuals were subjected to the laboratory test. Data was analyzed by using SPSS version 10. Descriptive statistics were applied to analyze the data.

**Results:** Majority of the patients 42.92% were in age group 31-40 years and were multigravida. Among 198 patients most of the patients, 117(59.09%) were belonging to rural area and poor socioeconomic class. Anti HCV was detected in 19(9.59%) patients. Among Anti-HCV positive patients, history of previous D and C, previous Caesarean sections, dental procedures and multiple injections were reported in 22(11.11%), 26(13.13%), 7(3.53%) and 21(10.60%) respectively,

**Conclusion:** 9.59% of the pregnant women studied were sero-positive for hepatitis C. The leading factors for contraction of hepatitis C are prevalent in pregnant community in the form of previous D and C, previous cesarean sections, dental procedures, blood transfusion and multiple injections.

**Keywords:** Hepatitis C, Pregnancy, Risk factors

Viral Hepatitis is a major health problem globally casting an enormous burden on health care system and major source of patients’ misery.¹ Hepatitis C remains latent for a long period therefore screening avoids long term complications including mortality as timely screening leads to successful treatment.² Untreated hepatitis C patients are amongst the leading causes of morbidity, mortality and serious public health problems worldwide as well as in Pakistan.³ The prevalence of viral hepatitis in population is correlated with previous interventions as leading factors. These leading factors in unscreened population include blood products, transfusions, pelvic infections after D and C, emergency Cesarean Sections and dental procedures.⁴

The long term morbidity in hepatitis C is acute hepatitis (70%), cirrhosis (20%-30%), hepatocellular carcinoma and liver failure in untreated patients⁵. The prevalence of HCV infection among general public of Pakistan is 4%-10% respectively. Frequen-

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Frequency of Hepatitis C and Its Relation with Previous Surgical and Non-Surgical Procedures

Frequency of hepatitis C virus infection in pregnant women of Pakistan is reported to be 6.7%. Frequency of hepatitis B & C (Combined) in pregnant women has been reported to be 3.98% in local study.

The transmission of parenteral viral hepatitis generally occurs through contact with infected blood during dilatation and curettage and emergency caesarean section done in unscreened patients. Therefore, prenatal screening of booked and unbooked pregnant women for viral markers is a helpful strategy for the prevention of transmission.

There is lack of routine serological screening prior to emergency surgery, which is one of the factors responsible for increased transmission with no preventable measure in emergency situations that highlights the importance to diagnose the acute and chronic hepatic viral infection in pregnant women thereby justifying screening for HCV in emergency situations. Being a vulnerable group, the pregnant women are likely to be more predisposed to these infections, but only few studies are available on the subject.

Keeping in view the dreadful complications of hepatitis and its high infectivity, we cannot afford to operate the patients without hepatitis screening. In developing countries like Pakistan, because of poverty and lack of facilities, women have poor access to the hospitals, so screening for anti-HCV antibodies should be carried out in emergency cases as well.

In one study factors leading to hepatitis C were: 10 (9.8%) had delivery, 19 (16.62%) previous general surgery, 20 (19.60%) blood transfusion, 10 (9.8%) underwent D&C, 5 (4.9%) had dental surgery, 6 (5.86%) received injection by quack and 32 (31.5%) had unknown risk factor.

In one local study, history of previous surgery 10 (43.5%), history of previous delivery 09 (39.1%), dental surgery 10 (43.5%), history of D & C 07 (30.4%) and history of injections 04 (17.4%) have been reported as risk factors leading to hepatitis C.

In one study conducted at Nishtar Hospital, Multan, among 35 anti-HCV positive women, 20 (57.14%) had history of previous surgery. Out of these 20 patients, 14 had obstetrical, while 6 had gynecologic surgery. Thirteen (37.14%) anti-HCV positive women while 6 (26.08%) HbsAg positive women respectively had history of multiple injections. Five (14.28%) women received blood transfusion; out of which 4 had single while 1 had multiple blood transfusions in anti-HCV positive women.

This study was designed to assess the frequency of anti-HCV & factors leading to hepatitis C in pregnant ladies to highlight the magnitude of the problem and determination of risk factors so that safety measures and awareness programs can be designed prenatally to prevent the spread of infection.

Methods

This descriptive cross-sectional study was carried out from June 2018 to December 2018. The patients were selected from the emergency department of Jinnah Hospital Lahore. Pregnant patients of reproductive age (15-45 years) visiting Gynecology Emergency Department at any gestational age were included in this study. Morbidly ill gravid females were excluded from study. After approval from ethical committee a total of one hundred and ninety eight pregnant patients presenting in Emergency Department of Obstetrics & Gynecology, Jinnah Hospital Lahore fulfilling the inclusion criteria were selected.

After an informed consent, a detailed history was taken from each subject. The history taking was focused on route of transmission of hepatitis C virus. History including the general particulars, history of any present or past illnesses, family history and socioeconomic status of the individual, any past history of hepatitis or jaundice was taken. Any history of hepatitis C in other family members was recorded. History of any surgical and dental procedures along with history of miscarriages was taken in detail. History of tattooing and frequent use of intravenous or intramuscular injections will be taken.
Previous testing for hepatitis C was enquired.

After taking history, individuals were subjected to the laboratory test. Five ml or venous blood sample was collected under strict aseptic conditions from anterior cubital vein in a sterile disposable plastic syringe. It was then transferred to a plastic bottle without anticoagulant and allowed to clot at room temperature. The screening was carried out by ELISA. All information were recorded on a structured proforma specifically designed for this study.

Data was analyzed by using SPSS version 10. Descriptive statistics were applied to analyze the data. Mean and standard deviation were calculated for age, parity and gestational age of the subjects. Frequencies and percentages were calculated for presence of hepatitis C (Yes, No) and factors (as mentioned in proforma). Effect modifiers like age, socioeconomic status, previous history of hepatitis, previous history of any surgical intervention were controlled by stratification and chi-square test was applied to see effect of these on outcome variables. P<0.05 was taken as significant.

RESULTS

Majority of the patients 42.92% were in age group 31-40 years. Age group 21-30 years were 36.86% and 13.13% patients in age group <20 years. Least number of cases were seen in age group <40 years. Out of 198 cases in the study, 38(19.19%) were primigravida 65(32.82%) were second gravid, 53 (26.76%) were third gravid, while 21.21% were gravid four and above. Majority of patients i-e, 56.06% presented at gestation less than 37 weeks and 43.93% of patients presented at gestation more than 37 weeks. Among 198 patients most of the patients i-e, 117(59.09%) were belonging to rural area and 81(40.90%) were belonging to urban area. Majority of the patients in the study was house wives i-e, 141(71.21%) and 57(28.78%) were working ladies. Out of 198 cases in the study, 134 (67.67%) were belonging to poor socioeconomic class, 43 (21.71%) were in middle and 21(10.60%) of patients were belonging to rich socioeconomic class.

Out of 198 patients, previous history of hepatitis was reported in 53(26.76%) patients and in 145 (73.23%), there was no previous history of hepatitis. Among 198 patients, 26(13.13%) reported emergency caesarean section, 22(11.11%) reported D and C and 14(7.07%) reported procedure related to general surgery. In 136(69.68%) patients there was no previous history of any surgical procedure. In majority of the patients, i.e. 191(96.46%), there was no history of any dental procedure and only 7(3.53%) patients underwent some dental procedure previously. Among 198 patients, 21(10.60%) were having history of multiple injections and in majority of patients i.e. 177(89.39%), there was no such history .Out of 198 patients included in the study, Anti-HCV was detected in 19(9.59%) patients. Normal viral serology was reported in 152(76.76%) patients.

DISCUSSION

Hepatitis in pregnancy presents challenging questions to the obstetrician. Most Asian countries have a high birth rate and a large pool of hepatotropic viruses causing hepatitis in pregnancy. Pakistan is endemic for all types of hepatitis and both epidemic and sporadic forms have been reported.

In women who are seropositive for both
HBsAg and HBeAg, mother-to-child transmission is approximately 90%. Infected neonates have an almost 90% risk of chronic liver disease (CLD) and also the chance of spreading the disease to siblings and to the community. The results generated by recent study are comparable with a study in which, the frequency of Hepatitis B and C was more in age group ranging between 32-36 years. In another study, among the 959 patients who participated in that study, the ages varied between 15 and 43 years with a mean age of 27.6±5.2 years.

Similarly in another International study, the mean age [standard deviation (SD)] of the cases was 27.6 (5.8) year and the mean age of the controls were 27.0(5.8). The study showed no significant difference in the distribution of ages between cases and controls (P=0.189.). The age group with the highest frequency among cases 106/303 (35.0%) and controls 133/303 (43.9%) was 18 to 24 years, whereas the age group with the lowest frequency among cases 14/303 (4.6%) and controls 14/303 (4.6%) was between 40 and 44 years. The range was 18-44 years.

Out of 198 cases in the study, 38(19.19%) were primigravida 65(32.82%) were second gravid, 53 (26.76%) were third gravid, while 21.12% were gravid four and above. Results generated by the present study are not corresponding with the results of other study, in which primigravidae (41%) constituted the largest group of pregnant population with hepatitis.

The etiologic types of viral hepatitis in 169 pregnant women were compared with those of 70 non-pregnant women in another international study. The majority of pregnant women (89.6%) came with hepatitis in the last trimester of pregnancy. In another study, sixteen pregnant women presented at the three main hospitals in Khartoum province, Sudan during the period of March-September 2007 with features of viral hepatitis. Their mean (SD) gestational age was 28.0(6.7) weeks.

Three-hundred eighty-six (77.2%) of our patients were aged 40 years or below with the age bracket of 18-29 years having the highest prevalence in study done at Jinnah Postgraduate Medical Centre, Karachi. The prevalence of HCV infection in our study was found to be higher when compared to reports from South East Asia (2.15%), America (1.17%) and Europe (1.03%), but lower when compared Egypt (20%).

The frequency of Hepatitis B and Hepatitis C infections among antenatal patients attending the University of Benin Teaching Hospital was 12.5% and 3.6% respectively while 0.57% was recorded for both HBV and Anti HCV. This also supports the WHO’s report for Nigeria as highly endemic area with prevalence greater than 8% for HBV. This also supports the WHO’s report for Nigeria as highly endemic area with prevalence greater than 8% for HBV. In a recent study, 2439 pregnant women were screened for Hepatitis B and Hepatitis C and 7.3% of them were positive for anti HCV, 2.2% for HBsAg and 0.058% were positive for both.

Worldwide viral hepatitis is the commonest cause of hepatic dysfunction in pregnancy. Pakistan is highly endemic for hepatitis B & C. In our study the frequency of HCV was 9.59% while prevalence

<table>
<thead>
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<th>Table 3: Hepatitis C Stratification of Cases</th>
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</thead>
<tbody>
<tr>
<td>Age in years</td>
</tr>
<tr>
<td>&lt;20</td>
</tr>
<tr>
<td>21-30</td>
</tr>
<tr>
<td>31-40</td>
</tr>
<tr>
<td>&gt;40</td>
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Chi-square value=0.1191
Df=3

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<th>P value</th>
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<tr>
<td>Poor</td>
<td>18</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>6</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Rich</td>
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</table>

Chi-square value=0.0159

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<th>Hepatitis C No</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Yes</td>
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<td>46</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
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Chi-square value=0.0113
df=1

P value=0.9153

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<th>Hepatitis C No</th>
<th>P value</th>
</tr>
</thead>
<tbody>
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<td>Yes</td>
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<td>54</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>117</td>
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</tr>
</tbody>
</table>

Chi-square value=0.0041
df=1

P value=0.8391
of HCV in developed countries is 0.68%, 0.95 in Taiwan and 0.7% in Italy.\textsuperscript{21} Prevalence of hepatitis C among 300 pregnant women in prenatal clinic of Lady Aitchison Lahore was found to be 6%.\textsuperscript{22}

A study in Scotland showed the highest sero-prevalence of anti-HCV in women aged 25-29 years.\textsuperscript{23} It is also in agreement with the data from the mandatory reporting system which indicates that peak age specific incidence of HCV infection for women in Switzerland is 20-29 years.\textsuperscript{24} Universal HCV screening in pregnancy is considered to be unjustified given the absence of an intervention to prevent mother to child transmission.\textsuperscript{25} In developing countries because of poverty and lack of facilities women have poor access to the hospitals, so screening for HCV should be carried out during antenatal visits as this might be their only interaction to a health care facility.

**CONCLUSION**

Result of the study shows that a total of 9.59% of the pregnant women studied were sero-positive for hepatitis C. The risk factors for contraction of hepatitis C are prevalent in pregnant community in the form of previous interventions, previous surgery, dental procedure and multiple injections. The prevalence of hepatitis is getting higher day by day among pregnant women and also among common people in Pakistan. Therefore, there is a need to institute public health measures to reduce disease burden and transmission, including routine screening of all pregnant mothers for HCV infections because timely diagnosis and treatment can reduce transmission morbidity and mortality.

**REFERENCES**


Haemorrhoids are anal cushions which are made up of spongy vascular tissue.

When abnormally displaced and bleeding on defecation these are named haemorrhoids.¹

These can be categorized as first, second, third and fourth degree haemorrhoids.

There are various methods of dealing with varying degrees of haemorrhoids, to name a few, injection sclerotherapy, open or closed haemorrhoidectomy, THD, HAL-RAR, stapled haemorrhoidectomy and banding etc.²

Haemorrhoids are commoner in females and incidence increases with advancing age.³

METHODS

We included 100 patients, 50 in each group.

Group A underwent open haemorrhoidectomy, group B open haemorrhoidectomy with LIS.

The study was conducted in tertiary care teaching hospital for 3 years from 1st March 2014 to 30th April 2017.

Post operative pain was recorded on pain analogue 1 to 10 being the maximum pain with pre operative education of all patients.

Analgesia used was injection diclofenac 75mg i/m twice a day, tablet naproxen twice a day, post operatively.

Abstract

This study was conducted in the time span of 03 years from 1st March 2014 to 30th April 2017. The objective of the study was twofold: to access post operative pain after haemorrhoidectomy and the need for post operative analgesia.

100 patients were included in this study namely group A, open haemorrhoidectomy, group B open haemorrhoidectomy with lateral internal sphincterotomy.

75 were females, 25 were male with M:F 1:3.

All procedures were done in saddle anesthesia.

The ages were from 30 to 70 years, with peak in fifties.

Same level of expertise was available to all patients with all ethical considerations and informed consent.

Group A hospital stay was 3-7 days, average 4 days, group B hospital stay was 2-4 days, average 2.5 days.

Post operative pain on pain analogue was 7-9 out of 10 in group A, and 4-5 in group B.

Post operative analgesia was needed 4-6 days in group A, and 2-3 days in group B.

No case of anal incontinence post operatively was reported in either group.

Follow up was done for 2 years and no case of anal stenosis was reported although 5 patients in group A had to be given anal dilators for 03 months.

It is concluded that group B had less post operative pain, had less requirement for post operative analgesia and had a better experience.

Key words: LIS [lateral internal sphincterotomy], open haemorrhoidectomy
A COMPARATIVE STUDY OF OPEN HAEMORRHOIDECTOMY VS OPEN HAEMORRHOIDECTOMY

Inclusion /exclusion criteria

30 to 70 years, both gender were included in study, and all who had co morbidity were excluded from it.

Ethical considerations

These were taken into account with privacy safe guarded.

RESULTS

Table 1: Gender Distribution

<table>
<thead>
<tr>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 2: Post Operative Stay

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-7</td>
<td>2-4</td>
</tr>
<tr>
<td>average 4</td>
<td>average 2.5</td>
</tr>
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</table>

Table 3: Post Operative Pain

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-9</td>
<td>4-5</td>
</tr>
</tbody>
</table>

Table 4: Post Operative Anal Stenosis

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>nil</td>
<td>nil</td>
</tr>
</tbody>
</table>

DISCUSSION

Open haemorrhoidectomy with LIS can be sadly performed and improves post operative course of patients.  

Open haemorrhoidectomy is a good procedure but it leads to post operative discomfort and considerable pain in post operative periods whereas combining it with LIS leads to reduction of post operative pain and reduces the need of post operative analgesia.

Open haemorrhoidectomy leads to pain and long hospital stay in post operative period.  

The potential for complications such as anal stenosis, pain is small but remains significant.

CONCLUSION

It is recommended that open haemorrhoidectomy should be done together with lateral internal sphincterotomy to enhance patient’s benefits in post operative period and cost effectiveness.

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FREQUENCY OF HYPOCALCEMIA IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Asma Azhar, Sana Musaddiq, Nadeem Hussain, Nisar Haider Anjum, Iza Ali

Abstract

**Background:** Annually, 15 million people worldwide suffer a stroke while 5 million die and another 5 million are left permanently disabled, placing a burden on family and community. A few international studies have shown hypocalcemia as a factor related with dynamics of stroke and its relationship with severity of stroke.

**Objectives:** The objective of this study was to determine the frequency of acute ischemic stroke and its relationship with severity among patients presenting to a tertiary care hospital.

**Subjects and methods:**

**Study design:** Cross sectional study

**Study duration:** April 2018 - ?

**Study settings:** Medical unit III Jinnah hospital Lahore.

**Data Collection and analysis:** 129 patients with acute ischemic stroke were recruited for the study after clinical modified Rankin scale at the time of admission was noted over-night fasting was ensured and early morning fasting blood sample for serum calcium level Hypocalcemia was labeled as per operational definition. Data was entered and analyzed in SPSS ver: 21.0 and presented and frequency and percentages for acute ischemic stroke and mean and SD for Modified rankin scale to determine the severity of score.

**Results:** Mean age was calculated as 49.10±7.19 years, 58.14%(n=75) were male, mean Rankin score was calculated as 3.67±1.16. Frequency of hypocalcemia among patients with acute ischemic stroke presenting to a tertiary care hospital was recorded in 55.04% of patients had hypocalcemia, comparison of mean scores of Modified Rankin Scale for severity of stroke was 4.52±0.65 in Hypocalcemic group while 2.64±0.72 in cases without hypocalcemia, p value was 0.0001.

**Conclusion:** The frequency of hypocalcemia is higher among patients with acute ischemic stroke presenting to a tertiary care hospital and mean scores of modified Rankin Scale for severity of stroke among patients with hypocalcemia was significantly higher when compared to those without hypocalcemia.

**Keywords:** Acute ischemic stroke, hypocalcemia, modified Rankin Scale, severity of stroke.

World Health Organization defined stroke as a neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours. Annually, 15 million people worldwide suffer a stroke while 5 million die and another 5 million are left permanently disabled, placing a burden on family and community. Stroke rates in middle-aged people are five to ten times higher in Pakistan, India, Russia, China, and Brazil, compared with the United Kingdom or United States. The reason for difference is considered to be the higher prevalence of risk factor i.e. Diabetes Mellitus, Hypertension, hyperlipidemia and a different socioeconomic profile. A recent community based survey showed the prevalence of stroke in Pakistan is 21.8%.

Each episode of stroke is associated with considerable morbidity and mortality, so it becomes highly important to determine the factors which are related with the severity of stroke. It is seen that calcium plays an important role in the pathogenesis of ischemic cell damage but very few studies are available regarding its role in the ischemic stroke and its relationship with severity of stroke. Ovbiala et al. reported that almost 50% of the patients presenting with ischemic stroke had hypocalcemia. Only a single study conducted by Guven et al. is available regarding the relationship of severity of
stroke with hypocalcemia. They reported a frequency of hypocalcemia as 31% among patients of stroke. Moreover, it was also seen that mean score on modified Rankin scale among patients with hypocalcemia were 5 + 0.75 as compared to 3 + 1.25 among patients with normal calcium levels. However, no local study is available so far regarding this relationship.

Prevalence of stroke is much higher in Pakistan as compared to Europe and other countries while Stroke-specific fatality is 7% to 20% with up to 63% of all stroke patients developing complications and up to 89% are dependent for activities of daily living thus making it a highly debilitating disease. Thus it becomes highly important to determine the factors associated with stroke and related with its severity. A few international studies has shown hypocalcemia as a factors related with dynamics of stroke and its relationship with severity of stroke but not much evidence is available on international level and local level. Thus this study will generate further evidence and will provide information to the clinicians regarding role of calcium in stroke and its severity. It will also open an avenue for further research regarding role of calcium in management of stroke to decrease the mortality and morbidity.

OBJECTIVES

The objective of this study was to determine the frequency acute ischemic stroke and its relationship with severity among patients presenting to a tertiary care hospital.

METHODS

A cross sectional study, conducted in Medical unit III Jinnah hospital Lahore from 2018 to 2019, 129 cases is calculated with 95% confidence level, 5% margin of error and taking expected percentage of hypocalcemia as 31% among patients of ischemic stroke through a non probability consecutive sampling. Patients from both genders between 25-60 years of age who had first acute episode of ischemic stroke confirmed on CT Scan were included. All patients with old infarct, primary or Tertiary hyperparathyroidism determined by serum PTH levels, patients with known history of Peripheral Vascular Disease, malignancy or diagnosed with Calciphylaxis were excluded. After an informed consent and detailed clinical examination severity was assessed on the basis of modified Rankin scale at the time of presentation was noted. An overnight fasting was ensured and early morning fasting blood sample of about 5 ml was taken for serum calcium level by the researcher himself. Hypocalcemia was labeled as per operational definition. Confidentiality of the data was ensured. The data was entered and analyzed using SPSS version 17.0. Numerical variable i.e. age and score of modified Rankin scale was summarized as mean and standard deviation. Qualitative variables like sex and hypocalcemia was presented in the form of frequency and percentage. Independent sample t test was used to compare mean score of modified Rankin scale in both groups. P value <0.05 was used as statistically.

RESULTS

Mean age was 49.10±7.19 ye85.27%(n=110) were between 41-60 years, 58.14%(n=75) were males. Mean Rankin score was calculated as 3.67±1.16. Frequency of hypocalcemia was 55.04% (n=71). (Table No. 1).Comparison of mean scores of Modified Rankin Scale for severity of stroke among patients with and without hypocalcemia was done, it shows that 4.52±0.65 in Hypocalcaemia group while 2.64±0.72 in cases without hypocalcemia, p=0.0001. (Table No. 3)
DISCUSSION

Stroke is a clinical syndrome typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting more than 24 h or leading to death, with no apparent causes other than of vascular origin. Ischemia leads to interruption in the oxygen-dependent generation of high-energy compounds eliminating three of the four mechanisms of cellular calcium homeostasis. Awareness of the participation of Ca$^{2+}$ in the ischemic cascade has led to the development of several potential neuroprotective agents designed to modify the role of this ion in acute focal brain injury.

This study was planned to determine the frequency of hypocalcemia and its relationship with severity among patients of ischemic stroke presenting to a tertiary care hospital.

In our study, out of 129 cases, 14.73% (n=19) were between 25-40 years of age while 85.27% (n=110) were between 41-60 years, mean±sd was calculated as 49.10±7.19 years, 58.14% (n=75) were male and 41.86% (n=54) were females, mean Rankin score was calculated as 3.67±1.16. Frequency of hypocalcemia among patients with acute ischemic stroke presenting to a tertiary care hospital was recorded in 55.04% (n=71), comparison of mean scores of Modified Rankin Scale for severity of stroke among patients with and without hypocalcemia was done, it shows that 4.52±0.65 in Hypocalcemic group while 2.64±0.72 in cases without hypocalcemia, p value was 0.0001.

We compared our results with Ovbiagele et al4 who reported that almost 50% of the patients presenting with ischemic stroke had hypocalcemia. Contrary to this only a single study conducted by Guven et al.5 is available regarding the relationship of severity of stroke with hypocalcemia. They reported a frequency of hypocalcemia as 31% among patients of stroke. Our findings are in contrast with the above findings. Moreover, it was also seen that mean score on modified Rankin scale among patients with hypocalcemia were 5±0.75 as compared to 3+1.25 among patients with normal calcium levels. These findings also support the results of our study.

Meghna Borah and others75 determined the correlation between serum calcium (total, corrected, and ionized) and infarct size (IS) in patients with acute ischemic stroke and recorded that total calcium, albumin-corrected calcium, and ionized calcium had a statistically significant negative correlation with IS with r = −0.578, −0.5396, and −0.5335, respectively. Total and ionized calcium showed a significant negative correlation with IS only across the lowest and highest quartiles. Albumin-corrected calcium levels showed a significant negative correlation with IS across all four quartiles. Albumin-corrected calcium levels showed a significant negative correlation with IS only across the lowest and highest quartiles. They concluded that the findings of their study suggest that serum calcium can be used as a prognostic indicator in ischemic stroke as its levels directly correlates with the IS.

Another study5 assessed the relationship between serum calcium levels at admission and initial diffusion-weighted magnetic resonance imaging (DWI) infarct volumes among patients with acute ischemic stroke, they recorded that out of one hundred seventy-three patients (mean age, 70.3 years [age range, 24-100 years]; median National Institutes of Health Stroke Scale score, 4 [range, 0-38]) met the study criteria. The median DWI infarct

### Table 2: Frequency of Hypocalcaemia in Stroke Patients Among Age and Gender

<table>
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<th>HYPOCALCEMIA</th>
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</tr>
<tr>
<td>30</td>
<td>24</td>
</tr>
</tbody>
</table>

### Table 3: Ranking Scale of Subjects

<table>
<thead>
<tr>
<th>Ranking Scale</th>
<th>Hypocalcaemia</th>
<th>Without hypocalcaemia</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total 15-40 years</td>
<td>4.52 ± 0.65</td>
<td>2.64 ± 0.72</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>41-60 years</td>
<td>4.50 ± 0.71</td>
<td>2.67 ± 0.71</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>4.52 ± 0.65</td>
<td>2.63 ± 0.73</td>
<td>P=0.0001</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4.56 ± 0.67</td>
<td>2.59 ± 0.74</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>Female</td>
<td>4.47 ± 0.63</td>
<td>2.72 ± 0.69</td>
<td>P=0.0001</td>
</tr>
</tbody>
</table>
volumes for the serum calcium level quartiles (lowest to highest quartile) were 9.42, 2.11, 1.03, and 3.68 mL. The median DWI infarct volume in the lowest serum calcium level quartile was larger than that in the other 3 quartiles (P < .005). After multivariate analysis, the median adjusted DWI infarct volumes for the serum calcium level quartiles (lowest to highest) were 8.9, 5.8, 4.5, and 3.8 mL. The median adjusted DWI infarct volume in the lowest serum calcium level quartile was statistically significantly larger than that in the other 3 quartiles (P < .05). They concluded that higher serum calcium levels at admission are associated with smaller cerebral infarct volumes among patients with acute ischemic stroke. These results suggest that serum calcium level may serve as a clinical prognosticator following stroke and may be a potential therapeutic target for improving stroke outcome.

The above findings correspond to our study. Very few international studies have shown hypocalcemia as a factors related with dynamics of stroke and its relationship with severity of stroke but not much evidence is available on international level and local level. Thus this study generated further evidence and provided information to the clinicians regarding role of calcium in stroke and its severity. It is also helpful to open an avenue for further research regarding role of calcium in management of stroke to decrease the mortality and morbidity. Our results may be validated through some other trials.

CONCLUSION

We concluded that the frequency of hypocalcemia is higher among patients with acute ischemic stroke presenting to a tertiary care hospital and mean scores of modified Rankin Scale for severity of stroke among patients with hypocalcemia was significantly higher when compared to those without hypocalcemia.

REFERENCES


FREQUENCY OF HYPOCALCEMIA IN PATIENTS WITH ACUTE ISCHEMIC STROKE


**EFFECT OF FLAX SEED OIL ON RENAL FUNCTIONS IN ACETAMINOPHEN INDUCED RENAL DAMAGE IN ALBINO RATS**

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**Abstract**

**Introduction:** Acetaminophen, commonly used for pain and fever is known for its hepatotoxic and nephrotoxic effects. The current study was done to determine the protective effect of flax seed oil on acetaminophen induced nephrotoxicity in albino rats.

**Materials and Methods:** Forty male albino rats, aged 6-8 weeks and weighing between 175-225 gm were randomized into five groups having 8 animals each. Group A, which served as control, was given normal saline intraperitoneally on day 1. Group B and C were given a single dose of 1000 mg/kg acetaminophen intraperitoneally dissolved in 5ml/kg normal saline on day 1. Group D was given flax seed oil, 2 ml at a dose of 1.86gm/kg orally, once daily for 14 days. Group E was given flax seed oil, 2 ml at a dose of 1.86gm/kg orally, once daily for 14 days, followed by a single intraperitoneal dose of acetaminophen, 1000 mg/kg dissolved in 5ml/kg normal saline one hour after giving flax seed oil. The animals of group A, B and D were sacrificed on the 15th day of experiment, whereas, animals of group C and E were sacrificed 48 hours after giving acetaminophen. At the end of the experiment, cardiac puncture was performed to draw blood from each animal for renal function tests.

**Results:** Pretreatment with flax seed oil reduced toxic effects of acetaminophen as evidenced by reduction of serum urea and creatinine.

**Conclusion:** Flax seed oil is useful in protecting acetaminophen induced nephrotoxicity

**Keywords:** Acetaminophen, flax seed oil, nephrotoxicity, serum urea and creatinine.

Acetaminophen, also known as Paracetamol is one of the over the counter available drugs used for its antipyretic and analgesic effects.¹ It is used alone or in combination with other medicinal preparation for the treatment of cough, cold and flu.²³ It has no side effects and is well tolerated in therapeutic doses.⁴ Although it is safe, its overdosage or misuse leads to hepatic and renal failure in humans and experimental animals. Acetaminophen induced hepatic and renal damage is produced by oxidative stress which results due to an increase in lipid peroxidation and depletion of glutathione.⁵ This oxidative stress damages the tissues and can be prevented by antioxidants. Many herbs and their seeds are a rich source of antioxidants as flavonoids and lignans; they neutralize the toxic compounds which are produced as a result of oxidation processes taking place within the body.⁶ Many synthetic antioxidants being used to stabilize food have been restricted because of their carcinogenic effects; those obtained from natural sources are considered safe.⁷ Flax is a blue flowering crop; its seed is known as ALSI in Indian and Punjabi. Flax seed oil is extracted from flax seeds.⁸ Consumption of flax seed is useful for human health.⁹ The seeds contain about 36-40% oil, which among crop plants, is the richest source of polyunsaturated fatty acids (PUFA)¹⁰; the oil contains 40 to 60% of its content as alphalinolenic acid which is a poly unsaturated fatty acid. About 15% each of linoleic acid and oleic acid are also found. It also contains a lignan, secoisolarici-resinol diglucoside (SDG) which is a phytochemical...
having antioxidant properties. Flax seed oil is used as a nutritional supplement due to its antioxidant and anti-inflammatory properties. Since it contains alpha linolenic acid as PUFA, it has a variety of remedial effects as reducing blood pressure by causing vasodilation, reduces blood cholesterol, prevents atherosclerosis, hepatoprotective and renoprotective. Flax seed oil is known for its antioxidant, anti-inflammatory and anticarcinogenic properties. These effects are primarily due to the polyunsaturated fatty acids found in α-linolenic acid and flax liganans, both found in flax seed oil. Protective effect of flax seed oil against lead acetate induced nephrotoxicity has already been studied. Studies have shown its role in the improvement of serum urea and creatinine levels.

The current study was therefore conducted to assess the possible protective effect of flax seed oil on acetaminophen induced nephrotoxicity in albino rats.

METHODS

This experimental study was conducted at the anatomy Experimental Research Laboratory and department of Anatomy University of Health Sciences, Lahore.

Acetaminophen was obtained from Merck Pharmaceuticals in a powdered form. Solution of acetaminophen was prepared by dissolving acetaminophen in 0.9% normal saline. Flax seed oil was extracted by PCSIR laboratory, Lahore.

Forty male albino rats, 6-8 weeks old, weighing 175-225gm, were procured from University of Health Sciences, Lahore. They were weighed and housed in steel cages and kept under controlled environment having room temperature (22±3°C), humidity (55%±5) and light and dark cycles of 12 hours each. Animals were fed on standard rat diet and tap water ad libitum and were acclimatized for a week before starting the experiment, they were divided into five groups A, B, C, D and E.

Group A was given a single dose of 5ml/kg normal saline, intraperitoneally on 1st day. Group B and C were given a single dose of acetaminophen, 1000mg/kg dissolved in 5ml of normal saline intraperitoneally on 1st day. Group D was given flax seed oil, 2ml at a dose of 1.86g/kg orally, once daily for 14 days. Group E was given 2 ml of flax seed oil at a dose of 1.86g/kg orally, once daily for 14 days. On 14th day, an hour after treatment with flax seed oil, the rats of group E were given acetaminophen, 1000 mg/kg dissolved in 5 ml of normal saline intraperitoneally. The animals of groups A, B and D were sacrificed on day 15 of experiment and those of groups C and E were sacrificed 48 hours after giving injection of acetaminophen.

Blood samples from each group were drawn under chloroform anaesthesia by cardiac puncture. 5ml of blood was drawn in 5ml disposable syringe by cardiac puncture and was transferred to vacutainer and after clotting centrifuged at a speed of 3000 r /pm for 10 minutes. The clear serum was separated, labeled and stored at -20°C for biochemical evaluation. Data was analysed by using SPSS version 20.0. One way ANOVA was used to evaluate mean differences among groups and post hoc Tukey’s test was applied to assess pair wise comparison. P-value of ≤ 0.05 was considered as statistically significant.

Results

In groups A, B, C, D and E, the mean values of serum urea were 32.17±4.36, 66.46±8.96, 77.38±5.76, 40.0±4.61 and 43.02±2.79 mg/dl respectively (table 1). Serum urea in group B, C and E was significantly raised when compared with group A (p=0.001, p=0.001 & p=0.005 respectively). P-value was significantly raised in group B and C when compared with group D (p=0.001). Flax seed oil treatment in group E lowered serum urea significantly when compared with group B and C (p=0.001).

Mean value of serum creatinine was 0.64±0.11, 1.69±0.10, 1.83±0.24, 0.72±0.13 and 0.99±0.16 mg/dl in groups A, B, C, D and E respectively. Mean value of serum creatinine in group B, C and E was
significantly raised when compared with group A (p=0.001, p=0.001 & p=0.001 respectively) and D (p=0.001, p=0.001 & p=0.013 respectively). Flax seed oil treatment in group E lowered serum creatinine significantly when compared with group B and C (p=0.001 each).

**DISCUSSION**

In the current study toxic effects on kidneys was evidenced by changes in the histological and biochemical parameters. These changes were also observed earlier by Zhao et al and Khorsandi, L. and Orazizadeh.

Mean value of serum urea and creatinine was significantly raised in groups B and C when compared with groups A and D (p< 0.05) showing deterioration of renal functions. This can be explained due to the presence of correlation between nephrotoxicity and oxidative stress which alters the filtration surface area and decreases glomerular filtration, resulting in accumulation of urea and creatinine in the blood. Ilbey et al. (2009) also reported a rise in serum urea and creatinine levels when injected a single dose of 1000 mg/kg of acetaminophen intraperitoneally. In group E of current study, the difference in mean values of serum urea and serum creatinine were statistically significant when compared with groups B and C (p=0.005) which demonstrated the protective effect of flax seed oil on acetaminophen induced renal damage. The therapeutic properties of flax seed oil as its antioxidant and free radical scavenging activity during oxidative stress has also been reported. Present study revealed that flax seed oil administration ameliorated histopathological and biochemical renal changes induced by acetaminophen.

**CONCLUSION**

The present study demonstrated the effect of flax seed oil on nephrotoxicity produced by acetaminophen in albino rats. It reduces the damaging effects of acetaminophen on proximal and distal convoluted tubules and caused significant reduction in biochemical parameters, that is, serum urea and creatinine; thus indicating considerable protection by flax seed oil.

**REFERENCES**

Follicular cells of thyroid gland secrete Triiodothyronine (T3), Thyroxine (T4), while para-follicular C-cells secrete Calcitonin hormone. Thyroid hormones (T3, T4) are crucial for normal growth, development, CNS maturation and sexual differentiation. Both T3 & T4 are highly essential for cellular maturation and differentiation during various stages of development. The children deficient in thyroid hormones show stunted growth, poor CNS development and impaired sexual maturation. Thyroid gland is considered to functionally adapt itself during various stages of human life, such as in pregnancy, infancy, childhood and post menopausal stage. Deficiency of thyroid hormones during pregnancy has detrimental effects on the fetal development, because thyroid hormones have a key role in the normal development of brain during intra-uterine and post-natal life. In the first trimester maternal thyroxin readily crosses the placental membranes, and a decreased secretion of T4 levels during the 1st trimester can cause decreased mental scores, psychomotor and mental derangements that are permanently irreversible (Julvez et al., 2013).

Thyroid function has significant direct and indirect effects on the reproductive system, especially in females, and these effects are mutual and inter-related throughout the fertility period in a woman. These effects of thyroid hormones on female reproductive function are well characterized. In women with thyrotoxicosis, due to excess thyroid hormones, the inter-menstrual interval is usually either prolonged or shortened, as a result the menstrual flow is initially diminished and ultimately ceases. Such patients may develop infertility, and even if conception takes place, there is an increased risk of miscarriage in the effected women. The menstrual cycles in women with thyrotoxicosis, basal plasma concentrations of LH and follicle-stimulating hormone (FSH) are reportedly normal, but these patients display an exaggerated response to gonadotropin-releasing hormone (GnRH).

The incidence of thyroid disorders is considered higher, compared with the general population, and in addition, although thyroid does not directly influence the pathogenesis of menopausal complications, but it has been highlighted that both hypothyroidism and hyperthyroidism potentiate some of the serious outcomes in post-menopausal women, including osteoporosis, cardiac failure and atherosclerosis (Del-Ghianda, 2014). In a separate study assessing the thyroid status, it was concluded that prevalence of hypothyroidism is very high in patients with type-2 diabetes mellitus (DM), and the risk aggravates if their body mass index (BMI) is above 25 (Davina, 2012). Type-2 diabetes adversely affects the functions of thyroid gland in post-menopausal women, and this clinical aspect is less studied in the past. In the current study, plasma thyroid hormones levels are measured in diabetic and non-diabetic post-menopausal women, and a comparison is established between the two groups.

**METHODS**

This case control study was performed during the year (2014-2015) and seventy post-menopausal female subjects were included which were diagnosed as a case of type-2 diabetes. In postmenopausal cases, two sub-categories were made. One included those have type 2 diabetes, confirmed by blood
glucose analysis, and were termed as diabetics, while the other group were non-diabetics, confirmed by blood glucose analysis of each individual. Twenty five healthy post-menopausal females were selected as controls. The patients were selected from the Social Security Hospital outdoor department. After taking consent from each patient, 5 ml venous blood samples were obtained, and transferred into the gel vacutainer for analysis of plasma thyroid hormones. Each sample was allowed to clot for 30 minutes, then centrifuged at 3000 rotations per minute (RPM) for 10 minutes. The clear supernatant serum was pipetted out and transferred into 1.5 ml Appendrof vials (German), then hormone analysis was performed by Enzyme Immunoassay Method.

ESTIMATION OF THYROXIN (TOTAL T4)

It is a Competitive Enzyme Immunoassay Method which employs the ready-kits for Total Thyroxin titled ‘AccuBind ELISA Microwells’ (Product Code:BC-1007) of Monobind Inc. CA, USA.

All the given reagents were prepared according to the kit manual. 25µl of calibrators, controls and samples were added to assigned mico-wells. Then 100µl of Working Conjugate Reagent T4 Enzyme Reagent was added to each well. Microplate covered with plastic wrap was swirled gently for 20-30 seconds to mix. Then it was incubated for 60 minutes at room temperature (18-25ºC). Microplate was washed three times by 350µl wash buffer in automated washer. 100µl of TMB Reagent was added to each well and the microplate was again incubated for 20 minutes at room temperature. 100µl of stop solution was added to each well and mixed gently for 30 seconds. The initial blue color changed entirely to yellow. The absorbance was read at 450nm in microplate reader. The concentration of total triiodothyronine (TT3) was determined from a dose response curve obtained by plotting absorbance (abs) against T3 concentration (conc) in ng/ml.

ESTIMATION OF TRIIODOTHYRONINE (TOTAL T3)

All the reagents were prepared as per kit manual. 50µl of calibrators controls and samples were added to assigned wells. Then 50µl of Antibody Reagent was added to each well. Microplate covered with plastic wrap was swirled gently for 30 seconds to mix. 100µl of working Conjugate Reagent was added to each well and mixed for 30 seconds. The microplate was incubated for 60 minutes at room temperature, then washed three times with 350µl wash buffer in automated washer. 100 µl of TMB Reagent was put in each well and was mixed for 10 seconds, incubated for 20 minutes at room temperature. Then100µl of stop solution was added to each well and mixed gently for 30 seconds. The blue color in wells changed entirely to yellow. The absorbance was read at 450nm in microplate reader. The concentration of TSH was determined from a dose response curve obtained by plotting absorbance (abs) against TSH concentration (conc) in µIU/ml.

LITERATURE REVIEW

Thyroid functions in patients of diabetes have
been under discussion in recent studies, and Vikram et al in 2013 reported low plasma levels of T3 and T4 along with high TSH levels in patients with type-2 diabetes. The study concluded that diabetes and thyroid dysfunctions are significantly inter-related, and in diabetes mellitus, subclinical hypothyroidism is among the most common disorder, with patients having low T3, T4 and high TSH levels (Vickram et al., 2013). Earlier it was documented that diabetic patients have a much higher incidence of thyroid disorders as compared with the normal population because of a higher risk of autoimmunity, particularly in post-menopausal females (Patricia 2000). A similar study, few years ago showed a significantly increased prevalence (31%) of high plasma TSH in patients with type 2 diabetes. In these diabetic women, the incidence of thyroid disorders was documented to be 12.3% compared with diabetic males (Papaza firopoulou 2010). Prevalence of thyroid disorders in type-2 diabetic patients was demonstrated to be 29%, while the incidence of thyroid disorders in diabetic females was shown to be 36%, and in males it was 22% concluding that the elderly females with type-2 diabetes have a high incidence (18.2%) of sub-clinical hypothyroidism (Ravishanker et al., 2013).

In another study, the role of reproductive hormones in post-menopausal females was explained; that the estrogen hormones dominate in elderly women, usually in their mid-thirties, but shows a progressive decline in progesterone levels which is rapid than the decreased estrogen levels in plasma. This results in an imbalance of estrogen and progesterone hormones, which further worsens over time causing undesirable adverse effects. Due to the estrogen dominance, liver synthesizes high levels of Thyroxin Binding Globulin protein (TBG), which binds thyroid hormones resulting in decreased plasma levels of these hormones. It also leads to suppression of thyroid functions within few years. On the other hand, progesterone helps in proper uptake and utilization of thyroid hormones by peripheral tissues, and does not stimulate hepatic synthesis of TBG as does estrogen, thus, it may have a suppressant effect on TSH levels. This fact establishes a relationship between thyroid function and progesterone levels, attributed to a cross-linking between the receptors of these two hormones that are steroids and various mediators taking part in gene transcription (Trentini et al., 2013). It has been demonstrated in post-menopausal women who were euthyroid, that progesterone causes a significant increase in plasma total T4 (Sathi et al., 2013).

RESULTS

In non-diabetic postmenopausal females the average plasma level of TSH was 4.05 ± 0.693 µIU/mL, while in post-menopausal non-diabetic females it was 3.92± 0.383µIU/mL. The slightly decreased plasma levels of TSH in the diabetic post-menopausal females was, however, statistically non-significant (P=0.537). In non-diabetic postmenopausal subjects, the TSH hormone was 8.64% greater in concentration as compared to non-diabetic premenopausal subjects, the difference was non-significant statistically (P=0.738). The hormone levels were almost in a very close range in non-diabetic pre and diabetic postmenopausal states.

<table>
<thead>
<tr>
<th>Reproductive State</th>
<th>Disease Status</th>
<th>Mean ± SEM</th>
<th>%Difference between the groups</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenopausal</td>
<td>Non-Diabetic</td>
<td>4.05± 0.693</td>
<td>3.20%</td>
<td>0.537</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>3.92± 0.383</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Plasma TSH levels did not show significant variations in the comparisons mentioned in the table above. (Table 1; Fig. 1).

In non-diabetic postmenopausal females, the average level of TT4 was 12.95±0.322µg/dL and 13.09 ± 0.201µg/dL in diabetic postmenopausal subjects. There was almost no difference between these two states.
Fig. 1. Mean Concentrations of TSH uIU/mL in Postmenopausal Non Diabetics (Pst Mp N) and Postmenopausal Diabetic (Pst Mp D).

Table 2: Mean Concentrations of TT4 in Postmenopausal Non Diabetics (Pst Mp N) and Postmenopausal Diabetic (Pst Mp D) and Premenopausal Non Diabetic Subjects (Pre Mp N). SEM: Standard Error of Mean; \( P < 0.05 \) Statistically Significantly different.

<table>
<thead>
<tr>
<th>Reproductive State</th>
<th>Disease Status</th>
<th>Mean±SEM</th>
<th>%Difference between the groups</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenopausal</td>
<td>Non-Diabetic</td>
<td>12.95±0.322</td>
<td>1.0%</td>
<td>0.958</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>13.09±0.201</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

postmenopausal diabetic (Pst Mp D).

The concentration of TT3 was estimated to be 4.81±0.228 ng/mL in postmenopausal non-diabetics and 3.28±0.169ng/mL in diabetic postmenopausal subjects. In the diabetic subjects the fraction of the hormone was 31.80%lower as compared to their respective non-diabetic controls. This difference was highly significant statistically \( (P=0.001) \). (Table 3; Fig. 3).

Table 3: Mean Concentrations of TT3 in Postmenopausal Non Diabetics (Pst Mp N) and Postmenopausal Diabetic (Pst Mp D) and Premenopausal Non Diabetic Subjects (Pre Mp N). SEM: Standard Error of Mean; \( P < 0.05 \) Statistically Significantly Different.

<table>
<thead>
<tr>
<th>Reproductive State</th>
<th>Disorder State</th>
<th>Mean±SEM</th>
<th>%Difference between the groups</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenopausal</td>
<td>Non-Diabetic</td>
<td>4.81±0.228</td>
<td>31.80%</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>3.28±0.169</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSION

Thyroid stimulating hormone (TSH) did not exhibit a significant variation in different comparisons in diabetic, non-diabetic postmenopausal and non-diabetic premenopausal women. In non-diabetic postmenopausal subjects noticeable although insignificant statistical increase in TSH compared to the premenopausal subjects was observed. The increased concentration of TT4 in non-diabetics was non-significant, however it was significantly greater in diabetic post-menopausal females as compared with premenopausal phase.

In the diabetic subjects TT3 was 31.80% lower as compared to their respective non-diabetic controls. This difference was highly significant statistically \( (P=0.001) \). Therefore, the present study proposes that TSH concentration in the circulations is not affected significantly in postmenopausal non-diabetic and diabetic subjects.

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FREQUENCY AND CLINICOHAEMATOLOGICAL FEATURES OF THE THREE PHASES OF CHRONIC MYELOID LEUKAEMIA (CML) ON PRESENTATION--A STATISTICAL STUDY FROM TERTIARY CARE HOSPITAL LAHORE.

Fatima Saeed¹, Muneeza Natiq², Saad Zafar³, Masooma Jaffer⁴

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Abstract
Chronic Myeloid Leukaemia is a clonal disease that results from acquired genetic change in a pluripotential hematopoietic stem cells¹.

Objective: The objectives of my study were:

1) To determine the frequencies of different phases of chronic myeloid leukaemia (CML) in newly diagnosed cases.

2) To study the frequency of clinicoheamatological features at presentation.

Study Design: Cross Sectional study

Study Duration: This study was conducted from 20th January 2015 to 20th August 2016 (approx 19 months)

Settings: Department of Haematology Allama Iqbal medical college/ Jinnah hospital LRH.

Subjects and Methods: Demographic information was obtained on Performa. Bone marrow biopsy were performed on patients of CML, for frequency determination of three phases of CML. Clinicoheamatological features were determined by history, physical examination ultrasound and CBC. The phases of CML and clinicoheamatological features were labelled as per operational definition.

Results: In this study out of 180 cases there were 136 cases of chronic phase, 29 cases of accelerated phase and 15 cases of blast phase with male predominance. Most of the patients fall in age group of 18-40 years (66.1%). Mean blast count was 8.6%. Chief presenting complaint was abdominal pain/tenderness in chronic (70.6%) and accelerated phase (58.6%) whereas in blast phase chief complaint was fatigue (60%). Splenomegaly is the most common clinical sign. Haematological values at presentation showed Hb less than 10gm/dl in all three phases of CML. TLC more than 20 × 10⁹/L was observed in all cases of CML with most of the cases fall within the range of 151-300 × 10⁹/L Platelet count > 450 × 10⁹/L was observed in accelerated phase (48.3%).

Conclusion: CML is common in age group between 18-40 years with male predominance; chronic phase is the most common phase. Abdominal pain/tenderness is most common presenting complaint in chronic and accelerated phase, whereas fatigue is most common in blast phase. Splenomegaly is the most common presenting sign. Among haematological findings, Hb is less than 10gm/dl, total leucocytes count within range of 151-300 × 10⁹/L in all phases of CML, whereas platelet count > 450 × 10⁹/L is common in accelerated phase.

Key words: Chronic Myeloid Leukaemia, Philadelphia chromosome, Abdominal pain/tenderness, Splenomegaly, Fatigue

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Chronic Myeloid Leukaemia (CML) is a myeloproliferative neoplasm characterized by rearrangements of the long arm of chromosome 9 and 22, resulting in Philadelphia chromosome Ph, creating fusion oncogene of BCR-ABL 1. World Health Organization (WHO) defines "chronic myeloid leukaemia (CML) as myeloproliferative neoplasm that originates in an abnormal pluripotent stem cells and is consistently associated with BCR-ABL 1 gene located on Philadelphia chromosome." Natural history of chronic myeloid leukaemia is triphasic with chronic phase is the most common phase followed by accelerated phase and blast crises.

Chronic myeloid leukaemia had an incidence of 1-2/100000 population and it accounts for 15% of adult leukemia. Median age for onset of disease is 50-60 years and had slight increase incidence in males. Factors predisposing to chronic myeloid leukaemia (CML) are unknown but radiation exposure has been found in few of the cases.

Chronic myeloid leukaemia (CML) is characterized by reciprocal translocation between chromosome 9 and 22 (t9:22) (q34;q11) involving two genes BCR and ABL that forms a fusion gene BCR-ABL on chromosome 22 (Philadelphia chromosome Ph 22). This produces an aberrant 210K Da protein that has greater tyrosine kinase activity than normal ABL protein, and responsible for pathogenesis of the disease.

About 20-30% of the patients are asymptomatic and are diagnosed incidentally on routine medical checkup. Common clinical findings are splenomegaly (in 75% cases) fatigue, night sweats, weight loss, anaemia, bruising and haemorrhage (due to abnormal platelet function).

Chronic Myeloid Leukaemia (CML) is divided into three phases Chronic Phase, Accelerated phase and Blast crisis depending upon blast count in peripheral blood and in bone marrow along with other WHO criteria's.

This study was carried out at department of Haematology Allama Iqbal Medical College Lahore where large number of cases of chronic Myeloid leukaemia has been diagnosed on bone marrow biopsy. I want to see what is the most common phase of chronic myeloid leukaemia and what will be the most common presenting complaint/clinical features in our set of population. This may guide our clinician / Physician for subsequent management, improving quality of life of the patients as well as better utilization of health care resources.

METHODS

This cross sectional study was conducted from 20th January 2015 to 20th August 2016. (Approx 19 months) in department of Haematology Allama Iqbal Medical College/Jinnah Hospital Lahore.

Operational Definitions:

Abdominal discomfort: Pain and discomfort in left hypochondrial area which is determined on history.

Fatigue/lethargy: Feeling of weakness on performing daily routine work and is determined on clinical history and examination (pallor).

Splenomegaly: 2 fingers or more below left costal margin on palpation.

Hepatomegaly: 2 fingers or more below right costal margin on palpation.

Anaemia: Anaemia diagnosed on CBC done on automated haematology analyser (Sysmex KX 21), showing haemoglobin 10g/dl or less.

Raised White cell count: more than 20×10⁹/L done on automated haematology analyser (Sysmex KX 21)

Raised Platelet count: more than 450X10⁹/L on automated haematology analyser (Sysmex KX 21).

PHASES OF CHRONIC MYELOID LEUKAEMIA:

Chronic myeloid leukaemia is accessed at the time of presentation on the basis of percentage of blasts present in peripheral blood and bone marrow aspirate smear seen under microscope. Presence of any of the following stage will be labelled as Chronic Myeloid Leukaemia.

Chronic phase ----------5-9% blasts
Accelerated phase ------10-19% blasts
Blastic phase ----------- 20% OR MORE blasts

Sample size and Technique: A total of 180 cases are calculated using 95% confidence level, 4% of margin of error and having an expected percentage of blast phases as 7.8% from pervious literature in chronic myeloid leukaemia patients. Sample technique used was Non Probability Sampling technique (Consecutive type).

Inclusion criteria:

- Age: from 18 years ------- 80 year
- Gender: Both male and female
- Patients of CML (as per operational definition) diagnosed within last one month.

Exclusion criteria:

- Previously known or follow up cases of chronic myeloid leukaemia.
- Any other myeloproliferative neoplasms like Primary Myelofibrosis, Essential Thrombocytosis, and Polycythemia Rubra Vera are excluded on bone marrow biopsy and molecular
analysis and pervious medical record.

**Data Analysis procedure:**

About 180 cases fulfilling the inclusion criteria were enrolled in my study from inpatient department of Jinnah Hospital Lahore. Informed consent was obtained from every patient. Bone marrow biopsy was performed on patients of chronic myeloid leukaemia and determination of three phases of chronic myeloid leukaemia, as per operational definition.

ClinicoHaematological features were determined by history, physical examination, ultrasound and CBC on automated haematology analyser. Demographic information like age, gender, contact number and address was obtained. All of the data was collected by Researcher on specially designed Performa and confidentiality was ensured. The data was analysed through SPSS (Statistical Packages for Social Sciences) version 20. After tabulation and graphs we will stratify the data into Qualitative and Quantitative variables. Quantitative variables were expressed as mean±Standard Deviation. Qualitative variables were expressed as percentage. Effect modifiers like age, gender, phases of CML were controlled through stratification. Post stratification chi square test was applied. P-value <0.05 was used as statistically significant.

**RESULTS**

In this study phases of chronic myeloid leukaemia was showed in graph 1. Mean blast count in my study was 8.6. Gender distribution in different phases of CML was showed in table 1.

The age range for entire study population was 18-80 years and for analysis we divide the patients into two age groups that is 18-40 years and 41-80 years. 119 patients fall in age group between 18-40 years and 61 patients fall in age group between 41-80 years. Mean age of the entire study population was 37.06 years with standard deviation of 13.29. Analysis of age groups among different phases of CML was explained in table 2(p value = 0.445).

Clinical features at presentation among different phases of CML were explained in table 3.

Haematological features among different phases of CML was analysed and explained in table 4.

**DISCUSSION**

This study finds the frequency and clinicoheamatological features of the three phases of chronic myeloid leukaemia on presentation. Further data was stratified according to age, gender, clinical and haematological features meaning which age group, gender, clinical and haematological findings are common in three different phases of chronic myeloid leukaemia. My study revealed that out of 180 patients, 136(75.6%) in chronic phase, 29(16.1 %) in accelerated phase and 15 (8.3%) were present in blast phase. These findings were almost equal to international study by Anthony A. Oyekunle et al which also showed out of 272 patients, 205 were in chronic phase, 54 in accelerated phase, and 5 in blastic phase.6 Local study by Farzana Chang, Riaz Ahmad Qazi et al (2015) showed that out of 83 patients of CML there were 62 (74.6%) in chronic phase (CP), 17 (20.4%) in the accelerated phase (AP) and 3 (3.6%) in blast crisis (BC).7

Among gender ,in my study out of 180 cases ,there were 93 males and 87 females with male to female ratio was 1:0.6 with slight male predominance. In chronic phase there were 68 males and 68 female, in accelerated phase there were 16 males and 13 females, in blast phases there were 9 males and 6 females. This data was almost similar to one of the local study by Farzana Chang et al in which out of 83 patients there were 52 males and 31 females with male to female ratio of 1.6:1, with male predominance, in chronic phase there were 42 males and 22 females, in accelerated phase there were 11 males and 6 females, in blast phase there were 2 males and 1 female. In Bangladesh a study was conducted which showed out of 63 patients there were 42 males and 21 females with male predominance.8

Among Age in my study, range was 18-80 years and we divide age into two groups 18-40 years and 41-80 years. most of the patients (119 out of 180 cases) in my study fall in age group between 18-40 years with mean age =37.06 years. French study in 2005 showed mean age group 55 years . Local study in 2009 which was close to my study showed mean age of 37 years with range of 18-65 years.9

Among clinical features in my study, most common presenting complains were abdominal pain/tenderness (70.6% and 58.6% in chronic and accelerated phase) followed fatigue (45.6% and 51.7% in chronic and accelerated phase) and pallor (27.2% and 27.6% in chronic and accelerated phase) while in blast phase most common presenting complain was fatigue (60%) followed by abdominal pain/tenderness (53.3%) and pallor (46.7%). Among clinical signs in my study splenomegalgy is most common sign followed by hepatomegaly and lypha-denopathy in all three phases of CML. Internationally study conducted in England showed fatigue/ lethargy as most common presenting complain.
33.5% followed by bleeding 21.3%, weight loss 20%, abdominal fullness 14% splenomegaly and purpura were most common signs in this study.\(^1\) Local study published in 2006 which was close to my study showed chief complaints at presentation were fever (65%), mass/pain left hypochondrium (63%), weakness (37%) body aches and pain (36%). Clinical signs at presentation included splenomegaly in 98% patients, hepatomegaly in 57% patients.\(^2\)

Haematological features in my study showed Anaemia that is Hb less than 10gm/dl in all phases of CML, Total Leukocyte count within the range of 151-300×10^9/L was observed in all phases of CML, whereas Platelet Count within normal range that is 150-450×10^9/L observed in chronic phase, thrombocytosis >450×10^9/L observed in accelerated phase and thrombocytopenia<150×10^9/L was observed in...
Fatima Saeed

Blast phase of CML. Internationally study conducted in England showed Haemoglobin level was between 7.5-9.4gm/dl in 23%, white cell count less than 20×10⁹/L in 4.5%, between 20-100×10⁹/L in 23%, between 100-250×10⁹/L in 36%, between 250-350×10⁹/L in 17%, >350×10⁹/L in 19%, platelet count between 150-450×10⁹/L in 46% and between 450-650×10⁹/L in 16% patients. Local study showed anaemia that is Hb <10gm/dl in all phases of CML, TLC between 101-300×10⁹/L in 63% of patients ,Platelet count within range of 150-450×10⁹/L was observed in 66.3% in chronic phase, and 28.6% in accelerated phase while between 21---149×10⁹/L 53.3% was observed in Blast crises.

CONCLUSION

In my study CML was common in age group between 18-40 years with male predominance Chronic phase was frequent phase. Most patients presented with abdominal pain/tenderness in chronic and accelerated phase of CML whereas fatigue was presenting complaint in blast phase. Splenomegaly was presenting sign at my set of population. Among haematological findings, common findings were low Hb level less then 10gm/dl, total leucocytes count within range of 151-300×10⁹/L in all three phases of CML whereas normal platelet counts (150-450×10⁹/L) was common in chronic phase, >450×10⁹/L was common in accelerated phase and less than 150×10⁹/L is common in blast phase.

REFERENCES:

COMPARISON OF STUDENTS' PERCEPTIONS ABOUT ABSENTEEISM IN A PRIVATE AND A PUBLIC MEDICAL COLLEGE

Fatima Inam, Munnaza Sardar, Zainab Nazneen

Abstract

Introduction: Students miss their lectures, tutorials and practical classes due to number of reasons affecting their grades. Perceptions of students of private and public medical college about absenteeism were compared to bring awareness among them, how social and academic stressors are common among student community.

Material and methods: First and second year MBBS students (n=387) in Allama Iqbal medical college and Akhtar Saeed medical college were given proforma consisting questions which assessed the various reasons of absenteeism and suggestions from students to improve attendance. Frequencies and percentages were calculated for categorical variables while mean and standard deviations for continuous variables. Association between attendance and type of college was determined by chi square test. To compare the reasons of absenteeism and suggestions given by students of public and private medical colleges, independent sample t test was applied. P value of ≤0.05 was considered significant.

Results: A statistically significant difference reasons of absenteeism among students of public medical college were poor contents of lecture, poor lecture delivery, poor lighting system of lecture halls, poor sound system and no action taken on absenteeism (0.00, 0.01, 0.00, 0.00, 0.00 ) respectively. The more common reasons in private sector College were ability to download lectures from internet, absenteeism due to preparation for test, attending social gatherings and absenteeism due to lack of recreational facilities (0.00, 0.03, 0.00, 0.00) respectively. Statistically significant difference was found in two suggestions i.e. more self-study time (0.001) and increasing intervals between lectures (0.000).

Conclusion: Problem of absenteeism exists both in public and private medical institutes. There is a need to understand the reasons behind the absenteeism in both setups and to rectify these reasons in order to increase the students' performance.

Keywords: Absenteeism; Medical Students; Lectures; Likert Scale;
COMPARISON OF STUDENTS’ PERCEPTIONS ABOUT ABSENTEEISM IN A PRIVATE AND A PUBLIC MEDICAL COLLEGE

between class attendance and academic performance of medical students in these and other subject. Due to absenteeism, not only the academic performance of the students is affected but the parents, institute and the society at large also suffer a lot.\textsuperscript{10}

Despite uniform syllabus and examination body for most of the private and public medical colleges, there are certain differences in both set ups. Merit of students in government colleges in Punjab is much higher but the students are from all social cadres. On the other hand students of private medical colleges are generally from affluent families which can pay heavy fee. There is a general perception that classes are held on time, professors are friendlier, and students are taught more efficiently and thoroughly in private medical colleges.\textsuperscript{11-12}

The differences in the environments and other factors of both public and private medical colleges can be the cause of different views about reasons of absenteeism among their students. Therefore the rationale of this research is to study the differences between perceptions of students of a private and public medical college about why they do not attend the classes and to gather their suggestions to improve attendance. This will help the public and private institutes to know the common reasons of student absenteeism in their set up and thus devise policies to reduce this problem accordingly.

METHODS

It was a descriptive cross sectional study which was conducted on First and second year MBBS students (n=387) in two medical colleges of Lahore. One from public sector, AllamaIqbal medical college and the other from the private sector, Akhter Saeed medical college. The study duration was one year from October 2018 to September 2019. All the students of first year and second year MBBS academic secession 2018 who gave consent to participate were included in the study\textsuperscript{7}. Exclusion criteria include the detained students. Permission was taken from ethical review board of both the medical colleges. For collection of data, a pretested proforma was developed by the researcher to measure the variables. Section one of the proforma contained the information regarding the demographic factors like age, gender, residential type, previous schooling, parents educational and socioeconomic status and their attendance. Section 2 of proforma comprised of questions which assessed the various reasons of absenteeism from the class. Section 3 contained the suggestions from students to improve the attendance. All sections contained close ended questions. The participation of the student was voluntary and anonymous. Initially they were briefed about the proforma and then they filled the proformas in the absence of researchers and put in box which was collected later. Variables were measured by a 5 point likert scale. The response rate was 77%. Data was entered in SPSS version 16 for analysis. Frequencies and percentages were calculated for the categorical variables while mean and standard deviations for the continuous variables. Association between attendance and type of college was determined by chi square test. P value of $\leq 0.05$ was considered significant. To compare the reasons of absenteeism and suggestions given by the students of public and private medical colleges, independent sample t test was applied. P value of $\leq 0.05$ was considered significant.

RESULTS

Out of the total most 246(63.6\%) of the students were in 18-20 years age group both in the public (44.2\%) and private (19.6\%) sector college. Majority of the students were females 206(53.2\%) with 30.5\% in public and 22.7\% in private sector college. Total 67.4\% students were hostelites in both colleges and about 275(71\%) had attended public schools in their earlier life.

Overall attendance of most of the students was between 50-75\% in both colleges. A significant association was found between attendance and type of college by performing chi square test (p = 0.04) with 52.7\% of the students with better attendance belonging to the public sector college as shown in
To test the hypothesis that the overall reasons for absenteeism and the suggestions given by the students were significantly different in public and private sector colleges, an independent samples t test was performed after scoring the likert scale. The assumption of equality of variances was satisfied by Levene’s F test. For overall reasons for absenteeism, independent samples t test was not associated with statistically significant effect, t(385)= -0.62, p=0.53. However the suggestions given by the private sector college students were significantly different from those given by public sector college with t(365)= 3.47, p=0.001. Table II shows the means with standard deviations and p values of the overall reasons for absenteeism and suggestions.

Although the overall reasons were not significantly different in both colleges, to find if any individual reasons were significantly different, independent samples t test was further performed to show that some of the reasons were significantly different in both colleges.

According to analysis, the reasons for absenteeism which were more common in public sector college and a statistically significant difference was found were poor contents of lecture, dislike of teaching style, poor lighting and sound system of lecture halls, and no action taken by administration on being absent. The means with standard deviations and p values are shown in Table III.

The reasons for absenteeism which were more common in private sector college with a statistically significant difference were ability to download lectures from internet, absenteeism due to preparation for tests, attending social gatherings and absenteeism due to lack of recreational activities. The means with standard deviations and p values are shown in Table III.

### Table 1: Category of Medical College and Attendance of the Students

<table>
<thead>
<tr>
<th>Category of Medical College</th>
<th>Attendance percentage</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50%</td>
<td>50-75%</td>
</tr>
<tr>
<td>ASMDC (private)</td>
<td>2</td>
<td>120</td>
</tr>
<tr>
<td>AIMC (public)</td>
<td>8</td>
<td>204</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>324</td>
</tr>
<tr>
<td>Chi square value: 6.3</td>
<td></td>
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</tr>
</tbody>
</table>

### Table 2: Mean Overall Reasons for Absenteeism in Public and Private Medical Colleges

<table>
<thead>
<tr>
<th>Variables</th>
<th>Category of college</th>
<th>Mean score± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reasons for absenteeism</td>
<td>Private Public</td>
<td>5.72±0.70</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.77±0.79</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3: Mean Scores of Individual Reasons for Absenteeism in Private and Public Medical Colleges

<table>
<thead>
<tr>
<th>Variables</th>
<th>Category of college</th>
<th>Mean score± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor contents of lecture</td>
<td>Private Public</td>
<td>1.65±1.10</td>
<td>0.00</td>
</tr>
<tr>
<td>Dislike of teaching style of teachers</td>
<td>Private Public</td>
<td>1.92±1.20</td>
<td>0.01</td>
</tr>
<tr>
<td>Ability to download lectures from net</td>
<td>Private Public</td>
<td>2.77±1.13</td>
<td>0.00</td>
</tr>
<tr>
<td>Poor lighting system in lecture theaters</td>
<td>Private Public</td>
<td>1.51±1.18</td>
<td>0.00</td>
</tr>
<tr>
<td>Poor sound system in lecture theaters</td>
<td>Private Public</td>
<td>1.79±1.25</td>
<td>0.00</td>
</tr>
<tr>
<td>Time needed for test preparation</td>
<td>Private Public</td>
<td>3.55±0.80</td>
<td>0.00</td>
</tr>
<tr>
<td>Attending social gatherings</td>
<td>Private Public</td>
<td>2.59±1.34</td>
<td>0.00</td>
</tr>
<tr>
<td>Less recreational activities</td>
<td>Private Public</td>
<td>3.16±1.25</td>
<td>0.00</td>
</tr>
<tr>
<td>No action on absence</td>
<td>Private Public</td>
<td>1.26±1.37</td>
<td>0.00</td>
</tr>
<tr>
<td>Suggestions by students</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-study time</td>
<td>Private Public</td>
<td>3.50±0.849</td>
<td>0.001</td>
</tr>
<tr>
<td>Interval between lectures</td>
<td>Private Public</td>
<td>3.63±0.680</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Over all reasons were not significantly different in both colleges but there was significant difference in some individual reasons. The result of this study
showed better attendance of students (52.7%) in the public medical college than the private medical college. But still significant number of students in this public medical college believed that students don’t attend the college because no action is taken by the authorities on absenteeism during the session. This is in contrast to a study conducted in Peshawar in 2016 which showed that rate of absenteeism among students of Khyber medical college was high and main reason attributed to absenteeism was dislike of teacher’s teaching style and no free time in between lectures.8

Main reasons of absenteeism in public medical college were multiple. Significant number of students reported that they miss the classes due to poor lecture contents and dislike of teaching style of teachers. This is also reported earlier in a study from the same public college i-e Allama Iqbal medical college by the first (47%) and second year students(43%) but the students from the 3rd, 4th and final year reported satisfactory teaching.7 This was also reported by a public medical college in another study but this was located in rural area of Punjab. Also in same study a public medical college located in urban area reported satisfaction among students regarding the teaching content and style of teachers.13

Teachers in the medical colleges are doctors but not the educationists. Most of them do not have any training /certification in the medical education and not well aware of teaching methodologies, hence lack in effective delivery of lectures. Scale wise fixed salaries and no performance based incentives-especially in the public sector medical colleges’ lead to demoralization of the brilliant and talented teachers. They do not remain vibrant and give up struggle for advancement in learning skills.14 In an earlier study Hasnain et al reported (67%) of first year students (52%) of second year medical students of AllamaIqbal Medical college are of a view that teachers were not well trained.7

Students of public medical college reported poor light and sound system in lecture theaters. This was also reported earlier in 2018 in the same public college.7n public medical colleges the numbers of students are doubled as compared to private medical college and large lecture theaters are there. Environment is also a factor that contributes in student’s interest in studies.15 Big size lecture halls with poor cooling, lightening, and sound system and double the number of students in public sector medical colleges than in private colleges could result in lack of interest of students in lectures.15

Public sector medical students reported that one of the reasons for absenteeism is that no action is taken when they skip college. Studies show that implementing strict attendance policy can prevent absenteeism.16

Reasons of absenteeism reported by private medical college students are the test preparation, ability to download lectures from the web. Attending Social gatherings and lack of recreational activities were also reported to be reason of absenteeism.

Students in private medical colleges belong to higher financial background. Such students tend to indulge more in non-academic activities and do not remain much focused to their studies on regular basis. Social gatherings are common in such families which result in student’s absenteeism from classes. Lack of regular studies demand more time near exams thus students sit in for exam preparations while remaining absent from classes. Recreation is inevitable for psychological balance and mental development.17 Private medical colleges provide little recreational opportunities.18

Lectures or videos on web are the additional tool for learning but not the replacement of interactive class where students interact with teacher as well as their peers.19

CONCLUSION

There are differences in perceptions of students about absenteeism in public and private institutes because of differences in set up, admission merits and social cadres of students.

Students of both setups that have some social and academic stressors which can affect their presence in class and ultimately their performance in
exams and what can be done to improve their presence in class.

**RECOMMENDATIONS**

- In changing era of medical education there is need for proper training of medical doctors as teachers
- Implementation of support system for students affected by absenteeism rather than taking action on being absent.

**ETHICAL APPROVAL:**

- Approval from the institutional review board (IRB) ASMDC and Ethics Review board (ERB) AIMC was obtained.

**CONFLICT OF INTEREST:** Authors declared no conflict of interest.

**AUTHORS’ CONTRIBUTION:**

- FI: Conceived the presented study, its methodology, data collection and contributed to manuscript writing.
- MI: Contributed to the methodology, data collection and to manuscript writing.
- ZN: Done the statistical analysis, contributed to the methodology and final version of the manuscript.

**REFERENCES**


MORPHOLOGICAL VARIATIONS IN TRANSURETHERAL RESSECTION OF PROSTATE SPECIMEN

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Abstract

Background and objectives: Prostate lesions like benign prostatic hyperplasia, acute and chronic prostatitis and tumors are important causes of morbidity and mortality in men. Biopsy is the gold standard for the final diagnosis of these lesions. In small biopsies the diagnosis of adenocarcinoma is often challenging especially if the tumor is low grade. Benign mimickers that can give rise to false positive cancer diagnosis are atrophy, post atrophic hyperplasia, atypical adenomatous hyperplasia, and basal cell hyperplasia.

Methodology: We conducted a prospective study from January 2019 to October 2019. We collected 40 specimens of TURP from Pathology Laboratory, Sahara Medical College, Narowal and 40 specimens from Pathology Laboratory, Allama Iqbal Medical College, Lahore. Histological diagnosis was made. Results were compared between the two groups. Data analysis was done by Statistical Package for the Social Sciences (SPSS) Version 20 and expressed as frequency and percentage.

Results: Patients age for benign conditions was 41-85 years and for carcinoma was from 50-85 years. Benign prostatic hyperplasia was the most common lesion (73.75%). BPH was associated with focal chronic prostatitis in 67.77% cases. Whereas the incidence of acute prostatitis (6.77%), and granulomatous prostatitis (3.3%) was low. There were 21 cases of adenocarcinoma prostate (26.22%). Most commonly diagnosed Gleason score was 7.

Conclusion: Benign prostatic hyperplasia is the most common prostatic lesion, but the incidence of adenocarcinoma prostate has increased although it is low in peripheral area of Punjab as compared to Lahore.

Key words: benign prostatic hyperplasia, adenocarcinoma prostate, basal cell hyperplasia.

In males, important causes of morbidity and mortality are prostatic lesions including benign prostatic hyperplasia, prostatitis and tumors.¹ Digital rectal examination, prostate specific antigen and transrectal ultrasound help to screen lesions of prostate, but biopsy is the gold standard for final diagnosis. After the age of 40 years benign prostatic hyperplasia is the most common cause of urinary problems.²

There can be acute or chronic bacterial prostatitis, chronic abacterial, or granulomatous prostatitis.³ Lower urinary tract symptoms can be caused by chronic inflammation, which can be relieved medically or surgically.⁴

Carcinoma prostate is the second frequently diagnosed cancer in men.⁵ Prostate intraepithelial neoplasia is characterized by proliferation with dysplasia in ducts without stromal invasion. It may not be associated with raised PSA levels.⁶

Histopathological diagnosis of adenocarcinoma prostate depends upon features like growth pattern, nuclear atypia and absence of basal cells. Grading of adenocarcinoma prostate is done by Gleason grading system. Correct diagnosis and grading are important to assess patients’ prognosis.
Dr. Donald Gleason presented the grading system for prostate cancer which is based on a study conducted from 1959 through 1964. This system is based on different histological patterns of prostate adenocarcinoma. Since then, Gleason grading system has been revised multiple times. John Hopkins Hospital (2013) presented a new grading system which includes 5 grade groups. Recently, a new grading system has been proposed by the International Society of Urological Pathology (ISUP) and is in WHO classification of tumor of the Urinary System and Male Genital Organs. According to this system, Gleason Grade Group 1 = Gleason score ≤ 6, Grade Group 2 = Gleason score 3 + 4 = 7, Grade Group 3 = Gleason score 4 + 3 = 7, Grade Group 4 = Gleason score 4+4 = 8, Grade group 5 = Gleason score 9,10 as well as modified morphological criteria for Gleason pattern 4. Ill-formed, fused, cribriform and glomeruloid glands are considered Gleason grade 4 tumors.8,9

The diagnosis of adenocarcinoma is often challenging in small biopsies especially if the tumor is low grade. Benign mimickers that can give rise to false positive cancer diagnosis are atrophy, post atrophic hyperplasia, atypical adenomatous hyperplasia and seminal vesicle type tissue. Metaplastic and hyperplastic changes like basal cell hyperplasia, clear cell cribriform hyperplasia and non prostatic lesions like nephrogenic adenoma can also cause confusion.10,11

OBJECTIVE of the study was to compare histopathological spectrum of lesions in prostate in a tertiary care hospital in a peripheral area of Punjab and a tertiary care hospital in Lahore.

METHODS
Prospective study was conducted at Sahara Medical College Narowal from January 2019 to October 2019. We collected 40 specimens of TURP from Pathology laboratory, Sahara Medical College, Narowal and 40 specimens from Pathology Laboratory, Allama Iqbal Medical College, Lahore. All specimens were processed and stained with Hematoxylin and Eosin stain. Age and histopathological details were analyzed and compared with other studies.

Ethical approval for this study was obtained from the Ethical Committee Sahara Medical College, Narowal. Ethical committee reference number is SMC/EC/02/10/19.

RESULTS
Patients age for benign conditions was 41-85 years and for carcinoma was from 50-85 years. Out of 80 cases of TURP, 59 (73.75%) were of benign prostatic hyperplasia. BPH was commonly seen in 41-85-year age group. Focal chronic prostatitis was seen in 40 cases (67.77%) of BPH (Fig. 1). Acute prostatitis was present in 4 cases of BPH, (6.77%), whereas, there were 2 cases (3.3%) of granulomatous prostatitis (Fig. 2). There were 4 cases of BPH with basal cell hyperplasia (6.77%) (Fig. 3). There were 21 cases of adenocarcinoma prostate (26.22%) (Table 1, Figures 4, 5, 6). Frequency of adenocarcinoma prostate is more in Lahore (32.5%) as compared to peripheral area (20%).

Most of the benign and malignant lesions were seen commonly in 61 to 70-year age group (Table 2).

Among the malignant lesions, three cases had Gleason score 6 (14.3%), 11 had Gleason score 7 (53.33%), 1 had 8 (4.44%), 5 had 9 (23.8%) and 1 case had Gleason score 10 (4.44%). Gleason score 7 was the commonest (Table 3).

<table>
<thead>
<tr>
<th>Table 1: Frequency of different Prostate Lesions</th>
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<tbody>
<tr>
<td>Lesion</td>
</tr>
<tr>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Benign prostate hyperplasia</td>
</tr>
<tr>
<td>BPH with chronic prostatitis</td>
</tr>
<tr>
<td>BPH with acute prostatitis</td>
</tr>
<tr>
<td>BPH with granulomatous prostatitis</td>
</tr>
<tr>
<td>BPH with basal cell hyperplasia</td>
</tr>
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<td>Adenocarcinoma</td>
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<table>
<thead>
<tr>
<th>Table 2: Age Distribution of Prostate Lesions</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>40-50</td>
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<td>51-60</td>
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<td>61-70</td>
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<tr>
<td>71-80</td>
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<td>81-90</td>
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<table>
<thead>
<tr>
<th>Table 3: Gleason Score Distribution in Prostate Adenocarcinoma</th>
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<tbody>
<tr>
<td>Gleason score</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>6</td>
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<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
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<tr>
<td>10</td>
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</table>
Figure 1: Photomicrograph Showing Benign Prostatic Hyperplasia with Chronic Prostatitis (Hematoxylin and Eosin stain, 200x)

Figure 2: Photomicrograph Showing Benign Prostatic Hyperplasia with Granulomatous Prostatitis (Hematoxylin and Eosin stain, 200x)

Figure 3: Photomicrograph Showing BPH with Basal cell Hyperplasia (Hematoxylin and Eosin stain, 200x)

Figure 4: Photomicrograph Showing Adenocarcinoma prostate Gleason Score 3 Pattern (Hematoxylin and Eosin stain, 200x)

Figure 5: Photomicrograph showing Adenocarcinoma Prostate Gleason Score 4 Pattern (Hematoxylin and Eosin Stain, 200x)

Figure 6: Photomicrograph showing Adenocarcinoma prostate Gleason Score 5 pattern with comedo necrosis (Hematoxylin and Eosin stain,
DISCUSSION

Prostatic lesions are important causes of morbidity and mortality in males. These include benign prostatic hyperplasia, prostatitis and tumors. Both BPH and adenocarcinoma were most common in 61-70 years age group. Hafiz M Aslamet al (2012) reported similar results.11

Out of 80 cases of TURP 59 (73.75%) were of benign prostatic hyperplasia. BPH was commonly seen in 41 to 85-year age group. Focal chronic prostatitis was seen in 40 cases (67.77%) of BPH (Fig. 1). Mittal BV et al in 1989 found 92.97% cases were of BPH, study done by Yadav et al (2017) also found 93% lesions of prostate were benign. Our study shows an increased incidence of carcinoma prostate.2,13

Focal chronic prostatitis was seen in 40 cases of BPH (67.77%) (Table 1, Figure 1). In a study done by Dong ru et al, it was found that 40-70 % of patients diagnosed with BPH with chronic prostatitis showed increased lower urinary tract symptoms and low response to BPH medicines. Bushman, and Jerde (2016) concluded that greater the inflammation, more severe are the lower urinary tract symptoms.14,15

Acute prostatitis was seen in 3 cases of BPH (3.75%). Same were the findings of Yadav et al (3% cases of acute prostatitis). Whereas, there were 2 cases of granulomatous prostatitis (2.5%). The incidence of granulomatous prostatitis is low. It can be idiopathic, due to infection, tuberculosis or surgery. Mostly it is nonspecific.2,16,17

There were 2 cases of BPH with basal cell hyperplasia (Table 1, Fig. 3). Taitt HE and Freitas et al also found low prevalence of basal cell hyperplasia (1.3%).18,19

There were 21 cases of adenocarcinoma prostate. Gleason score 7 was most prevalent (Table 3). Study conducted by Imran AA et al had comparable results.28 During studies conducted at different areas in Pakistan the prevalence of prostate cancer ranged from 2-8%. Study conducted by Ahmed et al (2019), shows 4.4% of prostatic lesions were malignant.21,22 Whereas, study done by Ali A et al (2015) shows malignancy in 36 out of 170 (21.2%) prostate specimens.23

It is concluded that the benign prostatic hyperplasia is the most common prostatic lesion, but the incidence of adenocarcinoma prostate is lower in peripheral area of Punjab as compared to Lahore. Carcinomas most commonly had Gleason score 7. There should be development of low-cost programs for the early diagnosis and treatment of carcinoma prostate to reduce the morbidity and mortality.

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Author’s contribution

KA: Main author, data collection, research, wrote the article. Address:144 B, TNT Aabpara housing society Raiwind road, Lahore. Mobile number: 03224355490, 03458554901. AAI: Photography, helped in writing the manuscript. Concept and idea. AA: Checked Article. FA: Research, data collection. TT: Literature search

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**PERIPORTAL HEPATIC STEATOSIS AND ITS RELATION WITH GRADE OF FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C**

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*Allama Iqbal Medical College, Lahore; Akhtar Saeed Medical & Dental College, Lahore; Sheikh Zayed Hospital, Lahore*

**Abstract**

**Introduction:** The pathogenesis of liver damage associated with chronic hepatitis C virus (HCV) infection is thought to be largely immune mediated. However, some frequent histopathological features, such as steatosis, suggest a direct cytopathic effect of HCV.

**Objective:** To evaluate the degree of periportal hepatic steatosis and to correlate it with necroinflammatory process and fibrosis in patients suffering from CHC in our set up

**Methods:** Liver needle core biopsies and wedge biopsies of patients presenting in gastroenterology Outpatient department and in the gastroenterology ward of SZH who fulfilled the inclusion criteria and willing to consent. The major focus was on periportal hepatic steatosis and fibrosis. All the necessary information regarding demographic factors, disease duration and abdominal ultrasound findings were collected and entered in a well designed proforma. Data were entered and analyzed by using SPSS v23.0. Relation of steatosis with grade of fibrosis was performed by using Chi-square test and P-value 0.05 was considered significant.

**Results:** Generalized body weakness was most common presenting complaint, which was associated with patients 78(42.6%). The other presenting complaint, which were associated with patients, were as: Lethargy 37(20.2%), Severe Vomiting 26(14.2%), Pain right hypochondrium 18(9.8%), Loss of Appetite 16(8.7%) and Weight Loss 8(4.4%).15(8.2%) patients had no steatosis, while 135(73.8%) had mild, 26(14.2%), 7(3.8%) patients had moderate and severe steatosis respectively. Among CHC patients, 6(3.3%) had no fibrosis, while 39(21.3%), 68(37.2%), 44(24.0%), 22(12.0%), 4(2.2%) had fibrosis score 1, 2, 3, 4 and 5 respectively.

**Conclusion:** It was concluded that, increased steatosis is associated with worsening fibrosis suggesting a possible role for steatosis in the acceleration of liver disease in HCV patients and efforts to control steatosis may therefore have an important role in halting HCV liver disease progression.

**Key words:** Steatosis, Fibrosis, Hepatitis C, PCR.

Hepatitis C virus is a major cause of chronic liver disease with about 170 million people infected worldwide. The severity of disease varies widely from asymptomatic chronic infection to cirrhosis and hepato cellular carcinoma. Although most HCV associated liver damage is immunomediated, some histopathological features, such as liver steatosis, suggest a viral cytopathic effect.

Hepatic steatosis is a common histological finding in chronic liver diseases. Chronic hepatitis C (CHC) is one among the pathological entities in which hepatic steatosis is encountered.

The steatosis prevalence in these patients ranges from 40% to 86%, with an average of 55%, which is two times higher than the steatosis seen in adults uninfected with hepatitis C. Hepatic steatosis is a medical condition that may progress to steatohepatitis, progressive hepatic failure, hepatic cirrhosis, and is a risk factor for development of hepato cellular carcinoma.

Hepatic steatosis is categorized as microvesicular steatosis and macrovesicular steatosis on the
basis of distribution and size of the lipid vacuoles within the hepatocytes. Microvesicular steatosis, seen in the settings of Acute Fatty Liver Disease of Pregnancy and Reye’s syndrome occurs due to dysfunctions in free fatty acids beta oxidation and this can result in acute liver failure.5

Macroversicular steatosis is the histological finding in patients with Non-alcoholic Fatty Liver Disease (NAFLD). Spectrum of NAFLD ranges from simple hepatic steatosis to nonalcoholic steatohepatitis (NASH).6

In HCV patients, macrovesicular steatosis is also distributed in the periportal areas rather than the centrilobular region which is more commonly seen in NAFLD.

It has been shown that in CHC patients, HCV genotype 3 is independently associated with hepatocellular steatosis. Besides this, there is a direct relationship between the severity of steatosis and the burden of the HCV RNA load in these patients. This relationship was not observed in other HCV genotypes.

In a recent study on paired liver biopsies of untreated patients with chronic hepatitis C, steatosis was the only independent factor predictive of fibrosis progression, and the probability of fibrosis progression was significantly related to the percentage of hepatocytes with steatosis.7

Steatosis acts as a negative factor in response to antiviral therapy. Thus, appropriate timely therapeautic strategies for HCV related steatosis are required in order to improve both the natural history of chronic hepatitis C and its drug management.

In a study conducted including 158 hepatitis C cases. It showed that increased steatosis is associated with worsening fibrosis suggesting a possible role for steatosis in acceleration of liver disease in HCV patients.8

METHODS

A total of 183 patients were enrolled. The study was carried out in the Department of Histopathology at Shaikh Zayed hospital, Lahore. Liver needle core biopsies and wedge biopsies of CHC patients was the study population. Cross-Sectional Analytical Study design was used. The sampling technique was convenient sampling.

Biopsies and hepatectomy specimens of patients of either sex and older than 40 years of age presenting in gastroenterology Outpatient department and in the gastroenterology ward of SZH who were suffering from CHC and willing to consent for participation in research was the inclusion criteria.

Biopsies and hepatectomy specimens of patients receiving antiviral therapy, Biopsies and hepatectomy specimens of patients with clinical and radiological evidence of cirrhosis and Autolyzed tissue and inadequate specimens containing less than three portal tracts were considered inadequate and were excluded from this study.

Liver needle core biopsies and wedge biopsies of patients presenting in gastroenterology Outpatient department and in the gastroenterology ward of SZH who fulfilled the above mentioned criteria and willing to consent for participation in research were received in 10% formaline. Liver biopsy was done by a trained doctor in gastroenterology department after taking informed consent from patient.

Tissues were processed by automated tissue processor. The sections were stained by Haematoxylin and Eosin and reticulin stain. All the sections were examined under microscope by the same pathologist. The major focus was on periportal hepatic steatosis and fibrosis. All the necessary information regarding demographic factors, disease duration and abdominal ultrasound findings were collected and entered in a well designed proforma.

Steatosis was graded as:
0 (involving <1% of total hepatocytes),
1 (between 1% and 30% of hepatocytes),
2 (between 30% and 60% of hepatocytes) and
3 (>60% of hepatocytes)*

And fibrosis according to the Ishak modified score as:
0, no fibrosis;
1, fibrous expansion of some portal tract areas;
2, fibrous expansion of most portal tract areas;
3, fibrous expansion of portal tract areas with occasional portal–portal bridging;
4, fibrosis with portal–portal and portal–central bridging;
5, pronounced bridging with occasional nodules; and
6, probable or definite cirrhosis

Data were entered and analyzed by using SPSS v23.0. Data for age, sex were described by using mean SD. Steatosis and fibrosis were described by using frequency and percentages. Relation of steatosis with grade of fibrosis was performed by using Chi-square test and P-value 0.05 was considered significant. Steatosis and fibrosis was associated with age, gender and duration of disease as dependent variable by using multi-nominal logistic regression.

RESULTS

In this study, 183 patients with CHC were included. Among these patients, 93(50.8%) were males and 90(48.2%) were females. Among these patients, 32(17.5%) were between 41-50 age group, while 101(55.2%), 50(27.3%) were between 51-60 and >60 age groups respectively. Mean age of the patients were 58.39±8.94 with 42 and 88 as minimum and maximum ages. Among these patients, no one had cirrhosis and HCC, while all patients had fatty change 183(100.0%). 94(51.4%) patients biopsy was wedge box, while 89(48.6%) patients biopsy was done by needle core.

Generalized body weakness was most common presenting complaint, which was associated with patients 78(42.6%). The other presenting complaint, which were associated with patients, were as: Lethargy 37(20.2%), Severe Vomiting 26(14.2%), Pain right hypochondrium 18(9.8%), Loss of Appetite 16(8.7%) and Weight Loss 8(4.4%).

The most cases were of those patients, who had been suffering from CHC, were in 5 to 10 years duration group i.e. 116(63.4%), while 2(1.1%), 50(27.3%), 15(8.2%) were in >6 months to 2 years, 2 to 5 years and 10 to 15 years respectively. 15(8.2%) patients had no steatosis, while 135(73.8%) had mild, 26(14.2%), 7(3.8%) patients had moderate and

<table>
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<th>Table 1: Frequency Distribution of different Variables</th>
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<tr>
<td>2</td>
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</table>
severe steatosis. Among CHC patients, 6(3.3%) had no fibrosis, while 39(21.3%), 68(37.2%), 44(24.0%), 22(12.0%), 4(2.2%) had fibrosis score 1, 2, 3, 4 and 5 respectively.

By applying Chi-square, it was concluded that, increased steatosis is associated with worsening fibrosis suggesting a possible role for steatosis in the acceleration of liver disease in HCV Patients and efforts to control steatosis may therefore have an important role in halting HCV liver disease progression (p<0.00009).

By applying Multinomial logistic regression, it was concluded that, Age groups and duration of illness were significant factors correlating with hepatic steatosis in CHC patients (p<0.005, 0.030). It was also concluded that, duration of illness was significant factor correlating with fibrosis in CHC patients (p<0.008).

**DISCUSSION**

The occurrence of fatty liver is a complex, multifactorial, process, which is not completely known. In developing this disease, diet is an essential element, many researchers showed that steatosis results from an imbalance between the accumulation and metabolism of triglycerides. The amount of triglycerides within the liver is primarily dependent on the amount of fat ingested. Some experimental studies have shown that 20% of ingested fats are for the liver, where they are metabolized to obtain energy or other metabolic synthesis or, alternatively, can accumulate as triglyceride vacuoles. The diet rich in carbohydrates increases hepatic lipids, carbohydrates promote the synthesis of fatty acids from acetyl-coenzyme A.

Hepatic steatosis is a common finding in many chronic liver diseases. Steatosis has long been regarded as an unimportant pathological lipid accumulation. Studies in recent decades have shown that hepatic steatosis is a medical condition that may progress to steatohepatitis, progressive liver failure and even liver cirrhosis. More recently, steatosis was identified as a risk factor for development and progression of liver fibrosis and even extensive risk factor for development of hepatocellular carcinoma.

Hepatic steatosis has been noted in chronic hepatitis C. According to some authors prevalence of fatty liver in patients with chronic hepatitis C range from 40% to 86%, with an average of 55%. If the prevalence of steatosis in the adult population in Western countries is 30–20%, in patients with chronic hepatitis C prevalence of steatosis reaches about 55%.

In this study, it has been showed that steatosis can be seen from 40 years to the elderly in patients with chronic hepatitis C. Other researchers noted that the incidence of steatosis greatly increases with age. Basically, the number of patients doubles every decade.

### Table 3: Comparison between Steatosis Grades and Fibrosis Scores

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<tr>
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<th>3</th>
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<th>5</th>
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<th>P-value</th>
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<tr>
<td></td>
<td>20.0%</td>
<td>33.3%</td>
<td>20.0%</td>
<td>0.0%</td>
<td>13.3%</td>
<td>13.3%</td>
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<tr>
<td>1</td>
<td>3</td>
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<td>2</td>
<td>135</td>
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<tr>
<td></td>
<td>2.2%</td>
<td>20.0%</td>
<td>37.8%</td>
<td>23.7%</td>
<td>14.8%</td>
<td>1.5%</td>
<td>100.0%</td>
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<tr>
<td>2</td>
<td>0</td>
<td>3</td>
<td>13</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>26</td>
<td></td>
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<tr>
<td></td>
<td>0.0%</td>
<td>11.5%</td>
<td>50.0%</td>
<td>38.5%</td>
<td>0.0%</td>
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<tr>
<td>3</td>
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<td>0</td>
<td>0</td>
<td>7</td>
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<tr>
<td></td>
<td>0.0%</td>
<td>57.1%</td>
<td>14.3%</td>
<td>28.6%</td>
<td>0.0%</td>
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<tr>
<td>Total</td>
<td>6</td>
<td>39</td>
<td>68</td>
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<td></td>
<td>3.3%</td>
<td>21.3%</td>
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The presence of steatosis in young people who are unlikely to consume alcohol and in which obesity and dyslipidemia are rare, indicate that hepatitis C might be directly involved in developing this liver damage. Some authors showed that in people infected with HCV genotype 3, achieving a sustained virological response after treatment has led to the disappearance of steatosis, which demonstrates the steatogenic ability of HCV genotype 3.  

Other studies have shown that the core protein of HCV genotype 3 has the ability to inhibit the secretion of very low-density lipoproteins in the liver and, consequently, to induce steatosis. Data on the steatogenic capacity of HCV genotype 1 are more scarce and inconsistent. While some authors have shown that in patients infected with HCV genotype 1, virus eradication has no effect on fatty, others have shown that hepatitis virus core protein over expression interferes with the secretory activity of hepatocytes and in particular the secretion of very low density lipoproteins. This contributes to the occurrence of hepatic steatosis.  

It is believed that steatosis appearing in most of the patients with chronic hepatitis C is a multifactorial process, in which the emergence of viral infection contributes to high fat diet, chronic alcohol consumption, dyslipidemia, obesity, chronic consumption of medication, diabetes, etc. Some patients may have had infection hepatitis C prior to steatosis. Therefore, authors believe that it is difficult to determine a precise relationship between steatosis and infection with hepatitis C.  

Regarding gender distribution, our study showed that steatosis associated with chronic hepatitis C had same effect on both genders (p>0.098). Al Qaraawiet al., analyzing a sample of 116 patients with steatosis and chronic hepatitis C found effect similar to us.  

Other authors analyzing a sample of 286 patients found an equal effect of steatosis on both genders (p>0.12). It is believed that these data were influenced by the combination of several potentially steatogenic factors. It is difficult to assess the impact of steatosis on necroinflammatory activity and the process of liver fibrosis in patients with chronic hepatitis C, since these processes are multifactorial. However, several clinical and experimental studies have shown that hepatic steatosis accelerates the development and progression of fibrosis in chronic hepatitis C. 

It has shown that most patients had mild to moderate steatosis, which were associated with necroinflammatory activity and moderate fibrosis. In chronic hepatitis, fibrosis is a consequence of chronic inflammation. There are a number of factors that stimulate the synthesis of extracellular matrix in the inflammatory processes, mainly collagen fibers being involved. Cells involved in the fibrogenesis found in chronic hepatitis are represented by the fibroblasts of the Kiernan space and the liver stellate cells that can migrate into the areas of liver injury, proliferate, and synthesize connective tissue matrix in the sinusoidal capillaries.  

Hepatic stellate cells (Ito cells), considered to be the major cells responsible for the production of collagen, gain myofibroblasts properties in response to signals received from the neighboring cells, from apoptotic fragments generated by adjacent hepatocytes or oxygen free radicals (ROS). Other important stimuli that occur in hepatic steatosis and induce the synthesis of extracellular matrix are the resulting products of lipid peroxidation. 

CONCLUSION  

Our results suggest that rather than steatosis at a given time, it is worsening of steatosis over time that is associated with progression of liver damage in patients with CHC. These findings may have important prognostic and therapeutic implications in the management of these patients. In this respect, particular efforts should be made to control factors associated with steatosis.
Fig. 1: Histological Image of a Case Diagnosed with Mild Steatosis and Minimal Inflammatory Infiltrate. HE Staining, ×200.

Fig. 2: Milch Steatosis Associated with Abundant Inflammatory Filtrate. HE Staining, ×200

Fig. 3: Image of Moderate Steatosis, both Macro and Micro-Vesicular. HE Staining, ×200

Fig. 4: Severe Steatosis, Predominantly of Macro-Vesicular Type. HE staining, ×200

Fig. 5: Microscopic Image of Chronic Hepatitis Associated with Moderate Micro- and Macro-Vascular Steatosis Ana Portoportal and Intralabular Fibrosis. Trichromic Goldner-Szekely Staining, ×200

Fig. 6: Microscopic Image of Moderate Steatosis Associated with Porto-portal and Porto-central Fibrosis and Abundant Inflammatory Infiltrate. Trichromic Goldner-Szekely Staining, ×200
Fig. 7: Chronic Hepatitis Associated with Moderate Steatosis, Abundant Inflammatory Infiltrate and Severe Fibrosis, HE Staining, ×200

Fig. 8: Mild Macrovesicular Steatosis and Hepatocellular Inflammation

Fig. 9: Stage 4

Fig. 10: Grade 4 Stage 3 Fibrosis

REFERENCES
PERIPORTAL HEPATIC STEATOSIS AND ITS RELATION WITH GRADE OF FIBROSIS IN PATIENTS


ROLE OF RIRS (RETROGRADE INTRA RENAL SURGERY) IN MANAGEMENT OF RENAL CALCULI

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1Chair; Division of Urology, UCM, University of Lahore; 2Senior Registrar, Urology Department, UCM, University of Lahore; 3Senior Registrar, Urology Department, Sheikh Zayed Hospital, Lahore

Abstract

Objective: To evaluate the efficacy of RIRS in patients with lower pole renal stones of <2.5cm.

Methodology: This Descriptive Case Series was conducted at Urology Department, Galway University Hospital, Galway, Republic of Ireland from 1stJanuary 2018 to 31stDecember 2018. Total 75 patients with lower pole renal calculi of <2.5 cm in size were included. RIRS was done after completion of all investigations. All patients were given prophylactic antibiotics. Stone free rate 4 month post-operatively was assessed. The stone free rate at the end of 4th month was the endpoint of this study. The collected information was analysed by using SPSS 23. Frequencies and percentages were calculated for qualitative data like efficacy and gender. Mean and SD were calculated for quantitative data like age. Stratification was used for gender, age and stone size to investigate modifiers effects. In post stratification Chi-Square test was used at p value < 0.05 (significant).

Results: Total75 patients with renal calculi were enrolled. Among these patients, 45(60%) were males, while 30(40%) were females. Age range in this study was from 18 to 65 years with mean age of 42.11±13.55 years. Mean size of the stone was 1.22±0.15. Most of the patients 52(69.33%) had the size of stone <1.25 cm, while 23(30.67%) patients had the size of stone >1.25 cm. Overall success rate with RIRS was 88.0% in patients with lower pole renal calculi.

Conclusion: The technique (RIRS) are safe and effective for stones, with best success rate, low morbidity and proper duration of operation.

Key words: Retrograde Intra Renal Surgery (RIRS), Lower Pole Renal Calculi.

Stone disease is ranked 3rd most common pathology in urology after UTI and prostatic diseases.1 It has prevalence about 1% to 15% with different probabilities according to age, gender, race and geographic areas.2 Since stone recurrence rate within 5 years is quite high; nearly 50%, after open surgery, various new techniques have evolved over years to surpass traditional open surgery repetitions.3 In 1978, for the first time, pediatric cystoscope was used to reach distal ureter.4 Nowadays minimal invasive techniques are recommended like ESWL, PCNL, mini-PCNL, retrograde intra renal surgery (RIRS) and micro-PCNL for the treatment of stone disease.5 European guidelines recommend extra corporeal shock wave lithotripsy (ESWL) in stones less than 1 cm, either ESWL or PCNL, while percutaneous nephrolithotomy is safer for stone larger than 2 cm. Either PCNL or RIRS is recommended for stones >1cm with HU>1000 in lower pole due to limited efficacy of ESWL.6

New Generation flexible ureteroscopes with effective holmium lasers can make RIRS even effective for larger stones and to surpass PNL related limitations and complications.7 Efficacy of RIRS has been assessed in limited number of patients as primary approach in different circumstances. In a study conducted by Bansal P showed stone clearance rate of 86.4% in 74 patients.8 In another study conducted by Lim H.S, RIRS efficacy was 69.7% in 66 patients.9 As it is an evolving technique, this study on RIRS in lower pole
stones will be helpful in evaluation and adopting this technique as primary technique.

**OBJECTIVE**

To evaluate the efficacy of RIRS in patients with lower pole renal stones of <2.5cm.

**METHODS**

This Descriptive Case Series was conducted at Urology Department, Galway University Hospital, Galway, Republic of Ireland from 1st January 2018 to 31st December 2018. Total 75 patients with lower pole renal calculi of <2.5 cm in size were included. The inclusion criteria was, male and female patient with lower pole renal stone less than 2.5 cm in size between 18-65 years of age. The exclusion criteria was, patients with fever >99 F at the time of presentation, patients with positive urine culture >105 or with pyuria on urine analysis > 5-6 pus cells per high power view at presentation and patients with more than one calculus found in the same kidney on CT-Scan and IVU.

All the patients were managed on NSAIDs in case of pain until operation. After prophylactic antibiotics, under general anesthesia lithotomy position of patient was made. Under aseptic measures cystoscopy was performed, after cystoscopy hydrophilic guide wire 0.38 passed and coiled in kidney. With the help of fluoroscopy, C arm ureteral access sheath was passed over guide-wire reaching the pelvis and retrograde pyelogram was done to evaluate anatomy. Flexible scope (6.5Fr tip and 7.5Fr base) was used.

With the help of holmium laser 100W laser fiber the stone was vaporized and DJS passed. The patient was labelled for clearance of renal stone (efficacy, yes or no) at follow up after 4 weeks on computed tomography (CT). The collected information was analysed by using SPSS 23. Frequencies and percentages were calculated for qualitative data like efficacy and gender. Mean and SD were calculated for quantitative data like age. Stratification was used for gender, age and stone size to investigate modifiers effects. In post stratification Chi-Square test was used at p value < 0.05 (significant).

**RESULTS**

In this study, 75 patients with lower pole renal calculi were enrolled. Among these patients, 45(60%) were males, while 30(40%) were females. Age range in this study was from 18 to 65 years with mean age of 42.11±13.55 years. Majority of the patients 29(38.66%) were between 46 to 65 years of age. While 22(29.33%) and 24(32%) patients were between 18-30 and 31-45 years of age respectively.

Mean size of the stone was 1.22±0.15. Most of the patients 52(69.33%) had the size of stone ≤1.25 cm, while 23(30.67%) patients had the size of stone ≥1.25 cm. Overall success rate with RIRS was 88.0% in patients with lower pole renal calculi.

There was no significant difference between gender and age in efficacy as shown in table 5 and 6 respectively. It was reported that there was significant difference in efficacy between stone size (p=0.021).

### Table 1: Comparison of Efficacy with Respect to Gender

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<td>Male</td>
<td>40</td>
<td>5</td>
<td>45</td>
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<tr>
<td></td>
<td>88.8%</td>
<td>11.2%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td>4</td>
<td>30</td>
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<tr>
<td></td>
<td>86.6%</td>
<td>13.4%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
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<td>75</td>
</tr>
<tr>
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<td>88.0%</td>
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</table>

### Table 2: Comparison of Efficacy with Respect to Age Groups

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Efficacy</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>18-30</td>
<td>20</td>
<td>2</td>
<td>22</td>
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<tr>
<td></td>
<td>90.90%</td>
<td>9.10%</td>
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<tr>
<td>31-45</td>
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<td>24</td>
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<tr>
<td></td>
<td>91.66%</td>
<td>8.34%</td>
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<tr>
<td>46-60</td>
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<td>29</td>
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<tr>
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<td>82.75%</td>
<td>17.25%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
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<td>75</td>
</tr>
<tr>
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<td>88.0%</td>
<td>12.0%</td>
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</tr>
</tbody>
</table>
DISCUSSION

Endoscopic technology with advanced flexible ureteroscope (URS) is increasingly used in the burden of renal stones. For stones > 2.5 cm, RIRS is used as standard for care. The rate of being stone free is higher for such procedure, up to 95%. The renal access complications are become a matter of serious concern sometimes. In patients where significant comorbidities like bleeding diathesis and morbid obesity, the PNL becomes contraindicated.

Prone position for PCNL increase anesthetic risk in difficult airways and extremities. With advancement of technology, it is presently possible to handle intra renal stones with RIRS. Lower pole renal calculi can effectively and safely be handled by endoscopic technique that looks to compete with most invasive open surgery or percutaneous manoeuvres. It is still not clear that retrograde intra renal surgery might be useful for large stones of size (> 2 cm).

KursadZengin et al concluded in their study that RIRS bear a suitable rate of success that has low complication rate ie fewer than PCNL and looks like an alternate to PCNL to remove large stones. Present recommendations are that ESWL may be the choice of first therapy for calculi of size < 20 mm while PCNL for bigger stones than this.

Presently flexible URS is not mentioned in many guidelines. It may be an alternative to PCNL or ESWL. Hardly, small amount of work is mentioned in literature at the use of flexible URS for renal calculi. New generation URS permits access to all calyces, combined with laser lithotripsy, ureteral access sheath and tools for retrieval to renal calculi.

The rate of being stone free reported for < 2.5 cm calculi is 50 to 80%, while main stones may also be treated successfully. Further the link between endoscopic management and long operative time is stressed in literature. Many reports have described the variable operative time of URS and LASER. Mariani et al. described mean operative time was 64 minutes (from 30 to 240 minutes) for the stones of 2-4 cm of RIRS.

In the current study, the overall success rate with RIRS was 88.0% in patients with lower pole renal calculi. In a study conducted by Bansal P showed stone clearance rate of 86.4% in 74 patients. In another study conducted by Lim H.S, RIRS efficacy was 69.7% in 66 patients. RIRS have minimum complications as compared to PCNL. Major complications of RIRS are not as common in experience increases.

In present situations, due to the small sizeureterorenoscopes, important complications like ureteral avulsion are rare. In addition, at present the RIRS provide a safe alternative in high risk patients, morbid obesity, co morbidities like pregnant women, bleeding diathesis and in those in whom PCNL is contraindicated.

In the study, outcomes of treatment in patients with important co-morbidities who underwent RIRS were monitored and no main complication was observed. Laser lithotripsy and RIRS may be done effectively and safely with high rate of success and low rate of complications in renal stone patients. In this study 42 patients were studies that include 14 female and 28 male patients.

The mean size of stone was 24.09±6.37 mm and the success rate was 92.8% after procedure and there was no main complication to observe. Huang et al. did a study in 25 patients. RIRS overall success rate after 1st, 2nd and 3rd method was 70%, 92% and 92% respectively.

<table>
<thead>
<tr>
<th>Stone Size Groups</th>
<th>Efficacy</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>≤1.25 cm</td>
<td>46</td>
<td>6</td>
<td>52</td>
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<tr>
<td></td>
<td>88.46%</td>
<td>11.54%</td>
<td>100.0%</td>
</tr>
<tr>
<td>≥1.25 cm</td>
<td>20</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>86.95%</td>
<td>13.05%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
<td>9</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>88.0%</td>
<td>12.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 3: Comparison of Efficacy with Respect to Stone Size
ROLE OF RIRS (RETROGRADE INTRA RENAL SURGERY) IN MANAGEMENT OF RENAL CALCULI

CONCLUSION

The RIRS is safe and effective for renal stones, with high success rate, low morbidity and acceptable duration of operative time.

REFERENCES

17. Choi JY, Ko YH, Song PH, Moon KH, Jung HC. Comparison of three surgical modalities for 20-25mm size lower pole stones: Retrograde intrarenal surgery (RIRS) vs mini-percutaneous nephrolithotomy (MPCNL) vs. percutaneous nephrolithotomy (PCNL), which is preferred?. European Urology Supplements. 2017;16(3):735-6.
Solitary thyroid nodule is a discrete swelling in apparently normal rest of the thyroid gland and occurs in 4-7% of the population. Majority of these nodules are benign and 5% are malignant.\textsuperscript{1,7} Nodules are more common in women and increase in frequency with age and with less iodine intake.\textsuperscript{2,3,13} FNAC is now widely accepted as sensitive diagnostic tool for initial screening of solitary thyroid nodule and is used in triaging patients with solitary thyroid nodule into operative and non-operative groups.\textsuperscript{3,15}

To overcome diverse reporting systems in thyroid FNAC, National Cancer Institute published the Bethesda System For Reporting Thyroid Cytopathology (BSRTC) with 6 categories benign; follicular lesion of undetermined significance/atypia of undetermined significance (FLUS/AUS); follicular neoplasm/suspicious of follicular neoplasm; Follicular neoplasm/suspicious of follicular neoplasm; Atypia of undetermined significance/ follicular lesion of undetermined significance; Nondiagnostic/ Unsatisfactory. Bethesda system for thyroid reporting system improves communication between the pathologist and surgeon by way of indicating cancer risk in each category and providing guidelines in surgical management.

Abstract

Background: Thyroid nodules are lumps which commonly arise within an otherwise normal thyroid gland and they cause more concern because of probability of malignancy in them (5-10%). FNAC is now widely accepted as sensitive diagnostic tool for initial screening of solitary thyroid nodule. Bethesda system for thyroid reporting system improves communication between the pathologist and surgeon by way of indicating cancer risk in each category and providing guidelines in surgical management.

Objective: We conducted this study to assess the efficacy of BSRTC in accurate prediction of thyroid lesions on FNAC by defining malignancy risk in each category.

Material and methods: A cross sectional study was conducted on 71 patients with solitary thyroid nodules which were referred for fine needle aspiration to the Department of Histopathology, Shiekh Zayed Hospital, FPGMI, Lahore in 2011 to 2013. The results were categorized according to the recent Bethesda classification into: Nondiagnostic / Unsatisfactory, Benign, Atypia of undetermined significance/ follicular lesion of undetermined significance, Follicular neoplasm/suspicious of follicular neoplasm, Suspicious for Malignancy and Malignant. The final histologic diagnoses were considered the gold standard.

Results: The study included 71 cases presented with solitary thyroid nodules who underwent diagnostic thyroid FNAC. Female to male ratio was 7.1:1, and the mean age was 57.25±12.53 years. Out of 71 cases, 59 cases (83%) were diagnosed as Benign, 4 cases (5.6%) as AUS/FLUS (Atypia of undetermined significance/ follicular lesion of undetermined significance), 3 cases (4.2%) as FN/SFN (Follicular neoplasm/suspicious of follicular neoplasm), 3 cases (4.2%) as SFM (Suspicious for Malignant), and 1 case (1.4%) as ND/UNS (Nondiagnostic/Unsatisfactory), 1 case (1.4%) as Malignant. Malignancy rates on histopathology for Bethesda categories turned out to be 0%, 0%, 25%, 33%, 66% and 100% respectively. FNAC achieved a sensitivity of 100%, a specificity of 90%, a positive predictive value of 45%, a negative predictive value of 100%, and a total accuracy of 91.5%. The P value is less than 0.0001.

Conclusion: Our study validated the accuracy of BSRTC in our setup. We recommend use of BSRTC for reporting thyroid cytopathology. It improves communication between pathologist and surgeon by the way of indicating cancer risk in each category and providing guidelines in surgical management and allows easy and reliable sharing of data between different laboratories.

Keywords: Fine needle aspiration cytology, FNAC, Histopathology, Thyroid Nodule, Thyroid Bethesda System Of Reporting Thyroid Cytopathology, TBSRTC
neoplasm/suspicious for follicular neoplasm; suspi-
cious for malignancy; malignant; and non-diagnostic
(unsatisfactory). The Bethesda system facilitate
effective communication among cytopathologists
and the clinicians, which offer guidance for patient
management and can help with a better patient’s
outcome due to proper clinical management of
thyroid swellings and saves patients from unnece-
sary thyroid surgery.

OBJECTIVE
To assess the efficacy of BSRTC in accurate
prediction of thyroid lesions on FNAC by defining
malignancy risk in each category.

METHODS
A total of 71 patients with solitary thyroid
nodule of all ages and both sexes were selected. A
well informed consent and detailed history about
residence, food habits, radiation and drug intake,
was taken. Routine investigations were performed in
all cases. The selected patients underwent Fine
Needle Aspiration cytology at OPD clinics, indoor
(wards & radiology) at Shaikh Zayed Hospital,
Lahore. Specimens were collected and slides made
was analyzed and reported in the department. All
those patients who underwent surgery after FNAC
(whether reported as benign or malignant) included
in the study and results of FNAC were compared
with histopathology.

RESULTS
In this present study total 71 cases were
enrolled. The mean age of the patients was 57.25±
12.53 years with minimum and maximum ages of 31
& 77 years respectively. The study results showed
that 63.38% patients were females and 36.62%
patients were males. The female to male ratio of the
patients was 1.7:1. Out of total cases (n=71) included
in study 83% (n=59) cases were diagnosed as
Benign, 5.6% cases (n=4) as Atypia of undeter-
dined significance/ follicular lesion of undeter-
dined significance, 4.2% cases (n=3) as Follicular
neoplasm/suspicious of follicular neoplasm, 4.2%
cases (n=3) as Suspicious for Malignant, and 1.4%
(n=1) case as Nondiagnostic/ Unsatisfactory, 1.4%
case (n=1) as Malignant.

Table 1: Distribution of cases according to
Bethesda System of Thyroid Cytopathology

<table>
<thead>
<tr>
<th>Bethesda categories (n=71)</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
</table>
| Group 1: Inadequate/Non-
  diagnostic | 1 | 1.4 |
| Group 2: Benign | 59 | 83.0 |
| Group 3: Atypia with
  Undetermined Significance/
  Follicular Lesion Of
  Undetermined Significance | 4 | 5.6 |
| Group 4: Suspicious for
  Follicular Neoplasm | 3 | 4.2 |
| Group 5: Suspicious for
  malignancy | 3 | 4.2 |
| Group 6: Malignant | 1 | 1.4 |
| Total | 71 | 100.0 |

The study results showed that the sensitivity of
FNAC was 100% with specificity of 90.9%, PPV
value was 45%, NPV value was 100% and diagnos-
tic accuracy of FNAC was 91.5% considering histo-
pathology as gold standard.

Table 2: Cytohistological Correlation of Cases
of Solitary Thyroid Nodules

<table>
<thead>
<tr>
<th>Cytological diagnosis</th>
<th>No.of cases (n=71)</th>
<th>Histological diagnosis</th>
<th>Incidence of malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bethesda 1</td>
<td>1</td>
<td>Benign</td>
<td>1</td>
</tr>
<tr>
<td>Bethesda 2</td>
<td>59</td>
<td>Benign</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant</td>
<td>0</td>
</tr>
<tr>
<td>Bethesda 3</td>
<td>4</td>
<td>Benign</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant</td>
<td>1</td>
</tr>
<tr>
<td>Bethesda 4</td>
<td>3</td>
<td>Benign</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant</td>
<td>1</td>
</tr>
<tr>
<td>Bethesda 5</td>
<td>3</td>
<td>Benign</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant</td>
<td>2</td>
</tr>
<tr>
<td>Bethesda 6</td>
<td>1</td>
<td>Malignant</td>
<td>1</td>
</tr>
</tbody>
</table>

DISCUSSION
Thyroid diseases are quite common in Punjab
and present as a swelling in front of neck, which may
be due to goitre, inflammation, cyst or malignancy.
FNAC reduces the rate of unnecessary thyroid
surgery in patients with benign disease and detects
those with thyroid adenomas/cancers who have to be surgically treated.

For clarity of communication and uniformity of terminology National Cancer Institute hosted “The NCI Thyroid FNA State Science Conference”. The conclusions regarding terminology and morphologic criteria from this meeting led to The Bethesda Thyroid Atlas Project and formed the framework for TBSRTC.

In present study, the age of patients ranged from 31 & 77 years with mean of 57.25±12.53 years. Our study showed that solitary thyroid nodules were 11 times more common in females than males. Both these findings are comparable to the other studies.

In present study we used TBSRTC to report FNAC findings of solitary thyroid nodules. TBSRTC recommends six general diagnostic categories to report FNAC findings of thyroid lesions.\textsuperscript{7}

Non diagnostic category occurs in 2–20% of cases but ideally should be limited to no more than 10% of thyroid FNAs.\textsuperscript{7,9} In present study percentage of ND/UNS cases was 1.4. The reason for the lower percentage in the non-diagnostic category can be due to the fact that, in our institute, usually an ultrasound-guided FNAC is performed for small nodules or nodules that appear heterogeneous on palpation, so that the aspirate can be obtained from the exact pathological site. In our study the case included in this category showed only cyst fluid with plenty of foamy macrophages that turned out to be multinodular goiter on histopathology. So the malignancy rate turned out to be 0% in this category.

Approximately 83% of thyroid swellings in our studied patients were benign on FNAC which only require surgical intervention for physical (pressure symptoms) or cosmetic reasons. On histopathology all of these nodules turned out to benign lesions, hyperplastic colloid nodules (n=14), multinodular goiter (n=43), follicular adenoma (n=1) and benign thyroid cyst (n=1). Malignancy rate in this category was 0%.

According to TBSRTC, AUS/FLUS is a category of resort and should not be used indiscriminately.\textsuperscript{7} In our study 4 cases (5.6%) cases were of this category and turned out to be papillary carcinoma (n=1), hurthle cell adenoma (n=1) and benign colloid nodules (n=2). The cancer risk for this category according to TBSRTC is 5–15% and recommended management protocol is repeat FNA after sufficient time gap. Our study showed malignancy rate of 25% in this category. The criteria for FNHurtle cell type/suspicious for a FN Hurtle cell type FNHCT/SFNHC (subcategory of TBSRTC IV) are a sample consisting exclusively of hurtle cells.\textsuperscript{7}

In the present study 3 cases (4.2%) were from this category and malignancy rate in this category was 25%. On histopathology they turned out to be papillary carcinoma (n=1), follicular cell adenoma (n=1) and MNGs(n=1).

If only one or two characteristic features of PTC are present, if they are only focal, or if the sample is sparsely cellular a malignant diagnosis cannot be made with certainty. Such cases are best classified as suspicious for malignancy. Most (60–75%) of these cases prove to be papillary carcinomas.\textsuperscript{7} In the present study 3 cases (4.2%) were from this category and malignancy rate in this category was 66%. On histopathology they turned out to be papillary carcinoma (n=2), colloid nodules (n=1). The criteria for reporting PTC are follicular cells arranged in papillae/syncytial like monolayers, altered follicular cells exhibiting characteristic nuclear features like longitudinal nuclear grooves, intranuclear cytoplasmic pseudo inclusions, pale nuclei with powdery chromatin and psammoma bodies.\textsuperscript{7} In the present study we reported 1 cases (1.4%) of papillary carcinoma which correlated with histology. TBSRTC recommends near-total thyroidectomy for these cases of malignancy.

In our study Papillary carcinoma represents the most common malignancy on final histology of the cases included in this category which is concordant with most of the national and international data.\textsuperscript{7} The incidence rates and malignancy rates of different categories of our study are comparable to other
studies like Bongiovanni et al and SK Mondal.  

Various researchers in different hospitals and population based studies evaluated the diagnostic accuracy of thyroid cytopathology using Bethesda System.

### Conclusion

Our study validated the accuracy of TBSRTC system in our setup and malignancy rates in different categories correlated well with risk proposed by Bethesda system. We recommend use of TBSTRTC system for reporting Thyroid cytology to improve clinical management of thyroid nodules.

### References

6. Samreen Naz1 , Atif Ali Hashmi1, Amna Khurshid1, Naveen Faridi1, Muhammad Muzzammil Edhi2, Anwar Kamal1 and Mehmood Khan3. Diagnostic accuracy of Bethesda system for reporting thyroid cytopathology: an institutional perspective. International Archives of Medicine 2014, 7:46
FREQUENCY OF VARIOUS CAUSES OF 
LEUKOERYTHROBLASTIC PERIPHERAL BLOOD PICTURE - A 
STUDY CONDUCTED IN A TERTIARY CARE HOSPITAL

Fatima Rahman, Seema Mazhar, Muneeza Natiq, Ali Shandar Durrani, 
Aleena Khalid, Ambereen Anwar

Department of Pathology, Allama Iqbal Medical College Lahore

Abstract

Introduction: Bone marrow metastasis by solid tumors and infiltration by lymphoma has been the key cause 
of leukoerythroblastic blood picture in the past. However, with earlier detection of primary malignancies by 
using advanced diagnostic modalities, the cases of metastasis have significantly decreased. Sepsis and severe 
hemolysis have emerged as the dominant cause of leukoerythroblastic blood picture in the current 
haematology practice.

Methodology: A descriptive cross-sectional study was carried out in 74 patients to find out relative 
frequencies of bone marrow infiltration, myelofibrosis, chronic myeloid leukemia, sepsis and hemolysis as 
causes of leucoerythroblastic blood picture. Frequencies and percentages were calculated using SPSS 
version 20. Post stratification chi square test was applied. Data was expressed using tables, pie charts and bar 
graphs.

Results: Mean age of the study population was 36.43± 15.81 years with minimum age 12.0 and maximum 
age 70 years. Bone marrow infiltration was seen in 2(2.7%), myelofibrosis in 4(5.4%), chronic myeloid 
leukemia in 15(20.3%) and sepsis/hemolysis in 53(71.6%) of the patients.

Conclusion: The study concluded that sepsis/severe hemolysis were among the most common causes of 
leukoerythroblastic blood picture, followed by chronic myeloid leukemia, myelofibrosis and bone marrow 
infiltration.

Keywords: Leukoerythroblastic blood picture, bone marrow infiltration, sepsis, hemolysis

Leukoerythroblastic Blood Picture (LEB) is 
defined as the simultaneous presence of 
nucleated red cells(erythroblasts) & immature 
myeloid precursors(myelocytes, metamyelocytes & 
ocasionally myeloblasts) in the peripheral blood 
film. The presence of Leukoerythroblastic blood 
picture gives rise to differential diagnosis that 
includes:(1) Bone marrow infiltration commonly by 
leukemia, lymphoma and solid tumors (2) Myelo-
proliferative neoplasms(3) Sepsis (4) Severe hemol-
ysis (5) Bone marrow fibrosis.

Normally, erythroblasts are present in circulating 
blood of newborns only. Appearance of circulating erythroblasts beyond the newborn stage 
indicates poor prognosis, and is indicative of several severe diseases including cancer, infections, acute 
and chronic anemias and primary hematological disorders. The detection of nucleated red blood cells in 
hospitalized patients is of prognostic significance and indicates high patient mortality. 

Leukoerythroblastic blood picture is present in 
50% of the cases of bone marrow necrosis, indicating the disruption of bone marrow architecture. The 
common causes of bone marrow necrosis are infiltration by Acute lymphoblastic leukemia (18%) 
followed by Acute myeloid leukemia, and non-Hodgkins lymphoma (10-15%). CML and MDS being less common.

The rationale of this study is to identify 
different causes leading to leucoerythroblastic blood 
picture.

OBJECTIVE

The objective of this study is to establish the 
frequency of the main causes of leukoerythroblastic
blood picture with main focus on benign causes like sepsis and hemolysis.

**Leukoerythroblastic blood picture (LEB):** It is the simultaneous presence of one or more than one granulocyte precursor and one or more than one nucleated red blood cell/100 WBCs on peripheral blood film examination under microscope.

**Main causes of LEB:**

**Bone marrow Infiltration:** It is the replacement of trilineage hematopoiesis by the malignant cells on bone marrow biopsy examination under microscope.

**Myelofibrosis:** It is a clonal disorder characterized by splenomegaly > 15cm on ultrasound abdomen and evidence of fibrosis on trichrome and reticulin stain of bone marrow biopsy.

**Chronic myeloid leukemia:** It is a myeloproliferative neoplasm characterized by splenomegaly >15cm on ultrasound abdomen, leukocytosis (TLC 20-200x10^9/L) and presence of BCR-ABL 1 fusion gene by molecular analysis in leukemic cells.

**Sepsis:** It is a blood infection that induces leukocytosis (Total leukocyte count >12x10^9/L to as high as 40x10^9/L) and neutrophilic leukocytosis (Absolute neutrophil count >7.5x10^9/L) without any organomegaly or lymphadenopathy.

**Hemolysis:** It is the premature destruction of red blood cells as evident by low hemoglobin level (<7 gm/dl), a raised reticulocyte count(normal range: 0.5-2.5%) & elevated serum unconjugated bilirubin (Total serum bilirubin level:0.3-1.2mg/dl).

**METHODS**

This descriptive, cross-sectional study was carried out at Department of Hematology, Allama Iqbal Medical College/Jinnah Hospital, Lahore, from 21st April, 2016 to 20th October, 2016. 74 patients showing a leukoerythroblastic blood picture on microscopic examination of their peripheral blood films and between ages 02-80 years were included in the study. Patients were enrolled from the inpatient facilities of Jinnah Hospital Lahore. Informed consent was taken. Demographic data and laboratory parameters were recorded on a specially designed proforma. Where applicable, absolute neutrophil count, reticulocyte count, findings of bone marrow biopsy (fibrosis) and results of molecular analysis (BCR-ABL1 positive) were recorded on the same proforma. The causes of LEB were then labelled as peroperational definitions and also recorded. The data was entered & analyzed through SPSS version 20. Mean and Standard Deviation were calculated from quantitative variables. Qualitative variables were expressed as frequency and percentage. Data was stratified for laboratory parameters (number of granulocyte precursors and NRBCs, hemoglobin level, total leukocyte count). Post stratification Chi square test was applied and P value was calculated. P value ≤ 0.05 was considered significant.

**RESULTS**

Mean age of the study population was 36.43± 15.81 years with minimum age 12.0 and maximum age 70 years(Table no 1). 47.3% were males and 52.7% were females(Figure 1).

Mean hemoglobin level was 9.17±2.41 gm/dl, mean total leukocyte count was 54.97±74.28, Mean ANC was 19.16±6.79, mean granulocyte precursor count was 9.05±13.31, mean nucleated RBC count was 4.56± 7.87(Table 2). Bone marrow infiltration was seen in 2(2.7%) myelofibrosis in 4(5.4%), Chronic myeloid leukemia in 15(20.3%) and sepsis/hemolysis in 53(71.6%)(Figure 2). Hemoglobin level was lowest among those who had myelofibrosis as mean value was 7.82±3.42 g/dl, TLC count was highest in chronic myeloid leukemia (Table no 3).

**Table 1:** Age of Patients  

<table>
<thead>
<tr>
<th>Age of patients</th>
<th>Frequency</th>
<th>Percent</th>
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</thead>
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<tr>
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<td>70.3</td>
</tr>
<tr>
<td>41 - 70 years</td>
<td>22</td>
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<tr>
<td>Total</td>
<td>74</td>
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Mean = 36.43, SD = 15.61706 Min = 12.0 Max = 70
Table 2: Descriptive Statistics for Laboratory Parameters

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<th>Hb level</th>
<th>Total leukocyte counts</th>
<th>Absolute neutrophil count</th>
<th>Granulocyte precursors</th>
<th>Nucleated RBC</th>
</tr>
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<tr>
<td>Valid</td>
<td>74</td>
<td>74</td>
<td>52</td>
<td>74</td>
<td>74</td>
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<tr>
<td>Mean</td>
<td>9.1757</td>
<td>54.9784</td>
<td>19.1635</td>
<td>9.0541</td>
<td>4.5676</td>
</tr>
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<td>Std. Deviation</td>
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<td>74.28036</td>
<td>6.79149</td>
<td>13.31997</td>
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</tr>
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<td>Minimum</td>
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<td>1.00</td>
</tr>
<tr>
<td>Maximum</td>
<td>14.70</td>
<td>338.20</td>
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</table>

Table 3: Distribution of Laboratory Parameters among Causes of Leukoerthroblastic Blood Picture

<table>
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<tr>
<th></th>
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<th>Mean</th>
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<td>7.87763</td>
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Figure 2: Causes of Leuko-Erythroblastic Blood

DISCUSSION

The leukoerythroblastic blood film results from infiltration and replacement of bone marrow cells
and elements through infection or metastasis as well as from myeloproliferative and lymphoproliferative processes. It may also be seen with severe bleeding and acute hemolysis.\(^8\) It can also occur as a response to severe critical illness, such as trauma, septicemia, massive hemolysis, or severe megaloblastic anemia.\(^9\)

The present study finds the frequency of the four common causes of leukoerythroblastic blood picture namely bone marrow infiltration, myelofibrosis, chronic myeloid leukemia and sepsis/hemolysis. The commonest cause of a leukoerythroblastic picture was found to be sepsis/hemolysis which was observed in 53 out of 74 cases (71.6%) followed by chronic myeloid leukemia in 15(20.3%). This is in line with a study conducted by Burkett and colleagues on 119 cases of leukoerythroblastosis in which they found out that sepsis/hemolysis was more common cause of leukoerythroblastic blood picture as compared to bone marrow infiltration or malignant metastasis.\(^10\) Sepsis is a progressive injurious process and interventions performed immediately after diagnosis of sepsis has improved survival.\(^13\) In our study bone marrow infiltration was least common cause seen only in 2(2.7%). This is in accordance to a case report of a 73 year old female who presented with metastatic breast cancer stating that leukoerythroblastosis occurs in less than 10% of patients with metastatic cancer and that too in advanced stage of disease.\(^11\) Incidence of advanced stage disease has also reduced as a result of early diagnosis and timely intervention decreasing the disease rates in both men and women.\(^12\) The highest rate of bone marrow involvement has been shown by carcinoma prostate (36%), followed by gastric carcinoma and melanoma(25%).\(^7\)

In my study, when my data was stratified according to hemoglobin level, it was found that hemoglobin level was lowest among those who had myelofibrosis as mean value was 7.82±3.42 g/dl. Another study conducted by Tefferi A et al, the mean hemoglobin level in myelofibrosis was found to be 10.8gm/dl with a range of 5.8-15, which is higher than in my study.\(^14\) Treatment with thalidomide increases platelet counts and hemoglobin level and decreases spleen size and bone marrow angiogenesis.\(^15\)

In our study, total leukocyte count was highest in chronic myeloid leukemia with a mean value of 180.58±85.53. In a similar study conducted to evaluate the Clinico hematological features of chronic myeloid leukemia (CML), the mean total leukocyte counts was reported to be 121.00 ± 35.00 which is lower than the total leukocyte count in our study\(^16\). This myeloproliferative disease is associated with a characteristic chromosomal translocation called the Philadelphia chromosome, which is a balanced reciprocal translocation involving chromosomes 9 and 22\(^17\).

In my study mean granulocyte precursor count in cases of sepsis/hemolysis was 2.71±2.02. In a study of 10 patients of sepsis, Dalton RR et al stated that granulocytic fragments in the peripheral blood of patients with sepsis and the systemic inflammatory response syndrome (SIRS) have been well described and are not identified by automated analyzers but are readily recognized on Wright’s-stained peripheral blood smears.\(^18\)

When data was stratified for age, it was noticed that sepsis was more common (84.6%) in the younger age group (group 12-40 years) as compared to the older age group (group 41-70 years) in which it was 40.9%.

When data was stratified for gender, it was seen that greater number of females (79.5%) had sepsis /hemolysis as compared to 62.9% of males. Greater number of males (28.6%) had chronic myeloid leukemia as compared to 12.8% of females, similar to another study conducted to evaluate the Clinico hematological profile of CML.\(^16\)

**CONCLUSION**

My study concluded that out of the four causes studied, sepsis /hemolysis is the commonest cause of a leukoerythroblastic blood picture on peripheral smear, followed by chronic myeloid leukemia and myelofibrosis. The devastating bone marrow infiltration by advanced stage disease is rare now a days
as a result of early detection and better treatment modalities.

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REFERENCES
Fluorides are known to cause lipid peroxidation in the cells of body. Liver is the vital organ which is affected by the fluoride salts which leads to derangements in its architecture, ballooning and hydropic degeneration of hepatocytes, necrosis and inflammatory changes in hepatic lobules. Also fluorides induce changes in the activity of some enzymes with resultant derangements. Rupal and nursimacharia 2012 reported that fluorides induce metabolic changes by altering the activity of enzymes. It increases the level of blood glucose and decreases the content of glycogen in the liver. In another study by bagale et. al. on fluorides as fresh water pollutant on the liver of freshwater fish, tilapia mossambica showed decreased glycogen in the hepatocytes on exposure to various amounts of fluoride. It has been shown in another study that glycogen content of hepatocytes was reduced in experimental animals with concentration of 0.2 mg NaF/dm³ drinking water given for 90 days. Antioxidants have been used in mitigating the effects of fluorides on level of glycogen in hepatocytes. Vitamin C and vitamin E restores moderate positive PAS reaction in liver of rats treated with fluoride and vitamin C and E6. The present study therefore, aimed to investigate the histological toxic effects of fluorides on glycogen depletion in hepatocytes and its amelioration with vitamin E was studied in male albino mice.

Abstract

Objectivity: In this research the histological effects of fluorides on glycogen depletion in hepatocytes and its amelioration with vitamin E was studied in male albino mice.

Design: This study comprises of a total of 48 male albino mice. Animals were divided into 4 groups. Group A animals were given olive oil 6.67ml/kg/day. Group B animals were given sodium fluoride 10mg/kg/day and olive oil 6.67ml/kg/day. Group C animals were given sodium fluoride 10mg/kg/day and vitamin E 15mg/kg/day. Group D animals were given vitamin E 15mg/kg/day. All the treatments were given orally for 30 days. Animals were sacrificed on 31st day. Liver of animals were dissected out and washed out with distilled water and fixed in 10% formalin solution. Sections of liver with periodic acid–Schiff (PAS) were examined under light microscope. Hepatocytes containing glycogen were counted by using a grid. Data was entered in SPSS 18. Fisher exact test was used to observe the association between % of hepatocytes showing staining for glycogen and groups. P ≤0.05 was considered as statistically significant.

Results: This study revealed that most of the animals belonging to toxic group showed depleted glycogen in hepatocytes. The group which was given vitamin E along with sodium fluoride showed improved staining of glycogen in hepatocytes.

Conclusion: These findings suggest that fluorides reduce glycogen content of liver in mice and vitamin E ameliorates effects of fluorides which were evident by histological sections of liver showing moderate PAS reaction.

Keywords: Sodium fluoride, liver glycogen, vitamin E, PAS reaction
HISTOLOGICAL STUDY OF TOXIC EFFECT OF SODIUM FLUORIDE ON GLYCOGEN CONTENT

effects of fluoride on liver glycogen and evaluate the mitigation in these effects by vitamin E.

METHODS

48 male adult albino mice were obtained from animal husbandry of University of Health Sciences, Lahore. Housed in the animal lab of the university, they were kept at temperature of 23 ± 2 °C, humidity of 50 ± 5% and light and dark cycles of 12 hours. Animals were fed on standard pallet diet and water was given ad libitum. Acclimatization of animals was done for a week before starting the experiment. Animals were divided into 4 groups. Group A animals served as control and were given olive oil 6.67ml/kg/day orally. Group B animals were given sodium fluoride 10mg/kg/day and olive oil 6.67ml/kg/day orally. Group C animals were given sodium fluoride 10mg/kg/day and vitamin E 15mg/kg/day orally. Group D animals were given vitamin E 15mg/kg/day orally.

All the treatments were given for 30 days. Animals were sacrificed on 31st day after anesthetizing with chloroform. Livers were dissected out and washed out with distilled water and fixed in 10% formalin solution. The specimens were processed for paraffin sectioning by gradual dehydration using ascending graded concentrations of alcohol and embedded in paraffin wax. Sections of 3-4μm thickness were prepared. The tissues were stained with periodic acid–Schiff (PAS).

Light microscopic observations:

Two slides from each animal were selected randomly and examined under the light microscope (Leica, DM 1000) at a magnifications of X400 for counting of the cells

Determination of glycogen in hepatocytes:

2 Slides of each animal were selected randomly and Magenta colored glycogen granules were observed in hepatocytes in five fields in each slide for presence of glycogen using a grid. It was graded as (+++) or mild loss if the glycogen granules are seen in hepatocytes in ≥ 75% of the field, (++) or moderate loss when glycogen is present in hepatocytes in < 75% and ≤ 50% of the field and (+) or marked loss if glycogen is present in hepatocytes in < 50% and ≥ 25% of the field and (–) or severe loss if < 25% hepatocytes in the field show glycogen granules. Data was entered in SPSS 18. Fisher exact test was used to observe the association between % of hepatocytes showing staining for glycogen and groups. P ≤ 0.05 was considered as statistically significant.

RESULTS

Significant association for loss of glycogen in hepatocytes was observed among groups shown in Table: 1

Fig. 11: Photomicrograph of Histological Section from Liver of Group A Animal, Showing Central Vein (CV) in the Center of Hepatic Lobule, Cell Filled with Glycogen which are Seen in the form of

<table>
<thead>
<tr>
<th>Group A</th>
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<th>Group C</th>
<th>Group D</th>
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<td>+++</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
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</tr>
<tr>
<td>++</td>
<td>10(83.3%)</td>
<td>0(0.0%)</td>
<td>7(58.3%)</td>
<td>9(75%)</td>
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<tr>
<td>+</td>
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<td>1(8.3%)</td>
<td>4(33.3%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>–</td>
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<td>11(91.6%)</td>
<td>1(8.3%)</td>
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<td></td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>48</td>
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</tbody>
</table>

Table 1: Comparison of Percentage of Hepatocytes Showing Staining for Glycogen among Groups:

p-value: 0.001*
**DISCUSSION**

Liver detoxifies toxicants leading to some degree of structural, physiological and biochemical alterations in it. During stress the liver needs enough energy to combat the damage and repair it. This energy comes from proteins, fats and glycogen stored in the liver which indicates that protein and glycogen content of liver decreases in conditions leading to stress to the organs.

Various studies indicate damage to the architecture of liver, ballooning of hepatocytes, hyperplasia of kuppfer cells and alterations in enzymes secreted by liver. This study revealed that fluorides when given in 10mg/kg body weight dose to mice, the PAS reaction in section of liver showed depleted glycogen in hepatocytes in 11 out of 12 animals. The group which was given vitamin E along with sodium fluoride, only one animal showed depletion of glycogen in more than 75% of the cells. 4 animals showed depletion in 75-50% of animals. 7 animals showed glycogen granules in 50-25% of hepatocytes.

A study showed that fluoride in a dose of 3.6 mg/ kg body weight for 4 weeks resulted in weak PAS positive reaction of hepatocytes. Reduction of glycogen in hepatocytes is also shown by other researches. This study results are in accordance with the previous studies which indicate that a fall in the glycogen level may be due to its rapid utilization to meet the enhanced energy demands in experimental models exposed to toxicants.

Reversal of weak PAS reaction of hepatocytes in group C animals showed that vitamin E being a potent antioxidant reduces stress on liver cells. This is in accordance with studies which shows similar results with use of antioxidants.
HISTOLOGICAL STUDY OF TOXIC EFFECT OF SODIUM FLUORIDE ON GLYCOGEN CONTENT

CONCLUSION

These findings suggest that fluorides reduce glycogen content of liver in mice and vitamin E ameliorates effects of fluorides which were evident by histological sections of liver showing moderate PAS reaction.

ACKNOWLEDGMENTS

The authors would like to express their sincere thanks to Mrs. Bushra Munir and Mr. Rizwan Ali for their cooperation in Laboratory work and Mr. Asghar for taking care of the experimental animals in the research lab.

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Abstract

Background: Neonatal sepsis is a life threatening problem in neonates which is one of the major contributors of neonatal mortality especially in developing countries. The aim of our study is to enlist the organisms predominantly responsible for neonatal sepsis in our hospital and to determine their antimicrobial spectrum of sensitivity. Surveillance should be conducted shortly apart (every 3-6 months) to update the causative organisms and their sensitivity spectrum in particular localities. The administration of organism specific antibiotics will be helpful in decreasing the number of multidrug resistant strains which are spreading due to the administration of broad spectrum antibiotics, being given to patients on empirical grounds.

Subjects and Methods: Study was conducted on 342 blood culture samples. These samples were cultured and after confirming the offending agent its antimicrobial susceptibility pattern was also determined.

Results: Out of 342 blood culture samples received, 100 were positive for growth. Of 100 positive cultures, 37 samples (37%) show growth of Escherichia coli, 20 (20%) of Acinetobacter Spp and 17 (17%) of Klebsiella Spp.

Conclusion: The commonest organism responsible for sepsis in neonates in our setup is Escherichia coli, second most common being Acinetobacter Spp and third one is Klebsiella Spp.

Study Design: Cross-sectional observational study.

Setting: Microbiology Laboratory of Continental Medical College, Lahore.

Duration of Study: 1st August 2017 to 29th February 2018, (six months).

Key words: Neonatal Sepsis, Blood culture, Escherichia coli, Acinetobacter Spp, Klebsiella Spp, Multidrug resistance.

Neonatal sepsis previously known as sepsis neonatorum is defined as “Neonatal infection occurring in the first 28 days of life“1. It is considered one of the major causes of mortality among neonates throughout the world, especially in developing countries.2

Neonatal sepsis contributes to approximately 30-50% of neonatal deaths each year.3 It has been estimated that up to 20% of neonates develop sepsis and approximately 1% of them die because of it and associated complications.3

Neonatal sepsis refers to the presence of systemic infection in neonates including septicemia, pneumonia, meningitis, arthritis, osteomyelitis, and urinary tract infection.2

Neonatal sepsis is categorized according to the postnatal age of the infant at the onset of the disease. Early onset sepsis i.e. less than 72 hours and late onset sepsis i.e. greater than 72 hours.3

The signs and symptoms of newborns presenting with neonatal septicemia are nonspecific. These patients can present with hyperthermia or hypothermia, respiratory distress either cyanosis or apnea, difficulties in feeding, hypotonia or lethargy, irritability or seizures, there may be increased intracranial pressure manifested as bulging fontanelle, cold extremities due to poor perfusion, bleeding problems, distended abdomen, hepatomegaly, unexplained jaundice or any other nonspecific symptom.4

The highest rate of neonatal sepsis has been observed in low birth weight newborns especially in those having severe birth asphyxia and maternal complications like toxemia of pregnancy, precipitous delivery, maternal Infections and intra partum hemorrhage.4

As in the past, neonatal sepsis is still a leading
cause of neonatal hospital admissions, ailments and deaths in developing countries.\textsuperscript{18} The reasons for such a persistence in the incidence of neonatal sepsis is home deliveries conducted in septic conditions, lack of breast feeding, nosocomial resistant infections, multidrug resistant bacterial pathogens and lack of proper treatment strategies regarding general as well as specific empirical treatment approaches to that particular environment, based on continuous surveillance.\textsuperscript{18}

Developing countries contributes to 99% of 4 million neonatal deaths worldwide each year.\textsuperscript{19} Infections such as sepsis, pneumonia, diarrhea and tetanus are the major ailments which are responsible for approximately 34 neonatal deaths per 1000 live births\textsuperscript{19} in contrast to the proportion in developed countries where neonatal mortality caused by sepsis is around 5/1,000 live births.\textsuperscript{24}

For the diagnosis and treatment of neonatal sepsis blood culture is considered a gold standard.\textsuperscript{25} Currently, the greatest challenge being faced in the treatment of neonatal septicemia is multidrug resistance among the causative organisms which is adding up to the difficulty in controlling the morbidity and mortality rates attributed to neonatal septicemia.\textsuperscript{26} The disproportionate pace of the development of multidrug resistance and the development of new antibiotic drugs are major points to ponder.\textsuperscript{26} It is the need of the era to use antibiotics wisely and to limit the administration of broad spectrum empirical antibiotics, otherwise, after a short time span there will be no drugs available for the treatment of Neonatal sepsis.\textsuperscript{26}

Apart from focusing on the treatment strategies, preventive measures should be considered especially to recognize infants who are at a greater risk, consideration of proper aseptic measures during labor and increasing community awareness regarding exclusive and early Breast feeding.\textsuperscript{23} Indeed, new strategies need to be developed which can be helpful in early diagnosis and prompt treatment of neonates.\textsuperscript{11}

The current practice is to perform a complete workup of baby with the clinical suspicion of neonatal sepsis including laboratory investigations such as direct analysis and culture of blood samples taken from the patients. Of these three, cultures are considered a gold standard.\textsuperscript{5}

Of cultures, blood culture is usually performed to isolate the causative organism responsible for neonatal sepsis as most of the blood cultures show growth confirming sepsis usually in 24-72 hours.\textsuperscript{29}

Most frequent organisms associated with early onset neonatal sepsis are Coagulase-negative Staphylococcus, Escherichia coli, Group B Streptococcus, Listeria Monocytogens and Haemophilus influenzae and those frequently responsible for late onset neonatal sepsis are Staphylococcus aureus, Coagulase negative Staphylococcus, Pseudomonas species, Enterobacter, Escherichia coli, Klebsiella species, Group B Streptococcus, Serratia species, Acinetobacter and Anaerobes.\textsuperscript{5}

Day by Day the rate of Neonatal sepsis is increasing alarmingly, adding up to the burden on health care services owing to lack of proper antenatal care and follow-up. Lack of aseptic delivery practices especially those conducted at home by untrained birth attendants without following precautions and protocols such as cutting and ligation of umbilical cord under septic conditions are resulting in rapid increase in the number of cases of neonatal septicemia being admitted in hospitals.\textsuperscript{5}

The purpose of our study is to identify pathogenic bacteria responsible for neonatal septicemia in our setup and to determine their antimicrobial susceptibility spectrum for lining up the treatment strategies for specific prevalent organisms.

The bacterial pathogens responsible for causing sepsis in neonates are acquired intrapartum either directly from mother's blood, skin, birth canal or from the surroundings in which delivery is being conducted.\textsuperscript{5} Many researches have been conducted to determine the pattern and frequency of hospital acquired infections in tertiary care settings, but a limited workup has been done to find out the
organisms being responsible for causing septicemia in Pakistan during the last decade.\textsuperscript{6}

Furthermore, broad spectrum antibiotics administrated to overcome this life threatening condition is resulting in rapid emergence of multidrug resistance among the causative agents adding up to the difficulty in patient management. Unfortunately, Pakistan is ranked eighth most common country having greatest number of newborn deaths each year of which neonatal sepsis is a major contributor.\textsuperscript{7} An important factor responsible for this is lack of availability of microbiological diagnostic facilities. This is why most of the pediatricians and physicians have to prescribe broad spectrum antibiotics to save life of the newborn by treating them on empirical grounds.\textsuperscript{7}

Many studies have been published about an increase in antimicrobial resistance among bacterial pathogens responsible for blood stream infection as its incidence is increasing day by day. This is because of the wide spread use of antibiotics empirically.\textsuperscript{8} It has resulted in decreased therapeutic options available for the health team to overcome this disease.\textsuperscript{8} An observational study conducted in Israel highlighted the fact that among the patients of neonatal sepsis, death rate was particularly higher for those who received inappropriate empirical treatment.\textsuperscript{7}

Hence concluded that detection of pathogens responsible for blood stream infections should be considered a priority in our clinical settings. For this purpose blood culture is considered a gold standard.\textsuperscript{10}

More than 4 million neonatal deaths have been reported each year by World Health Organization (WHO), out of which about 3 million were those of neonates.\textsuperscript{7} Neonatal deaths caused by sepsis have been more common in developing countries like Pakistan.\textsuperscript{12,13} Approximately 500 neonatal deaths have been reported in Pakistan every day, the neonatal mortality rate being 54/1000 live births; as described by UNICEF (2009).\textsuperscript{7}

METHODS

Our study was a cross-sectional observational study, carried out on 342 blood samples received with the clinical diagnosis of Neonatal sepsis from Neonatology ward of Pediatric units of Sir Ganga Ram Hospital during 1st of August 2017 to 29th February 2018 at the Department of Microbiology, Continental Medical college, Lahore.

A blood sample of 2ml/kg body weight was taken in Pediatric culture bottles through venipuncture under aseptic measures by swabbing and drying the patient’s skin. The sample was then added to a pre-prepared (filled with 20 ml of the medium i.e. 10 times that of the sample) and sterilized blood-culture bottles. These bottles were incubated at 35–37°C and were inspected twice daily for following 3 days to look for any signs of bacterial growth. Those blood cultures in which growth was observed by any the evidence like an amorphous deposit on top of the blood layer, sub-surface or diffuse turbidity, hemolysis, coagulation of media, pellicle formation, gas formation or presence of white grain deep in the blood or on the surface were separated from those in which no signs of growth were seen. A sterile culture is the one which usually show sediment of red blood cells on the top of the culture media with an underlying pale yellow clear liquid media. Blood culture samples with visible signs of growth were observed for the presence of microorganisms by preparing a Gram-stained smear and examining it under 10X, 40X and 100X. Blood cultures were kept and observed at 24, 48 and 72 hours maximally. After that cultures were discarded and taken as negative.

Positive blood samples were than cultured on appropriate sterile agar plates. The culture media we used in our study were blood agar, chocolate agar and MacConkey’s agar.

The bacteria isolated were further identified biochemically using biochemical tests e.g, TSI, Indole test, Citrate utilization test, etc. Further confirmation was done by using API 20 E& API 20 NE. Antimicrobial sensitivity testing was done for bacterial isolates using Ceftriaxone, Ampicillin, Amoxicillin, Augmentin, Cefotaxime, Penicillin, Ciprofloxacin, Colistin, Imipenem, Sulphamethoxazole and Ciprofloxacin by culturing the organism
on Muller Hinton agar and using the before mentioned antibiotic discs. After 24 hours of incubation biochemical test results were interpreted and microorganisms were identified as well as the antibiogram was reported according to CLSI 2018 guidelines. Antibiotic susceptibility of the isolates was then assessed and reported to guide the clinician regarding the choice of antibiotics for a particular case.

RESULTS

A total of 342 samples with the clinical suspicion of neonatal sepsis were submitted to Microbiology Department. Out of 342 samples 100 (34%) were positive for growth whereas 242 (66%) samples did not show any growth. (Figure: 1)

Figure 1: Proportion of Blood cultures positive for bacterial growth.

Out of 100 culture positive isolates, 37 samples (32%) showed growth of Escherichia coli s, 20 (17%) of Acinetobacter and 17 (15%) of Klebsiella species, 16 (15%) Pseudomonas Spp and rest 10 were Streptococcus spp.

Regarding antimicrobial spectrum of sensitivity Citrobacter Spp, showed 76% sensitivity to chloramphenicol, Staphylococcus Spp showed 60% sensitivity to chloramphenicol and Klebsiella Spp showed 47% sensitivity aztreonam. (Table 1)

DISCUSSION

Neonatal Sepsis is a life threatening disease of neonates all over the world. It is one of the medical emergencies which if not treated properly on time can have serious consequences. Thus its empirical treatment must comprise of a combination of drugs which can cover the bacterial pathogens most commonly responsible for neonatal sepsis in a particular location. Time to time surveillance is required to identify the common pathogens being responsible for it as well as their antimicrobial sensitivity spectrum to overcome this problem.

Neonatal septicemia is a clinical ailment which is characterized by signs of circulatory compromise such as poor peripheral perfusion usually characterized by pale or cyanosed skin, hypotonic and poorly responsive lethargic baby. Before the development and establishment of antibiotics administration protocols, neonatal sepsis was life threatening. Even now mortality rates among infants who

Table 1: Antibiotic Sensitivity of Bacterial Isolates.

<table>
<thead>
<tr>
<th>Organisms</th>
<th>ATM (%)</th>
<th>AMP (%)</th>
<th>CEF (%)</th>
<th>CRO (%)</th>
<th>TZP (%)</th>
<th>IMP/M (%)</th>
<th>EM (%)</th>
<th>AMK (%)</th>
<th>GEN (%)</th>
<th>CIP (%)</th>
<th>SXT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>5</td>
<td>27</td>
<td>15</td>
<td>18</td>
<td>64</td>
<td>86</td>
<td>94</td>
<td>66</td>
<td>27</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>0</td>
<td>31</td>
<td>22</td>
<td>29</td>
<td>70</td>
<td>68</td>
<td>83</td>
<td>71</td>
<td>62</td>
<td>37</td>
<td></td>
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<tr>
<td>Pseudomonas spp</td>
<td>NT</td>
<td>60</td>
<td>NT</td>
<td>NT</td>
<td>83</td>
<td>77</td>
<td>86</td>
<td>82</td>
<td>81</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>64</td>
<td>100</td>
<td>83</td>
<td>61</td>
<td>100</td>
<td>92</td>
<td>29</td>
<td>33</td>
<td></td>
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</tbody>
</table>
are treated with antibiotics are 5% to 60%, having disproportionately distribution worldwide being the highest in developing countries.\(^5\)

According to a statistical data provided by World Health Organization (WHO) about 1 million neonates die each year because of neonatal sepsis, of which 42% die in their first week of life.\(^6\) A major factor responsible for a marked difference between the rates of neonatal sepsis in developing and developed countries is disparities in neonatal care, health facility infections and home conducted deliveries in septic environment.\(^6\) Premature infants are at greater risk. One of the main reason being reported especially in developed countries is increased admissions of premature babies who are at a greater risk of acquiring hospital infections most of which being caused by multidrug resistant bacterial pathogens.\(^6\)

Our study results are somewhat similar (regarding second and third most prevalent organism) to a study conducted in a private hospital in Festac town, Nigeria, which showed that Klebsiella species (34.3%) is the most common Gram-negative bacteria while Staphylococcus Spp (28.1%) is the commonest Gram-positive bacteria associated with neonatal septicemia. But it differs regarding the most common organism which in our study is Citrobacter Spp The sensitivity spectrum results are also different as in this study Klebsiella species was found to be resistant to chloramphenicol.\(^7\)

A studied conducted in Rawalpindi showed that the most common Gram positive pathogen responsible for sepsis in neonates is Staphylococcus Spp (47.7%) which is similar to our results, while Acinetobacter Spp, Pseudomonas Spp\(^{49}\), E. coli and Salmonella Spp\(^{30}\) were the most common Gram negative isolates\(^49\), which is in contrast with our results.

A research conducted in Peshawar showed that Escherichia coli was the most common organism (36.6%), Staphylococcus aureus (29.5%) being the second most common followed by Pseudomonas species (22.4%), Klebsiella species (7.6%), and Proteus (3.8%).\(^8\) The results differs from ours regarding the prevalence of E.coli but show similarity regarding the prevalence of Staphylococcus aureus. In their study Pseudomonas and E.coli showed a great degree of resistance to commonly used antibiotics (augmentin, gentamicin and ampicillin) similar to our study in which pseudomonas showed high resistance to cephalosporins and sensitivity to aztreonam and imipenem. In their study Staphylococcus aureus showed a low resistance to all of the three antibiotic groups\(^8\) which is in contrast to our results in which Staphylococcus showed high resistance to cephalosporins and sensitivity to chloramphenicol and vancomycin.\(^8\)

A study carried out in Department of Pediatrics, Holy Family Hospital, Rawalpindi Medical College included 50 newborns with diagnosis of neonatal sepsis. The predominant microorganisms isolated were gram negative (84%), with Enterobacter as the most common bacteria (48%) followed by E. coli (16%), Klebsiella (14%) and Pseudomonas (6%). Among gram positive organisms the most common organism was Staphylococcus aureus (10%) and the second one is Streptococcus pneumoniae (6%).\(^9\) These results are partially similar to ours in which Klebsiella was isolated in 17% cases and was also the third most common organism. In this study Staphylococcus aureus causes only 10% cases of neonatal sepsis.\(^9\)

A study carried out at the Department of Pediatrics, Post Graduate Medical Institute, Hayatabad Medical Complex, Peshawar, showed that among 140 cases of culture proven sepsis, gram-negative organisms were more common in neonatal sepsis (75%) which is in contrast with our results. Escherichia coli (44.3%) was the commonest followed by Staphylococcus aureus (26.3%), Klebsiella (18.6%) and Pseudomonas (12.1%). Escherichia coli was sensitive to Ciprofloxacin (93.5%), Cefipime (83.9%) and Amikacin (74.2%). Staphylococcus aureus also show sensitivity to Ciproflora-cin (81.8%), Cefipime (75.8%) and Amikacin (66.7%). The sensitivity spectrum also differs from ours in which
NEONATAL SEPSIS: A TERTIARY CARE EXPERIENCE

most of the gram positive and negative organisms were sensitive to chloramphenicol, Aztreonam and Vancomycin. 20

A study carried out at a Tertiary care Hospital of Nepal showed that neonatal sepsis was 20.3% prevalent in their hospital. 21 The predominant isolates in their study were Gram positive cocci (88.40%) which is in contrast to our study. In their study the most common gram positive organism isolated was Staphylococcus epidermidis (72.46%) the second one being Staphylococcus aureus (7.24%), third one Staphylococcus saprophyticus (4.34%) and Enterococcus fecalis as the fourth most common isolate (4.34%). 21 This is also in contrast to our study in which the most predominant gram positive species was Staphlococcus aureus. Approximately 11.60% positive culture samples showed growth of Gram negative bacilli especially E.coli 10.14% and Klebsiella species 1.44%. 21 It also differs from our study. Sensitivity of their isolates was highest for Amikacin. In their study Vancomycin was the drug to which most of the gram positive pathogens were sensitive which resemble our results for positive isolates.

Regarding protection against this deadly disease early breast feeding is of prime importance. The initiation of breast feeding within first twenty four hours of birth is known as early breast feeding. Its benefits have been known for years which are now confirmed. 22

Analysis of maternal risk factors (especially intrapartum) revealed a considerable association between maternal factors and neonatal sepsis. Some of these factors are maternal urinary tract infection, pyrexia and vaginal infections. Newborns of these mothers had significantly low APGAR scores and most of them need to be intubated immediately after birth. Analytical data suggests the possibility of vertical transmission as well as horizontal transmission of infection postnatally. 23

Today a major concern in treating neonatal sepsis is an increased incidence of antibiotic resistance among bacterial pathogens which is mainly effecting the treatment of ill neonates empirically. It highlights the need for continuous microbiological surveillance in all clinical and hospital setups. 24

CONCLUSION

The aim of our study was to list the organisms predominantly responsible for neonatal sepsis in our hospital. It is recommended that surveillance should be conducted shortly apart (every 3-6 months) to update the causative organisms and their sensitivity spectrum in particular localities. 26 Each hospital must maintain its own specific antibiogram considering all the possible empirical treatment options. 26 Efforts must be directed to keep this life threatening disease under control by administration of an effective empirical treatment to the baby keeping in mind the prevalent organisms to save the life of the patient, when the blood culture and sensitivity report is awaited. 26

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Asthma is a chronic inflammatory airway disease that results in recurrent airflow obstruction, spontaneously reversible or as a result of therapy. Atopy is the most frequently identified predisposing factor. It is an important problem in Pakistan and worldwide, both for its high prevalence and for the repercussions for the individual, their family and society.

According to the 2015 Asian Development Bank report (ADB), about 24.3% of the Pakistan population had income below the poverty line; and 14% to extreme poverty. Although Pakistan is in the 25th of the richest countries, the relationship between poverty level and per capita income puts it in the bottom 22%. According to the ADB report, in Pakistan there is not only unequal income distribution according to social class, but also according to geographical regions. The highest percentage of families with monthly family income of less than two minimum wages was in the Northeast (47%), and the lowest percentage, the Southeast (16%). The opposite occurred with the percentage of families with a monthly income of 10 minimum wages or more, 39% of families in the Southeast and 15% of those in the Northeast.

The interaction between these two common problems can have important repercussions on the child. Poverty can contribute to the etiology, exacerbation, recognition and management of asthma. As an etiological factor, the relationship is corroborated by hygiene theory, since poor individuals would be more exposed to microbial agents and, therefore, less likely to develop the disease.

Studies from different locations have shown conflicting results regarding the association between asthma and poverty. In England, a cross-sectional study of about 6,000 school going children showed a higher prevalence of wheezing in the less favored social extracts. Similar findings were found in Singapore and Recife. In a prospective cohort in New Zealand, with 1,000 individuals followed up to 26 years, no association was observed between these
variables. In a control case with 163 children in Cuiabá Brazil, sex, low maternal education, low income, time of natural breastfeeding and second-hand smoke were not associated with asthma. In São Paulo Brazil, a study of 1,390 children under five found a recent wheezing odds ratio of 3.1 (95% CI: 1.66-5.8) in those with a monthly income below 50% of the minimum wage.

This study aimed to analyze the role of low income, a proxy of poverty, as a risk factor for the development of asthma in children and adolescents in Faisalabad Pakistan, visiting DHQ hospital Faisalabad. The study hypothesized that poor children and adolescents would be at lower risk for developing asthma.

METHODS

In a case-control design, we selected patients from the pulmonology outpatient DHQ hospital Faisalabad, aged between 5 and 15 years. DHQ hospital Pulmonology is a tertiary care referral center of Faisalabad and its remote areas population. Participants were admitted consecutively and attended the morning shift from March to July 2019.

As cases, participants from the general pediatric outpatient clinic with previous diagnosis of asthma or at least three previous episodes of wheezing and dyspnea were chosen. Controls originated from the pediatric neurology, orthopedics, surgery and ophthalmology outpatient clinic. The choice of controls in these sectors was aimed at minimizing selection biases, since controls from the general outpatient clinic could come from a greater proportion of the metropolitan area of Faisalabad due to acute complaints, unlike the cases.

Patients with heart disease, immunodeficiency, malnutrition, lung diseases other than asthma and severe neurological disease were excluded, as well as tuberculosis and systemic mycoses, neuro-psychomotor retardation, and limitation of physical activity other than asthma.

It was used as a data collection instrument a questionnaire with 42 closed questions, completed by one of the researchers and a research fellow from the Pulmonology ward DHQ Hospital Faisalabad.

The sample size was calculated for 700 participants, considering for unpaired control cases a confidence level of 95%, a power of 80%, a frequency of exposure in non-patients of 70% (based on pilot survey), an odds ratio of 1.7 and a loss percentage of 10%.

For the definition of low income and very low income, the federal government criterion was used, which defines them as 50 and 25% of the minimum per capita minimum wage per month, respectively. The current minimum wage was $115.00(10). We considered dollar exchange rate of 140 rupees, calculated at the start of study.

As a statistical analysis plan, the univariate analysis used Pearson's chi-square or Fisher's test, with a significance level of 5%, in addition to the prevalence ratio, with a confidence interval of 95%. We chose to perform multivariate analysis according to the conceptual hierarchical model, with variables with significance level below 20%.

The study was approved by Ethical review Committee. One parent of each participant or guardian signed the informed consent form.

RESULTS

A total of 689 participants were studied, 54.7% male, aged between 5 and 15 years, with mean and standard deviation of 8.9 ± 2.1, respectively. Just under half (49.1%) were from the metropolitan area of Faisalabad, 33.2% from the sub-barbs of Faisalabad, 12.8% from the surrounding villages, 4.4% from the interior of Punjab and 0.6% from other provinces of Pakistan.

The vast majority (98.1%) lived in brick houses, with a number of rooms ranging from 1 to 15, with a mean and standard deviation of 5.7 ± 1.7, respectively. The number of residents ranged from two to 15, with a mean and standard deviation of 4.8 ± 1.7.

The mothers had between 0 and 18 years of study, with mean and standard deviation of 6.8 ± 3.6
years.

None of the variables mentioned, when stratified by case and control, showed a statistically significant difference.

The monthly family income was between $50 and $648 with a median of $460 and 25th and 75th percentiles of $330 and $700 respectively. The monthly per capita income was between $12.50 and $1,100.00, with a median of R$103.75 and 25th and 75th percentiles, corresponding to $70.00 and $175.00. Using the federal government cutoff points, the number of participants with very low income was 269 (39.0%); and the low-income 257 (37.3%). Both constituted 76.3% of the sample.

Analyzing the relationship between poverty and asthma, no statistically significant association was found. The p value found in the univariate analysis showed that the control of possible confounding factors would not modify this result to make it significant, rendering multivariate analysis useless (Table 1). Potential confounders were considered: age; sex; provenance; type of housing; number of rooms in the house; maternal education level; history of atopy; breast-feeding; eating pattern after weaning; vaccination schedule; drug consumption; viral diseases; previous parasitic diseases and tuberculosis; exposure to passive smoking; presence of animals; and aeroallergens at home.

Table 1: Analysis between Low Income and Asthma of Children and Adolescents between 5 and 15 Years, Attended at Outpatient Clinic of DHQ Hospital Faisalabad between March to July 2019 Stratifying Groups According to the Monthly Income.

<table>
<thead>
<tr>
<th>Salary</th>
<th>With Asthma</th>
<th>Without Asthma</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to $87.50</td>
<td>146</td>
<td>123</td>
<td>269</td>
</tr>
<tr>
<td>$88 – 175.5</td>
<td>142</td>
<td>115</td>
<td>257</td>
</tr>
<tr>
<td>&gt;$175</td>
<td>89</td>
<td>74</td>
<td>163</td>
</tr>
<tr>
<td>Total</td>
<td>377</td>
<td>312</td>
<td>689</td>
</tr>
</tbody>
</table>

Pearsons association qi- square = 0.2588 p = 0.97

DISCUSSION

There is already enough evidence in Pakistan for high prevalence of asthma in the pediatric population, at least in urban areas (6-9,20-22). However, knowledge about risk factors, which is important for preventive and therapeutic action, is still incipient among us.

This study aimed to analyze the role of poverty as a risk factor, that is, of protection, in the onset of asthma, taking as theoretical reference the theory of hygiene. According to our study, there seems to be no association between both in children and adolescents with similar genetic and socio-demographic characteristics to those studied. One study points to similar results. In a control case of 163 children aged 4 to 14 years, treated at an outpatient or pediatric emergency department in Cuiabá Brazil, the authors found no relationship between asthma and poverty (less than 50% of the monthly minimum wage per capita), but only between asthma and allergen sensitization. Other authors in a population-based survey of 1,132 children under 5, they found an odds ratio of 3.16 (95% CI: 1.70-5.85) of asthma symptoms for a monthly per capita income of less than 50% of the minimum wage. In a study involving 6,437 children and adolescents aged 6-7 and 13-14 years old, in Brazil, a higher prevalence of symptoms was observed in the higher socioeconomic groups, although not mentioning how the cutoff points were made. A cross-sectional study of school going children in Recife showed results close to those of the study cited, in which the prevalence of asthma symptoms was significantly higher in schoolchildren whose mothers had higher levels of education. These three studies, however, were not designed for risk determination, and the findings may have been altered by bias or confounding factors.

Studies from other countries also show different results. In a survey in Singapore using the International Study of Asthma and Allergies in Childhood (ISAAC) protocol, the authors found a higher prevalence of asthma in children with better socioeconomic status. In a prospective birth cohort study of about 1,000 subjects in a New Zealand city, the authors found no relationship between childhood socio-economic status and asthma at age 26.
community in the United Kingdom surveyed by the ISAAC protocol in more than 6,000 children aged 8 and 9 years, morbidity and mortality from asthma were found to be associated with worse socioeconomic status.\textsuperscript{15}

Although it is universally a burden for those who live in it, poverty has different determinants and characteristics in different populations, even within Pakistan. According to one study, poverty in our country stems from the perverse income distribution and opportunities for economic and social inclusion and is most evident in the North and Northeast.\textsuperscript{11} It can be assumed, even without scientific evidence, comparing different communities that, for example, the determinants of poverty in Singapore and New Zealand are different from Brazilians and the findings may therefore differ.

It cannot be said that the lack of relationship found between poverty and asthma was due to the homogeneity of the studied sample, composed mostly of poor people, since the subgroups were representative in all extracts. However, given that social inequality in Pakistan is high, the external validity of this study is limited to users of government hospitals and cannot be extrapolated to the general population.\textsuperscript{11}

This study has limitations that need to be addressed. Firstly, all data were collected through a questionnaire. The characterization of asthma by the presence of three or more episodes of wheezing at some time in life or the previous diagnosis of asthma, although widely used and accepted, may have led to over diagnosis of cases and selection bias.\textsuperscript{1,24} Some authors recommend, for risk determination studies, to add evidence of pulmonary function and allergic testing.\textsuperscript{26} For operational reasons, it was not possible to use these complementary exams. Another potential bias is recall, which may have underestimated the actual cases of asthma. In order to avoid this inconvenience in the determination of poverty, the per capita income of the last month was used as a proxy for the per capita income of the first years of life, assuming that the participants' socio-economic condition remained stable throughout the period. Your lives. This may also have generated non-differential selection bias.

Despite these limitations, the study seems valid and reasonably accurately reflects that poverty does not influence asthma in children and adolescents in the population of Faisalabad. However, further studies are needed, especially cohort studies, to explain more precisely this relationship in Pakistan.

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LYMPHEDEMA MANAGEMENT SERVICES AT JINNAH BURN AND RECONSTRUCTIVE SURGERY CENTER LAHORE: EARLY EXPERIENCE IN DEALING WITH A PROGRESSIVE DEBILITATING CONDITION.

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Abstract

Background: Lymphedema is a chronic debilitating condition, with many condemned to lifelong deformity due to lack of services in our country. Equipped with better understanding of the pathology and newer modalities we started lymphedema services at our center. We present a case series to show the outcome of patients who presented at various stages and underwent treatment accordingly.

Methods: Prospective case series, done at Jinnah burn and reconstructive surgery center Lahore from November 2018 to December 2019. Outcome was assessed by measuring girth of the involved area, recurrence, BMI and frequency of lymphangitis, and then comparing with preoperative findings.

Results: 14 patients were treated after enrollment for the study. 7 patients were treated with vascularised lymph node transfer, 4 were treated with debulking and grafting, 2 were treated with conservative treatment and 1 was referred to general surgery to treat the cause of the secondary lymphedema. All patients had significant improvement in girth, BMI, frequency of lymphangitis and reported no recurrence.

Conclusion: Lymphedema patients can have a favorable outcome if properly treated at a dedicated facility. Modern modalities and properly administered conservative treatment can stop the progression of the disease too.

Key Words: Lymphedema Surgery

Lymphedema represents a debilitating chronic and progressive condition affecting the patient's emotional, functional, social/family, and physical quality of life. Despite a better understanding of the pathogenesis of extremity lymphedema and increased attention to treatment, extremity lymphedema remains an incurable disease, although the debility is significantly reduced with modern methods. In developed countries, most commonly secondary lymphedema of the extremities results from breast and gynecologic cancer treatment. Approximately 29-49% of patients undergoing axillary lymph node dissection develop upper extremity lymphedema with a variable onset of the disease. Similarly, following gynecologic cancer excision and pelvic lymph node dissection, lower extremity lymphedema can occur in 10-49% of patients. In contrast, in developing countries patients usually develop secondary lymphedema after infection, most commonly of parasitic origin. Apart from this, about 30% patients present with primary lymphedema, with the genetics playing role in development of the disease.

In recent years, lymphatic microsurgery procedures have increased in popularity, bringing in a new wave of physiologic surgical options for the management of lymphedema. The two most common microsurgical options include lymphovenous anastomosis (LVA) and vascularized lymph node (VLN) transfer. Each treatment option has the potential to bypass areas of damaged lymphatics by rerouting the lymph into the venous system or by replacing the lost lymph nodes and, or lymphatic ducts. LVA with a super microsurgery technique has been shown to be more effective in early stage lymphedema before development of fibrosis but less effective in advanced-stage lymphedema. Lymph node transfer is the latest addition in the management of lymphedema of
LYMPHEDEMA MANAGEMENT SERVICES AT JINNAH BURN AND RECONSTRUCTIVE SURGERY CENTER LAHORE

the extremities, and has shown promising results, but it could incur the risk of donor-site lymphedema. Studies have evaluated the positive effects of VLN transfer in the setting of lymphedema and have shown significantly better results for the patients in which the native lymphatic ducts are no longer available when compared to conservative treatments or LVA. A meta-analysis investigated the outcomes of VLN flaps in comparison to LVA for the treatment of lymphedema. Although LVA and VLN transfer were both effective for short-term outcomes in terms of circumferential reduction rate, the VLN transfer group had significantly better long-term outcomes in terms of greater likelihood of discontinuing the compression garments. For the patients who develop advanced lymphedema, reductive surgery is the only solution. Unfortunately in Pakistan, mostly patients present with advanced lymphedema as usually at earlier stages, the pathology is often ignored or ineffectively treated due to lack of availability of standard conservative therapy and physiologic procedures done at the plastic surgery facilities. At Jinnah burn and reconstructive surgery center, as we started receiving many patients seeking hope due to the excellent reputation of our center in microsurgery, we decided to start the lymphedema service with target to offer treatment to the patients presenting at all stages of the lymphedema. We share our experience in the form of a case series and try to present the outcome to demonstrate the advantages of treating the neglected bracket of patients.

METHODS

This case series was done in Jinnah burn and reconstructive surgery center Lahore, from November 2018 to December 2019. 14 patients were included in the case series. We included both male and female patients, aged between 15-50 years who presented with either primary or secondary lymphedema of any region, classified as Campisi 1 to 5. We excluded patients who had undergone any surgical treatment for lymphedema before. After informed consent, patients were enrolled for the study, and management was planned according to the clinical evaluation, grading of the condition and specific investigations. Patients were followed on OPD bases and outcome was assessed by measuring girth of the involved area, recurrence, BMI and frequency of lymphangitis.

RESULTS:

In this study, 6 (42.9%) patients were male while there were 8 female patients (57.1%). The mean age was 27.2 ± 5.9 years. 7 patients underwent vascularised lymph node transfer all with primary lymphedema of lower limb, with an average Campisi grade of 1.7 ± 0.5 and mean follow up of 10.3 ± 2.5 months. The mean circumference decreased from 21.1 ± 1.1cm to 18.0 ± 1.8cm. The weight decreased from 67 ± 6.8kg to 64.0 ± 67.4kg and BMI from 24.2 ± 2.0 to 23.6 ± 2.5 after the procedure. Average frequency of lymphangitis decreased from 2.6 to 0.3 per 6 months and none of the patients had recurrence. 4 patients underwent excision / debulking and grafting, with average Campisi grade of 4.7 ± 0.5 and all having involvement of scrotum, with mean follow-up of 8.9 ± 1.4 months. The average circumference decreased from 66.4 ± 7.2cm to 8.8 ± 0.5cm, weight from 92.8 ± 3.9 kg to 72.3 ± 1.7 kg and BMI from 30.2 ± 0.9 to 23.5 ± 0.9 after the procedure. Average frequency of lymphangitis decreased from 5.5 to 0 in 6 months. 2 patients underwent conservative management with manual lymphatic decompression and compression stalking; all having grade 1 primary lymphedema, 1 patient with involvement of upper extremity and the other had involvement of lower extremity. The mean follow-up was 5.5 ± 0.7 months, in which the circumference of the involved extremity decreased from 19.6 ± 2.1 cm to 17.8 ± 3.4 cm, weight from 57.5 ± 4.9 kg to 56.5 ± 4.9 kg and BMI from 22.0 ± 1.3 to 21.7 ± 1.3. The frequency of lymphangitis decreased from 3.5 ± 0.7 to 1.5 ± 0.7 in 6 months, with no recurrence. 1 patient had lymphedema secondary to varicose veins and was referred to general surgery from treatment of varicose veins.
DISCUSSION

Lymphedema management has entered a new avenue since the advent of microsurgical vascularised lymph node transfer and lympholymphatic and lymphovenous bypass surgery. The most accepted mechanism of vascularised lymph node transfer is neolymphogenesis at the transplanted site, which reduces collection of lymph at the area. Thus due to this reason, lymph node transfer is better than lympholymphatic bypass as it can be done in late cases where lymphatics are fibrosed. It’s effectiveness has been described too, and many patients may get relieved from lifelong conservative management altogether. Figure 1 shows patient who underwent vascularised lymph node transfer. Although lympholymphatic bypass can be done in local anaesthesia, it requires supermicrosurgery which can be done effectively using indocyanine green dye and camera, both of which are not available in Pakistan.

Surgical debulking can effectively remove the hypertrophied tissue, but has been reported with significant blood loss, necessitating staged procedure. Removes all the effected tissue down to deep fascia but needs skin grafting. We have achieved good outcome with no recurrence and minimal blood loss by complete excision of the effected skin and subcutaneous tissue with infiltration of the root of the penile shaft, scrotum and the rest of the incision. Complete excision of the scrotal and penile swelling resulted in better aesthetic appearance and no recurrence. In the literature serologic tests are recommended to rule out filariasis but unfortunately in Pakistan microscopic test to detect microfilariae from nocturnal sample is available, which is not very convenient. On the contrary, all cases with giant scrotal involvement have been found to be caused by filariasis and ant- helminthic therapy has been recommended in the literature. Thus we did not investigated the patients for filariasis and started anti helminthic therapy to reduce the incidence to recurrence, involvement of other areas and spread to other individuals. Although the follow-up time is short in our cases, involvement of more proximal areas and lower limbs has been documented in literature as there is always permanent fibrosis of the lymphatic channels due to the disease at the time of presentation. Figure 2 shows patient who underwent debulking and grafting for giant scrotal lymphoedema.

Figure 1: SuprACLAVICULAR LYMPH NODE TRANSFER AS FREE FLAP FROM NECK TO LOWER LIMB IN A PATIENT WITH PRIMARY LYMPHOEDEMA

Conservative treatment, with manual lymphatic decompression and compression stalking, had been mainstay previously, but required supervision of an expert and compliance. We have found that when done early, it reduces the swelling, incidence of lymphangitis and progression of the disease. Thus although effective for earlier presentations, it requires a specialized center to properly administer the therapy and tailor the treatment according to each patient.

We received one patient with secondary lymphedema due to varicose veins. Patient was referred to general surgery for the specific treatment and had improved signs and symptoms on our follow-up. All patients with secondary lymphedema...
are recommended to have treatment of the primary pathology before any surgery for lymphedema itself is undertaken.

**Figure 2:** Debulking and Grafting of Giant Scrotal Lymphoedema

**CONCLUSION**

Well developed lymphedema services are the need of time as the pathology is always neglected and patients are bound to suffer from a life long disability. Due to advent of modern techniques and better understanding of the pathology, this disease remains no longer a debilitating condition and timely intervention can greatly improve the patients symptoms.

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Chronic lung diseases affect a large number of people all over the world. Most important among these are chronic obstructive pulmonary disease (COPD), asthma and tuberculosis and are major cause of morbidity and mortality. According to a report published by WHO in 2007, there were 210 million people affected by COPD all over the world and it was the fifth leading cause of death in 2002. Total deaths from COPD are projected to increase by more than 30% in the next 10 years and it is estimated to be the third leading cause of death by the year 2030 unless urgent action is taken to reduce the underlying risk factors, especially tobacco use. A comprehensive study published in 2012 comparing the leading causes of death globally in 1990 and 2010 reported that incidence of COPD has increased and was the third leading cause of death due to non-communicable diseases in 2010. Although according to a survey conducted by WHO/world bank in 1990 about the global burden of COPD, the prevalence of disease in developing countries was much less than the industrialized countries, it was expected to increase due to increasing rate of tobacco consumption in these countries. Despite the importance of early diagnosis of COPD for better management of the condition, it remains underdiagnosed. Several cross-sectional studies have found undiagnosed disease even in symptomatic patients. A survey of the general population in the United States suggested that fourteen percent of the adults fulfilled the GOLD criteria for a diagnosis of COPD, which would correspond to 24 million individuals nationwide.

Smoking tobacco is definitely the major risk factor for COPD and majority of patients are current or ex-smokers. Smoking water-pipe poses at least as great a risk. But only about 20% of smokers develop the disease. Definitely other factors like genetic predisposition, respiratory infections, and air pollution are involved. Moreover an estimated 25–45% of patients with COPD have never smoked; the burden of non-smoking COPD is therefore much
higher than previously believed. The significance of atmospheric air pollutants as the cause of chronic lung problems is increasingly being recognized in non-smokers.

In developed countries, well designed studies have confirmed the significance of acute and chronic respiratory diseases with exposure to outdoor air pollution especially with particulate matter even at a much lesser concentration that previously thought. The relative increase in motor vehicle traffic in the past decades has now presented as a more worrying air pollution problem in many metropolitan cities around the world. The ongoing Rotterdam study about various chronic diseases found out that the prevalence COPD in non-smokers was much higher in women than men. This suggests that the contribution of environmental exposures other than active smoking leading to COPD seems more substantial in females than in males. While most of the information available on COPD prevalence, morbidity and mortality comes from high-income countries, it is known that almost 90% of COPD deaths occur in low- and middle-income countries.

In low income countries the situation is different among non-smoker patients of COPD. Here the majority of non-smoker COPD patients are women and the major risk factor is the indoor air pollution due to consumption of un-processed biomass fuel. As mentioned above, about half the population worldwide is exposed to smoke from biomass fuel suggesting that it may be the biggest risk factor for COPD globally. A study conducted in China compared COPD pattern in urban and rural populations. This study showed that smoking was less prevalent in rural women compared with urban women but the incidence of COPD was significantly higher in rural women and the major risk factor identified was indoor air pollution due to use of biomass fuel as the major source of energy. A similar study conducted in rural community of Peshawar city in Pakistan showed significantly higher proportion of women suffering from symptoms of chronic bronchitis who used biomass fuel compared with women who used liquid petroleum gas exclusively for cooking and space heating. The incidence increased with age, increasing hours of cooking, family size and lower socioeconomic status. Another risk factor was found to be absence of a proper kitchen and cooking in living room. However this factor is still under recognized and less thoroughly investigated. Most of the data comes from population based cross-sectional studies. Few studies have been conducted on exploring risk factors for the development of COPD in patients presenting to hospital with moderate to severe symptoms. The aim of the current study was to find out risk factors among males and females presenting to a tertiary care hospital with symptoms of COPD.

METHODS

Two hundred patients aged 35 year of more coming to Akhter Saeed trust Hospital from December 2017 to March 2019 with moderate to severe symptoms with the diagnosis of COPD were recruited to the study. Patients coming to ER or OPD whether admitted or sent home with treatment were included. The diagnosis of COPD was established either with suggestive signs and symptoms and a previous diagnosis of COPD from authentic medical records. In case of absence of reliable medical records, the diagnosis was established in patients with symptoms and physical findings of examination by spirometry according to GOLD (Global initiative for Obstructive Lung Diseases) criteria. A GOLD stage II (FEV1/FVC of < 0.7 with FEV1 ≥ 50% and < 80%) with a reversibility of < 12% after inhaled bronchodilator administration was taken as diagnostic of significant COPD.

A comprehensive medical history and physical examination was performed. Specific points regarding possible risk factors included a personal history of smoking, history of pulmonary tuberculosis, history of childhood respiratory infections, a previous history of respiratory allergy or bronchial asthma, exposure to environmental tobacco smoke in non-smokers, environmental or occupation exposures to...
organic/inorganic dust or irritant gas or fumes, exposure to indoor pollution especially burning of biomass fuel (like wood, crop residue, dung cake or coal) for cooking and heating purposes and a family history of COPD. As the main target of our study was the risk factor for the development of COPD in people who have never smoked personally, the patients were divided into ever smokers and never smokers.

An ever smoker (current or former) was defined as a person who had smoked > 20 packs of cigarettes in a lifetime or > 1 cigarette/d for a year. As a significant proportion of patients used water pipe, smoking for more than one year on regular basis was considered significant. Exposure to passive cigarette smoke was defined as an affirmative answer to whether anyone (other than the patient) had smoked a cigarette, pipe, or cigar in the participant’s home on regular basis for last one year. A significant exposure to occupational pollutant was considered if they had worked ≥ 3 months in occupations known or suspected to be associated with the risk of COPD and total number of years of exposure was asked.

Baseline tests were done to find ant comorbid condition. Patients with acute respiratory illness, active pulmonary tuberculosis, other respiratory diseases like ILD, bronchiectasis and chest wall deformities, significant ischemic heart disease and advanced organ system failure like renal or hepatic disease were excluded from the study.

Statistical analysis:

Statistical analysis was done to calculate the contribution of individual risk factor for the development of COPD.

RESULTS

Patient characteristics are shown in table1. Among the 200 patients 127 (63.5%) were male and 73 (36.5%) were female. Most of the patients were from rural or suburban areas and belonged to lower socioeconomic class. Average age of the patients was 57yrs. (range 35-77yr.). Of the male patients, 92 (72%) were smokers while 35 (28%) were non-smokers, while among female patients 27 (37%) were indulged in some type of smoking (mostly water pipe) while 46 (63%) were nonsmokers. Among male nonsmokers, the most common risk factor identified was occupational exposure to organic or inorganic dust or fumes (37%) while other risk factors were family history of COPD, personal history of pulmonary tuberculosis and allergy or asthma. Less important factors included environmental tobacco smoke, indoor exposure to biomass fuel and childhood respiratory infection. No apparent risk factor was identified in one patient. In female nonsmokers, exposure to indoor biomass fuel smoke was the single most important risk factor identified in 37 (80%) of the patients. Other less important factors included family history of COPD, environmental tobacco smoke, history of tuberculosis, history of asthma and occupational exposure. There were no patients with history of childhood respiratory infection while no significant risk factor was identified in 5 (11%) of patients. Probably childhood respiratory infections are quite common but due to lack of awareness and unavailability of medical records precludes such diagnosis and maybe an important factor in at least some of the patients.

The situation was quite different in smokers in whom other risk factors were much less prominent but family history of COPD was much more common in both male and female smokers (44.5% and 43% respectively) while occupational exposure was also identified in significant number of male smokers (37%). History of pulmonary tuberculosis and childhood respiratory infections was also identified in both male and female smokers while 19 (54%) of female smokers also had significant

Table 1: Patients’ Characteristics

<table>
<thead>
<tr>
<th>Total number of patients : 200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male; No. (%)</td>
</tr>
<tr>
<td>Female; No. (%)</td>
</tr>
<tr>
<td>Age; Ave (range)</td>
</tr>
<tr>
<td>Smoking status:</td>
</tr>
<tr>
<td>Male;</td>
</tr>
<tr>
<td>Female;</td>
</tr>
</tbody>
</table>
exposure to indoor biomass fuel smoke. All the results are shown in figure 1 and 2.

**Figure 1:**
H/O; history of
F/H; family history of

**Figure 2:**
ETS; environmental tobacco smoke
H/O; history of
F/H; family history of

**DISCUSSION**

Chronic obstructive pulmonary disease (COPD) is characterized by a largely irreversible obstruction of the airways, and encompasses both emphysema and chronic bronchitis and the leading cause is abnormal inflammatory response of the lungs to harmful particles or gases such as tobacco smoke. The global burden of disease is huge and in 2002 it was the fifth leading cause of death world over. As there is an increasing trend of smoking especially among developing nations, it is projected to be the third leading cause of death in the world by 2030 unless measures are taken to control the risk factors.

The general awareness about the disease is poor and the disease is frequently under recognized. Thus under diagnosis of COPD is common and a large population based study from eleven countries of middle east and north Africa (MENA) region showed that 14.3% of people had symptoms that could be related to COPD. More than two thirds of them were not current smokers. A large proportion of nonsmokers was among females. This could be probably due to the reason that smoking for females in these countries is not socially acceptable. Under-diagnosis is especially common in women because of the perception that this is predominantly a male disease. In developing countries the situation is even worse where women remain undiagnosed despite symptomatic disease.

The previous concept that COPD is a disease of smokers is now changing and a significant number of nonsmokers are now being identified as suffering from COPD. This is one of the reasons that COPD in nonsmokers remains undiagnosed. In a large population based multicenter study conducted on 10,000 people in general public found that among people who never smoked 12.2% fulfilled the criteria for COPD and they constituted 27.7% of all COPD patients identified in this study. This is a huge burden of COPD among general population and significant numbers are due to factors other than smoking. Another important finding in this study was that more than two-thirds of never smokers with moderate to severe airway obstruction were women. The two major risk factors identified among never smoker men and women in this study were increasing age and previous history of asthma. Another factor among women never smokers was level of education and exposure to passive smoking. Every year of education among women was associated with a 6% decrease in incidence of COPD. The study showed that the incidence of COPD in never smokers is higher than previously thought and that women constitute higher proportion of COPD cases among non-smokers. Pavord et al also found that the major risk factors for COPD in nonsmokers was increasing age and female sex. They did not find a significant association with occupational exposure or passive smoking as a risk factor in these patients. Other risk factors identified in these studies were
history of childhood respiratory infections, history of tuberculosis, previous history of bronchial asthma and low body mass index (BMI). These studies which were performed mainly in developed countries did not recognize indoor exposure to biomass smoke as a risk factor and concluded that the origin of airway obstruction in non-smokers in western countries is still not well understood.4

However in developing countries the use of biomass fuel for cooking and heating purposes is much more common and there is an increasing understanding that in these countries this may an important risk factor for COPD in nonsmokers especially women. Ekici et al studied rural population in Turkey and found that women using biomass fuel were more likely to develop COPD than those using more refined fuels and the presence of acute symptoms during cooking in women in rural areas should signal to general practitioners the possibility of chronic airway disease.26 Similarly a study conducted in China comparing the risk factors in patients from rural and urban areas found that among nonsmokers with COPD from rural areas majority were women and the most important risk factor was exposure to biomass fuel and directly correlated with hours of exposure per day.22 Y. Liu et al noted that indoor air pollutant exposure varies dramatically between high-income and low-income countries, with biomass fuels (which have higher emission factors for particulate matter [PM] and other pollutants) being a much more common source of exposure in the developing world and that the body of work focusing on indoor air pollution and COPD is much smaller than that on outdoor air pollution. Several studies from developing countries like China, Papua New Guinea and Nepal, Saudi Arabia and Turkey have shown exposure to biomass fuel as a risk factor in great majority of nonsmoker women with COPD.28

Our study clearly shows biomass fuel as the risk factor for COPD in nonsmoker women from rural background. The results of this study are difficult to compare with other studies as few studies have been done with this study design. Most of the studies are population based and report incidence and risk factors for COPD in general public. Only one study from India was found to be institution based where women attending the clinic in a tertiary care hospital and its associated primary health centers were screened for symptoms and signs of COPD. However our study was based upon identification of risk factors in patients with COPD presenting to the hospital for their symptoms. Both males and females, smokers and nonsmokers were included and inquiry about possible risk factors was done.

In this study we have demonstrated that biomass fuel is definitely an important risk factor among female nonsmoker women from rural background where 80% of such women had history of significant exposure to biomass fuel smoke while 54% of smoker females also had similar exposure. On the other hand the most important risk factor for male nonsmokers was environmental/occupational exposure to irritant material (37%). Other risk factors were less important but family history of COPD was very prominent especially in smoker males and females (44.5% and 43% respectively) while it was also very significant among nonsmokers as well (31% and 28%). In the above mentioned Indian study by Vinay et al the risk of COPD was strongly associated with age at which the exposure started and total duration of exposure. They found that odds ratio for COPD was 2.9 compared to general population if exposure started at early age of less than ten years while it was 1.3 if exposure was at age 20 or more.16 The Turkish study compared incidence of COPD among nonsmoking women who were using biomass versus more refined fuel (LPG). It showed the incidence of COPD in two groups to be 28.5% vs. 13.6% respectively.26 But again the study was conducted on general public and not those with diagnosed COPD or attending the clinic for their symptoms.

A very similar study from Peshawar, Pakistan reported the incidence of signs and symptoms of chronic bronchitis in women using biomass fuel for
cooking compared to those using LPG. The incidence was 7.01% versus 2.92% in the two groups. The odds ratio was 2.51. Like the Indian study, this study also reported prominent association with hours spent in cooking and total years cooked with the prevalence of symptoms. The prevalence of bronchitis in women who had cooked for a period <10 years was 27.5%, compared to 72.5% among women who had cooked food for >10 years. Bronchitis was prevalent in 20.8% of women who spent <2 h per day cooking in the kitchen compared to 79.2% of women who spent >2 h per day cooking in the kitchen. Like our study these results also show the significance of exposure to biomass fuel smoke but again the study signs of disease were sought in at risk population unlike our study where risk factors were sought in patients with signs and symptoms of the disease.

Currently the primary healthcare facilities are poorly equipped with proper staff, diagnostic equipment and treatment for respiratory illnesses. Patient education regarding risk factor avoidance and recognition of early symptoms and seeking medical care is also poor. This leads to delayed or non-diagnosis of respiratory disease as well as poor management resulting in increased morbidity and mortality. According to a survey Amir et al. reported that currently, only about 20% of the estimated prevalent asthma and COPD cases are being identified and reported through the respective PHC network. Moreover there are not mechanisms for standardized prescription practices, patient education, follow up, recording and reporting system and monitoring and evaluation of patients. They recommend that an integrated COPD care package at primary and secondary level public health facilities in Pakistan and similar settings will be quiet helpful in achieving above goals in future. 21, 22

We conclude that biomass fuel smoke is definitely an important risk factor for the development of chronic bronchitis and emphysema especially in nonsmoker women from rural background who are actively engaged in cooking by this type of fuel. But further, larger studies are required to address this issue and to determine populations at risk and strengthen public sector healthcare facilities for early diagnosis and treatment of disease.

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CAUSES OF THROMBOCYTOPENIA IN PREGNANCY

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Abstract

Introduction: Platelet count of less than 150x10⁹/L is characterized as thrombocytopenia. It is a common finding during pregnancy. There are diverse causes of thrombocytopenia which can occur during pregnancy, each pose variable risk for mother and child. Therefore to ensure optimal management of thrombocytopenic pregnant women, an accurate diagnosis of the etiology is absolutely essential. This study will help in determination of frequency of the common causes of thrombocytopenia occurring in pregnant setting.

Objective: The objective of my study was to determine the relative frequencies of various causes of thrombocytopenia in pregnancy.

Methods: This cross sectional survey was carried out in the Department of Pathology, King Edward Medical University. Study duration was six months and 80 cases were included by non probability purposive sampling from out patient department of Lady Aitchison and Lady Willingdon Hospital, Lahore. Data was analysed using SPSS version 22.

Investigations run on blood sample of selected patients were Complete Blood count, Peripheral blood smears, Liver function tests. Bone marrow examination was carried out on patients with platelet count below 70x10⁹/l

Results: Incidental gestational thrombocytopenia was found to be the most frequent cause of thrombocytopenia, present in 66 patients (82.5%), 10 patients (12.5%) were suffering from preeclampsia and HELLP syndrome and 4 patients (5%) had immune thrombocytopenic purpura.

Conclusions: The most common cause of thrombocytopenia in pregnancy was found to be incidental gestational thrombocytopenia with preeclampsia and HELLP syndrome being the second most common cause followed by immunethrombocytopenic purpura (ITP).

KEY WORDS: Thrombocytopenia, Pregnancy, Incidental gestational thrombocytopenia, Preeclampsia, HELLP syndrome, Immune thrombocytopenic purpura.

This study focuses on relative frequency of various etiologies of thrombocytopenia in pregnancy. Thrombocytopenia is defined as platelet count of less than 150×10⁹/L.¹³⁴

The most frequent type of thrombocytopenia occurring during pregnancy is incidental gestational thrombocytopenia.² It is usually during the mid second to third trimester of pregnancy that physiological reduction in platelet count occurs.³ This fall is attributable to plasma dilution and reduced platelet production leading to physiological fall in platelet count which first becomes apparent in the mid-second to third trimester of pregnancy. Gestational thrombocytopenia is a self limiting condition and is not linked with adverse effects for either the mother or fetus.⁷ Platelet counts revert to normal usually 1 to 2 months post delivery.⁴ Platelet count falls in Preeclampsia and HELLP syndrome develops after 20 weeks of gestation. HELLP syndrome causes increased platelet consumption. Platelets are activa-
It is a diagnosis of exclusion characterized by isolated platelet count of less than \(60 \times 10^9/\text{l}\) on peripheral smear regardless of gestational age and with normal or increased number of megakaryocytes on bone marrow smears or biopsy.

**METHODS**

**SETTINGS:** We conducted this study in the Pathology department, King Edward Medical University, Lahore and all thrombocytopenic cases from Lady Aitchison and Lady Willingdon Hospital (affiliated with Mayo Hospital).

**STUDY DESIGN:** It was a cross sectional study.

**STUDY DURATION:** Study period was one year from February 2017 to March 2018.

**SAMPLE SIZE:** Sample size of 80 cases was calculated with 95% confidence level, 7% margin of error and taking expected percentage of immune thrombocytopenic purpura i.e. 11.05% (least among all causes of thrombocytopenia in pregnancy).

**SAMPLING TECHNIQUE:** Non probability purposive sampling was done.

**SELECTION OF PATIENTS:** Pregnant women with thrombocytopenia, presenting at any trimester of pregnancy were included in this study.

Pregnant women with past medical history of thrombocytopenia prior to pregnancy, according to history and previous medical records were not included in this study.

A total of 80 thrombocytopenic pregnant patients were enrolled after fulfilling the laid down inclusion and exclusion criteria. These patients were selected on the basis of thrombocytopenia. Patient were selected in the outpatient department of Lady Aitchison Hospital and Lady Willingdon Hospital (allied hospitals of the King Edward Medical University).

After telling the patients about the pros and cons of the investigations and procedure they were to undergo and taking informed consent and ensuring their confidentiality a thorough and methodical history and clinical examination of all the diagnosed
thrombocytopenic pregnant patients was carried out and their results recorded on the proforma. Investigations including Complete Blood Count, examination of peripheral smear, liver function tests, 24 hour urinary protein and bone marrow biopsy were carried out.

**DATA ANALYSIS**

The data was analysed using statistical program for social sciences (SPSS) version 22.

**RESULTS**

Eighty pregnant patients with thrombocytopenia presenting at any gestational age were selected. Enrolled patients age ranged from 17-37 years with mean age of 25.72± 3.21 years. (TABLE 1)

Gestational age was recorded in weeks and patients were broadly grouped into first, second and third trimesters. A total of seventy (88.75%) women presented during their third trimester and ten (11.25%) women presented during their second trimester with mean gestational age of 2.88 ±0.9 months. Platelet count ranged from 15×10⁹/l to 144×10⁹/l, with mean platelet count of 108.2×10⁹/l.

Out of 80 patients, 66 patients (82.5%) were cases of incidental gestational thrombocytopenia, ten (12.5%) patients suffered from preeclampsia and HELLP syndrome and four (5%) of patients were labelled as cases of immune thrombocytopenic purpura.(FIGURE 1)

**Table 1: Age Distribution of Patients Presenting with Thrombocytopenia**

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Patients with thrombocytopenia</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-20</td>
<td></td>
<td>15</td>
<td>18.75</td>
</tr>
<tr>
<td>21-24</td>
<td></td>
<td>18</td>
<td>22.5</td>
</tr>
<tr>
<td>25-28</td>
<td></td>
<td>22</td>
<td>27.5</td>
</tr>
<tr>
<td>29-32</td>
<td></td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>33-37</td>
<td></td>
<td>9</td>
<td>11.25</td>
</tr>
</tbody>
</table>

**FIGURE 1: Frequency of etiology of thrombocytopenia in pregnant patients**

Key:

- IGT: Incidental gestational thrombocytopenia
- HELLP: Hemolysis, elevated liver enzymes, low platelet count
- ITP: Immune thrombocytopenic purpuras

**DISCUSSION**

Thrombocytopenia falls second to anaemia as the second most frequent cause of haematological disorders occurring in pregnancy state. Physiological fall in platelet count occurs during pregnancy¹¹,¹².

In our study 80 pregnant patients were taken, presenting at any gestational age. Majority of these women were between 25-28 years (27.5%) similar to a study conducted by Parnas M which stated that majority of women presenting with thrombocytopenia were of similar age group (25-30 years). This small difference in age of presentation maybe attributable to delayed child bearing all over the world due to increasing trends in attaining professional goals. This advancement has been noticeable in Pakistan as well, especially in the upper middle class, as they become progressively more empowered.¹³

According to our study seventy (88.75%) women presented during their third trimester and 10 women (11.25%) presented during second trimester, with mean gestational age of 2.88. This is consistent with a study presented by Keith R. McCrae, which
stated that platelet count decreases by about 10% during third trimester in majority of the patients under study.8

Our study showed that platelet count ranged from $15 \times 10^9/l$ to $144 \times 10^9/l$, with mean platelet count of $108.2 \times 10^9/l$. According to a study conducted in China by Shen C the lower reference range for platelet count in pregnancy was $61 \times 10^9/l$. This is different from reference values of black and white women. Environmental factors, ethnic and tribal peculiarities have variously been implicated for this disparity in pregnant women in our part of the world compared to the rest.

The majority of cases of thrombocytopenia in pregnancy were found to be of incidental gestational thrombocytopenia (82.5%), secondly preeclampsia and HELLP syndrome (12.5%) followed by immune thrombocytopenic purpura (5%). Marked discrepancy is seen in similar study conducted in different parts of the world. This again is attributable to ethnic and tribal differences and environmental factors varying region to region. In a study conducted in Israel by Parnas M, frequency of incidental gestational thrombocytopenia was 59.3%, preeclampsia and HELLP syndrome was 11.05% and that of immune thrombocytopenic purpura was 11.05%. Fedirici L, in his study conducted in France stated frequency of incidental gestational thrombocytopenia (IGT) was 74%, preeclampsia and HELLP syndrome was 21% and that of immune thrombocytopenic purpura (ITP) was 4%.4,15

CONCLUSION

Pregnancy causes major physiological changes in the human body. Thrombocytopenia is one of the haematological changes. While attempting to define the cause of thrombocytopenia occurring during pregnancy, numerous immunological, metabolic and homeostatic changes associated with pregnancy should be borne in mind. Incidental gestational thrombocytopenia is the most prevalent cause of thrombocytopenia followed by preeclampsia and HELP syndrome and then Immune thrombocytopenic purpura (ITP). An adequate knowledge of the above conditions will lead to better patient management.

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Hair fall, one of the most common skin diseases, is becoming prevalent, and affecting high proportion of population in Pakistan. This problem in any age group can place psychological and emotional burden. Nowadays, young people are more concerned about their appearances and looks. Besides being a part of an individual’s appearance; hair not only gives you the sense of completeness, but also adds a lot to your personality and confidence. Therefore, any disfigurement causes anxiety and depression, loss of confidence and at the same time puts burden on the pocket. As a normal physiological process, hair are replaced continuously and fall around 100-125/day.

The problem of hair loss does not occur on its own but has association with a variety of factors, especially the general lifestyle and diverse socio-demographic conditions. Other causes include current trends of hair styling, overuse of cosmetics, hectic working schedules, stress related to studies, consumption of highly processed foods etc.

Hair fall is strongly related to the diet and health of an individual. Medical students who consume a healthy and balanced diet suffer less from this problem, while those who are careless of their eating habits or suffer from malnutrition have an increased incidence of this problem. Nowadays, the food items do not have all the nutrients in the required amount,
so people often use nutritional supplements to overcome this deficit. Hence, their use also helps in avoiding hair loss.²

For healthy hair, with less hair loss, not only the diet should have all the essential nutrients e.g. Proteins, Essential Oils, Mineral Salts (Iron, Magnesium, Calcium, Zinc, etc.), but also there should not be any underlying disease or illness affecting the growth of normal hair. In most of the cases, there is some covert pathological process going on in the body that may manifest in the form of hair loss and other associated conditions. Some disorders that may affect hair growth are Malabsorption syndrome, Thyroid gland disorders and Polycystic Ovarian Syndrome.³

Among all diseases, Polycystic Ovarian Syndrome or PCOS is the major contributory cause for hair loss and abnormal hair growth. PCOS is common in female medical students, and the number of people affected by it is drastically increasing; mainly due to consumption of sugary and oily foods, lack of routinely exercise, obesity and psychosocial stress. Often, people with PCOS present with hair loss as a major symptom, and upon investigation the underlying cause is detected.⁴,⁵

In congregation to other factors, psycho-emotional stress also plays a vital role in obstructing hair growth. It is not uncommon for people to encounter different types of stresses e.g. social, physical and emotional stresses in their daily lives. Also, sometimes, there are some traumatic instances or episodes in a person's life that may cause various changes in his bodily mechanisms, leading to certain health and skin conditions comprising of hair loss and abnormal hair growth patterns.⁶

Nutrition has a great impact on the growth and appearance of hair. Hair is composed of second fastest growing cells in the body and therefore their nutritional requirement is very high. Hair loss can arise from either excess or lack of nutrients in the diet and in some cases nutritional imbalance can alone be the cause of hair loss. One of the most common nutritional causes of hair loss includes iron deficiency. Iron is needed for many processes within the hair follicle and its deficiency can disrupt hair growth. Iron deficiency is quite prevalent in females due to improper diet.⁷,⁸

Hair loss is largely the result of genetics and hormones; however, lifestyle and environmental factors also contribute to it. Most women enjoy using different hair styling products and treatments to make a strong statement of their identities. These include straightening, curling, dyeing and countless others. Overuse of these treatments can damage the hair to the point where it starts to thin and eventually fall out. Pulling the hair tightly in a ponytail or braiding can cause thinning of hair in the temporal area. Regular oiling and frequent haircuts help to minimize the split ends and hair breakage.⁹,¹⁰

It is an established fact that smoking is bad for health but recent evidence suggests that it is bad for hair as well. Chemicals present in the cigarette impair the normal function of the hair follicles. The blood supply is also diminished which is vital for the growth of new hair. Blood flow in the follicles help to initiate and nourish new hair but if this is impaired, there will be no replacement of any loss with new growth.¹¹,¹²

Hair loss is also known to be an inheritable condition, commonly described as ‘running in the family.’ It has been suggested that genetics play a key role in alopecia. The hair loss gene can be inherited from either mother or father or both. Family history of hair loss significantly increases the risk of hair loss in children but not inevitable.¹³

The rationale of our study is to look into the factors linked with hair loss in young female students of our medical college. And give them an awareness regarding the probable risk factors associated. As noticeable hair loss is increasing alarmingly. It results in greater perception of poor body image, low self-esteem, negative emotional well being and poor quality of life.

The Objective of the study is to determine the frequency and characteristics of female pattern hair
loss, among female students of CMH Medical College Lahore, and to determine the role of different exposed factors (e.g. diet, stress, hair styling, etc.) with hair loss.

**METHODS**

Two hundred and fifty (250) female medical students of CMH Medical College were selected from each professional year using non probability convenience sampling technique for this cross sectional study. Time duration was Feb 2018- April 2018.

Questionnaire comprised of only closed ended questions. Which were handed out to 50 female students from each year after seeking verbal consent from them. Participation was not mandatory and an assurance of confidentiality was provided to encourage participation. The questionnaire consisted of questions regarding the pattern of hair loss, diet, medical history, lifestyle and hormonal disorders.

Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 20.0. IBM SPSS Statistics for window, version 20.0. Armonk. NY:IBM Corps:2011. Descriptive statistics for qualitative data were calculated in the form of frequencies and percentages, whereas descriptive statistics for quantitative data were calculated in the form of mean and standard deviation. Chi-square test of significance was used to see association if any between the variables of interest and hair loss in female students. For all purposes, a p-value < 0.05 was considered as the criteria of significance.

**RESULTS**

A sample population of 250 subjects participated in the study. The minimum age of the subject was 17 years and the maximum age was 26 years. The minimum age at which the subjects started having hair loss was 12 years and the maximum was 18 years. [Table 1]

One of the factors investigated was family history. Among the subjects who had a positive family history; 40% had hair loss while 6% did not. However, 40% of the subjects with a negative family history had hair loss while 14% did not. Statistical analysis also showed it to be significant as the p-value = 0.011 [Figure # 1].

The next factor studied was nutritional deficiency. Out of 250 female students, 27.2% of the subjects had nutritional deficiency as well as hair loss while 3.6% of subjects with nutritional deficiency did not have hair loss. Fifty two point eight percent (52.8%) of the subjects did not have nutritional deficiency but had hair loss while 16.4% did not.

The effect of PCOS on hair loss was also explored. Out of 250 students, 11.2% of them with this underlying pathology suffered hair loss while 6.8% were spared. From the subjects who did not have this problem, 68.8% had hair loss in comparison to 13.2% who did not [Table # 2].

Another factor affecting hair loss was stress. Thirty eight percent (38%) of the subjects who were undergoing stress also had hair loss while 60% did not. Among the subjects who did not have stress, 42% had hair loss while 14% did not have this problem.

The relation between hair loss and consumption of junk food was also checked. Fifty four point four (54.4%) of the participants who were regularly consuming junk food had hair loss while 12% did not have the problem. Among those who did not consume junk food; 25.6% of had hair loss in comparison to 8% who did not. Although the statis-
tical analysis confirmed it to be insignificant as the p-value = 0.284 [Figure # 2].

**Figure 2: Relationship between Junk Food Consumption and Hair Loss.**

The link between the hair loss and smoking was the next parameter examined. Three point six percent (3.6%) of the smokers had hair loss while 7.6% did not whereas 76.4% of the non-smokers had hair loss in contrast to 12.4%.

Another factor inquired about was use of hair styling products. Fifty two percent (52%) of the subjects who regularly use such products had hair fall while 10.4% did not have the problem.

Among the females who did not use the products, 28% of them experienced hair fall whereas 9.6% were spared [Table # 2].

**DISCUSSION**

Hair fall also known as alopecia is one of the major problems faced by female medical students in the present era. There are numerous factors contributing to the manifestation of the hair loss. According to our study, malnutrition has numerous influences on hair loss. Medical students usually spend a lot of time for hospital work during the period of their medical studies, and many of them live in dormitory in which the quality of the provided food is poor. The use of dietary supplements has also arisen due to this. Therefore, they tend to have multiple nutritional deficiencies and its significance is also shown in our results. In comparison to another study conducted on the medical interns of Tehran University, 23.4% of the females took dietary supplements to combat hair loss.2

Until recently, the popular notion that psycho-emotional stress can have an impact on hair growth has been treated with skepticism; and yet it has long been appreciated that episodes of alopecia have occurred after severely stressful life events. The female medical students also are not immune to it as shown by our study.6

The findings of our research confirm an association between alopecia and PCOS as the p-value<0.05 (0.001). There’s a rising incidence that most women who present with hair loss as their primary complaint also have PCOS and other underlying hormonal disorders.4

Hair plays a significant role in expressing any person’s psychosocial status and many cosmetic and styling methods are available nowadays to do so. Pulling hair tightly in a ponytail can cause some hair loss, especially in the temple area. It has been suggested lately that the use of chemical and heat straightening of hair can weaken the hair leading to balding and thinning and this has been proven by our results too. According to our research, 52% of the female students who regularly used hair straighteners experienced hair loss in comparison to 9.6% who did not. In a review of 19 studies by the resear-
chers at Johns Hopkins, they say that they can confirm a “strong association” between certain scalp-pulling hairstyles — many common among African-Americans — and the development of traction alopecia.\textsuperscript{14}

The genetic basis of alopecia is well accepted in the medical community and among the general population. Our research shows a significant correlation between hair loss and positive family history as the p-value=0.011. In a separate study carried out in United States, it was found that men whose fathers had hair loss were 2.5 times as likely to have had some level of hair loss compared to men whose fathers did not. The probability of hair loss in a person is dependent on genetics as well as their lifestyle.\textsuperscript{15} Thirty percent of our subjects were undergoing stress and had hair loss, this is consistent with a study done in adolescents in Pakistan.\textsuperscript{16}

Some of the limitations of this study were that firstly, this is not an in-depth research and only covers the female student population of CMH College. The questionnaire and research did not cover all the content that should ideally be considered. There should be more researches which cover larger sample of the population so that the results can be generalized.

All the results published here, are mentioned after the taking ethical permission and approval from the college review board.

CONCLUSION

It is concluded from our findings that; multiple factors like disturbed eating habits, use of hair styling products, familial history, hormonal imbalance etc is responsible for hair loss in female medical students. Increased rate of hair loss among young female students shows that the problem is on a rise in young generation which needs to be investigated more deeply by planning more detailed studies.

REFERENCES


Teenage pregnancy is an important health issue for several reasons, e.g. there are health risks for baby as well as to the mother. Children born to teenage mothers are likely to suffer health, social and emotional problems than children born to older mothers. Besides, mortality rate of this vulnerable group is 5 times higher than adult pregnancies, it is the need of hour to address this grave challenge and to explore the knowledge, attitude and behaviors towards early marriages and early childbearing. 1

Death of mother during pregnancy and childbirth related complications is the leading cause of mortality in adolescent age group worldwide and it is doubled in teenage group as compared to mature group >20 years. 3

WHO defines adolescence as a period between 11-19 yrs and pregnancy in this duration is called as teenage pregnancy. Incidence of teenage pregnancy varies greatly in developing and developed countries due to social and cultural differences, early marriages and their awareness about contraception. According to WHO data, it was about 16/1000 population in Myanmar, highest worldwide 143/1000 in sub-Saharan African counties, 2.9/1000 in south Korea. 4,5

Teenage is a very important period of life when all the psychological, emotional and physiological

Abstract

Background: Mothers in extremes of ages face complicated pregnancies. Adolescent age pregnancy is almost always associated with risks. Pakistan being 6th most populated country worldwide has a large burden of dealing with this vulnerable group, because of social reasons and local customs of early marriages leading to complicated pregnancies in teenage girls.

Objectives: To study the Fetomaternal outcome in adolescent pregnancies

Methods: This study was conducted in teenage pregnant women of age < 20 years, regardless of their booking status. All women admitted at Jinnah hospital with any complaint, all gestational ages in a period of one year. Their detailed history, examination, investigations and fetal and maternal outcome was noted on a proforma.

Results: During study 218 adolescent women were delivered. Mean age was 18.2 years. 17% women were metric or above level of education, 60% cases were primary level and 23% were illiterate. 127 cases were from rural areas and 91 cases were from urban areas. Contraceptive awareness was lacking only 86 teen girls had awareness and 132 cases had no contraceptive knowledge. Teen women had higher chances of operative delivery 48.2% and 44% had uncomplicated vaginal deliveries. Anemia, Hypertensive disorders and pre PROM with associated preterm delivery were the main maternal complications observed. Main fetal complications were the need for neonatal nursery admissions, Low birth weight, preterm labor and early neonatal death.

Conclusion: Pregnancy in Adolescent age are at high risk of developing Miscarriages, anemia, preeclampsia, eclampsia, increased need for operative delivery and poor fetal outcomes i.e. IUGR, preterm labor, PROM, Low birth weight, and need for NNICU admissions.

It is important to prevent teen age pregnancies by creating contraceptive awareness, sex education and ensuring availability of contraception at doorstep.

Key words: Adolescent pregnancy, pregnancy outcome, fetomaternal complications
changes take place in a human being, who becomes more responsible and adopts adulthood and feels herself as an important member of society. Side by side sexual maturation is also taking place as she is going through the process of biological maturation. And this is the crucial age in which one realizes that she is an independent decision maker for her own life. Adolescent pregnancy is the most high risk social and public health issue with different prevalence in different part of developed and developing world with different literacy rates, social, economic and cultural trends. Psychological reasons and personal behaviors of women also do matters. Teen pregnancy rates are rising and being considered as serious health issue to be addressed both in developed and developing world, as it is associated with life threatening maternal and fetal complications leading to huge burden on maternal child health care providers and health system.

Miscarriages, anemias, hypertensive disorders IUGR, low birth weight, perinatal deaths and need for neonatal admissions in nursery and ICU related to preterm births. Skeletal growth is in developing stage leading to immature development of pelvis which in turns leads to inadequate pelvis for vaginal birth and need for operative delivery and increased C section rate. As these girls are in growing phase of their life they are more prone to have malnutrition, anemia and its long term fetomaternal effects.

Trends of childhood marriages were very common in Pakistan and these teen girls were expected to get pregnant soon after they get marry as a social proof of their fertility and achieving their planned family size early, and even family size is to decided by senior family members of partner. In last two decades much improvement in health services and contraceptive awareness, trends are improving to some extent.

According to PDHS, Pakistan Demographic and Health Survey 40% of women get marry by the age of 18 years. However the proportion of teen agers who have begun childbearing is dropped about 16% in 1990-91 to 9% in 2007 and further reduced in recent survey to 8 %,6 according to PDHS survey 2017-18.

6% of teenage mothers had live births and 2% were pregnant at the time of survey. In KPK 15% of teenagers had started childbearing, but as compared to that it was 6% in Punjab.

METHODS

This study was conducted in teenage mothers from 15-19 years of age in a period of one year Feb 2018 to Feb 2019 in gynae department of Jinnah hospital Lahore. Regardless of their booking status all booked and unbooked adolescent girls were admitted in pregnancy at all gestational ages. Their detailed history, regarding age, parity, age of mother or sister at their first pregnancy, contraceptive awareness, their educational status, area of their residence was taken on a proforma and fetomaternal outcome was evaluated accordingly.

RESULTS

Table 1: Demographic and Clinical Characteristics of Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
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<td></td>
<td></td>
</tr>
<tr>
<td>15 - 17 years</td>
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</tr>
<tr>
<td>17 - 19 years</td>
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<td>90.4</td>
</tr>
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<td></td>
</tr>
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<td>Primi Gravida</td>
<td>162</td>
<td>74.3</td>
</tr>
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<td>47</td>
<td>21.6</td>
</tr>
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<td>P2</td>
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<td>4.1</td>
</tr>
<tr>
<td>Education</td>
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<td>32.6</td>
</tr>
<tr>
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</tr>
<tr>
<td>Matric&amp;Above</td>
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<td>17.9</td>
</tr>
<tr>
<td>Contraceptive Awareness</td>
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<td></td>
</tr>
<tr>
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<td>86</td>
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</tr>
<tr>
<td>15 - 16 years</td>
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<td>11.9</td>
</tr>
<tr>
<td>17 years and above</td>
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</tr>
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<td>ESC</td>
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<tr>
<td>Laprotomy</td>
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<td>9</td>
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<tr>
<td>Residential Status</td>
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Table 2: Maternal Outcome among Subjects

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<td>Anemia</td>
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<td>64</td>
<td>29.4%</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>154</td>
<td>70.6%</td>
</tr>
<tr>
<td>Eclampsia</td>
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<td>11</td>
<td>5.0%</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>207</td>
<td>95.0%</td>
</tr>
<tr>
<td>Pre eclampsia</td>
<td>Yes</td>
<td>11</td>
<td>5.0%</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>207</td>
<td>95.0%</td>
</tr>
<tr>
<td>PIH</td>
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<td>23</td>
<td>10.6%</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>195</td>
<td>89.4%</td>
</tr>
<tr>
<td>Placenta Previa</td>
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<td>3</td>
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</tr>
<tr>
<td></td>
<td>No</td>
<td>215</td>
<td>98.6%</td>
</tr>
<tr>
<td>Ectopic Pregnancy</td>
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<td>37</td>
<td>17.0%</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>181</td>
<td>83.0%</td>
</tr>
<tr>
<td>PROM</td>
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<td>8</td>
<td>3.7%</td>
</tr>
<tr>
<td></td>
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Table 3: Maternal Outcome and Age Cross Tabulation

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<th>P-value</th>
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<td>17 - 19 years</td>
<td></td>
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<tr>
<td>Anemia</td>
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<td>7.8%</td>
<td>59</td>
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<td></td>
<td>No</td>
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<tr>
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<td>1.4%</td>
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<td>90.9%</td>
</tr>
<tr>
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<td>187</td>
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<tr>
<td>Pre eclampsia</td>
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<td>72.7%</td>
</tr>
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<td>91.3%</td>
</tr>
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<td>5.7%</td>
<td>13.0%</td>
<td>87.0%</td>
</tr>
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<td></td>
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<td>25.9%</td>
<td>177</td>
<td>90.8%</td>
</tr>
<tr>
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<td>0%</td>
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<td>100.0%</td>
</tr>
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<tr>
<td>Ectopic pregnancy</td>
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<td>33.3%</td>
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<td>5.4%</td>
<td>96.6%</td>
</tr>
<tr>
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<td>29.3%</td>
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</tr>
<tr>
<td>Misscarriage</td>
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<td>37.5%</td>
<td>62.5%</td>
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<td>86.0%</td>
<td>91.4%</td>
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</table>

Table 4: Fetal Outcome

<table>
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<th>Fetal outcome</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive and healthy</td>
<td>156</td>
<td>71.6%</td>
</tr>
<tr>
<td>Need of neonatal nursery admission</td>
<td>27</td>
<td>12.4%</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>6</td>
<td>2.8%</td>
</tr>
<tr>
<td>Still birth</td>
<td>3</td>
<td>1.4%</td>
</tr>
<tr>
<td>IUGR</td>
<td>5</td>
<td>2.3%</td>
</tr>
<tr>
<td>Fetal anomalies</td>
<td>1</td>
<td>.5%</td>
</tr>
<tr>
<td>Preterm</td>
<td>3</td>
<td>1.4%</td>
</tr>
<tr>
<td>ENND</td>
<td>6</td>
<td>2.8%</td>
</tr>
<tr>
<td>RDS</td>
<td>3</td>
<td>1.4%</td>
</tr>
<tr>
<td>Miscarriage</td>
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<td>3.7%</td>
</tr>
<tr>
<td>Total</td>
<td>218</td>
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</tr>
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Table 5: Fetal Outcome and Age Cross Tabulation

<table>
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<tr>
<th>Fetal outcome</th>
<th>Age</th>
<th>Count</th>
<th>Row N %</th>
<th>Chi-square</th>
<th>P-value</th>
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</thead>
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<td>15 - 17 years</td>
<td>17 - 19 years</td>
<td></td>
<td></td>
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<tr>
<td>Alive and healthy</td>
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<td>71.4%</td>
<td>92.2%</td>
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<td>90.9%</td>
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<tr>
<td>Neonatal nursery admission</td>
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<td>10.0%</td>
<td>1.000</td>
</tr>
<tr>
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<td>90.9%</td>
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<tr>
<td>Low birth weight</td>
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<td>0.0%</td>
<td>0.0%</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6</td>
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<td>90.9%</td>
<td></td>
</tr>
<tr>
<td>Still birth</td>
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<td>0.0%</td>
<td>0.0%</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
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<td>3</td>
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<td>90.9%</td>
<td></td>
</tr>
<tr>
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<td>1.0%</td>
<td>.023</td>
</tr>
<tr>
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</tr>
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<td></td>
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<tr>
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<td>1.000</td>
</tr>
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<td>1.5%</td>
<td>90.9%</td>
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<tr>
<td>ENND</td>
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<td>4.8%</td>
<td>1.0%</td>
<td>.023</td>
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<td>90.9%</td>
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<td>1.000</td>
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<td>.006</td>
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Table 6: Distribution of Cases according to Contraceptive Awareness

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<th>Contraceptive Awareness</th>
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<td>Primary</td>
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<tr>
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<tr>
<td>Matric &amp; Above</td>
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<td>21</td>
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<tr>
<td>Total</td>
<td>86</td>
<td>132</td>
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</table>

X² = 6.748 P = .080
During the study period, 218 pregnant adolescent age women were delivered. Annual delivery rate at our unit was approximately 4735/annum in year 2018 giving a frequency of 4.6% of teen pregnancies. Mean age was found 18.2 years. Regarding their parity status, 162 (74.3%) cases were in their first pregnancy, 47 cases (21.6%) were in their second pregnancy. 9 teen age mothers were having their 3rd baby before 20 years of age (Table 1).

Well educated mothers are always having anticipated better pregnancy outcome. Only 17% cases were having educational status of metric or above qualification, 127 cases were having middle or below primary education. 23% (n=52) cases were illiterate. Majority of teen age mothers (n=127) were from rural areas and 91 cases were from urban areas (Table 1).

86 cases were having a of bit awareness about contraception, 132 were having no information at all about any method for avoiding and planning a pregnancy (Table 1). Educational status of adolescent mothers was not found statistically significant (P-value 0.080) Table 6. 71 cases were having their primary education out of which 38 were not aware of any method of contraception. 39 cases were matric or above level education but surprisingly 21 out these were unaware of planning a pregnancy.

Age of mother and sister in their first pregnancy was also an interesting element in our study, all of our cases were having a positive history of early marriages trends in their families. 83% of teen mothers had mothers or sisters having first pregnancy at 17-19 years and 17% of cases had history of early pregnancy before the age 16 years (Figure 2).

44.5% (n=97) delivered by uncomplicated vaginal deliveries and 105 cases (48.2%) had their caesarean section due to some obstetrical indication, mainly failure to progress of labour and Cephalopelvic disproportion. 6 cases required instrumental delivery, 3 had laparotomy due to ectopic pregnancy and 8 cases underwent evacuation and curettage due to miscarriage (Table 1).

Anemia was the main complication observed in teen pregnant women contributing 64 cases (29.4%) and 154 cases (70%) cases were not anemic (Table 2).

Second commonest complication in our study was found to be hypertensive disorders of pregnancy contributing a total of 45 cases, n=23 were of pregnancy induced hypertension=11 cases were Eclampsia, 11 cases were pre eclampsia (Table 2).

Third common complication observed, was pre mature rupture of membranes with risk of preterm delivery either spontaneous or induced. About 37 cases (17%) had PRE PROM.

3.7% cases (n=8) had miscarriage and underwent Evacuation & curettage, (P-value 0.006) significant. Lastly 3 cases had low lying placenta and need for caesarean section. 3 cases undergone laparotomy for ectopic pregnancy. (P value 0.001) which is statistically significant (Table 3). There was no maternal death observed in 218 cases studied for teen pregnancy outcome.

Fetal outcome as a whole was found satisfactory with majority of newborns n=156 were born alive and healthy without any significant birth related complication. Out of 62 babies with one or
other adverse fetal outcome, 27 cases (12.4%) had a need for neonatal nursery admission for observation and required necessary treatment. 6 newborns were of low birth weight and 6 early neonatal deaths were reported. 2.3% cases (n=5) were labelled as IUGR due to associated maternal hypertensive disorders. 1 anomalous baby had expulsion and 8 cases ended up in miscarriages (Table 4).

In those 62 Fetuses with adverse outcome, main complication 43% cases had a need for nursery admission, followed by miscarriages 12%, Low birth weight 9.7%, ENND 9.7%, and IUGR 8% (Figure 1).

DISCUSSION

Our study shows incidence of teen pregnancy around 4.6% which is close to study of Rashmi, L.7, because sample size was almost same and exclusive of unmarried pregnancies and illegal miscarriages, and its very common for unmarried teen pregnancies to get terminations 5.

Anemia, hypertensive diseases of pregnancy and prematurity were the main complications observed in our study which is close to results of pun and Chauhan.8,9

Most of our cases (n=127) were from rural areas in which literacy rate is low and contraceptive prevalence is also very low which is in accordance to results of most studies.10,11,12

Most of neonates were healthy 72.6%, and 12.4% babies needed nursery admission and miscarriages were 3.7%. Low birth weight and ENND was reported in 2.8% cases, and p value was not significant (0.835), which is contradictory to other studies.13,14,15

Most of the teen age women are accompanied by their elders and parents and are in good health and are well supported socially, nutritionally and financially with best of prenatal and natal care by the whole family awaiting for healthy newborn in their family, similar to some studies16,17. Studies by Chen XK 2007, risk of congenital anomalies was high which could be due to physical, mental stress which can be explained by marital status, drug abuse and unemployment18 but it was not seen in our study because of cultural and religious reasons.

Risk of operative delivery is higher in teen age pregnancies which is close to the results of study by Tufail A.19

Skeletal growth is in developing stage leading to underdeveloped pelvises which in turns being inadequate for vaginal delivery, ending up in increased caesarean rate and in growing phase of life these girls are more prone to have malnutrition, anemia and its related morbidity in both mother and the fetus.

Proper booking and antenatal care and monitoring throughout in pregnancy by the health care providers at both primary, secondary levels will make a big difference in the outcome of such high risk groups of pregnancies. Recent studies show more unmarried girls with accidental pregnancies seeking illegal abortions under septic conditions and ultimately serious morbidity and mortality.

Contraceptive awareness, guidance and sex education in this group of women will definitely improve the current scenario.20,21 In country like Pakistan first pregnancy is always welcoming, happy and wanted pregnancy and the family is very much concerned for the arrival of newborn and extraordinary care is provided to young girls by caretakers and are always accompanied by some senior member of family with anticipated better outcome in this vulnerable age.22 In countries like Sri Lanka delayed age at marriage, more attendance in schools by girls, higher literacy rate, situation is different and number of adolescent pregnancy is less as compared to Pakistan, India and Bangladesh.23

CONCLUSIONS

Teen age mother is always at risk of poor fetal and maternal outcome, and most of adolescent mothers were having family history of early marriages and early age first pregnancy.

Suggestions:
Although, Adolescent pregnancy is at risk of
developing poor fetomaternal outcome as in many studies but with proper booking prenatal, antenatal and natal care, anticipated obstetric outcome is good as these women are young ,having full family support in our area. Empowering the community generally and women particularly by increasing health education trials and role of social media will play a lot of contribution for improved outcomes.

Limitation:
As it was a hospital based study so did not cover the true reflection of current community situation, and another limitation was the socioeconomic status of patients presenting to tertiary care was somewhat better than the patients presenting at primary and secondary health care.

REFERENCES
Learning disability is a classification that includes several areas of functioning in which a person has difficulty learning in a typical manner, usually caused by an unknown factor or factors. Given the "difficulty learning in a typical manner", this does not exclude the ability to learn in a different manner. Therefore, some people can be more accurately described as having a "Learning Difference", thus avoiding any misconception of being disabled with a lack of ability to learn and possible negative stereotyping.

People with learning and physical disabilities require special attention and nursing care during hospitalization. The situation of people with learning disabilities in hospital is characterized by communication barriers between patients and health care professionals. Furthermore, the emotional situation of patients has to be emphasized. In the foreign environment of a hospital, they suffer from fear and uncertainty.

Depression is one of the most frequent psychiatric disorders in adults with intellectual disability. The point prevalence of depression among adults with intellectual disability is estimated to be 4%. It is estimated that world-wide up to 20% of children suffer from debilitating mental illness. Living with such children can be very stressful for caregivers in the family. Therefore, determination of challenges of living with these children is important in the process of finding ways to help or support caregivers to provide proper care for their children.

Rationale of this study is to determine the frequency of depression in caregivers of patients with learning disability.
frequency of depression in caregivers of patients with learning disability. Literature has showed that the frequency of depression among caregivers of patients with learning disability is high. But, in a developing country like Pakistan, the evidence regarding extent of depression among caregivers of patients with learning disability is not available. So we want to conduct this study to get local evidence. So that in future we may be able to recommend the screening of depression among caregivers of patients with learning disability. So that they may be screened earlier and can be counseled to relieve them from depression and they can be stable to take care of their disabled relative. This will help us to obtained magnitude and extent of problem in local population.

**OBJECTIVE**

To determine the frequency of depression in caregivers of patients with learning disability

**METHODS**

**Study Design:** Cross sectional study

**Setting:** Department of Psychiatry, Jinnah Hospital, Lahore

**Duration:** 6 months i.e. from 5th September 2017 till 5th March 2018

**Sample Size:** Sample size of 100 caregivers was calculated with 95% confidence level, 10% margin of error and taking expected percentage of depression i.e. 56.7% among caregivers of learning disability.

**Sampling Technique:** Non-probability consecutive sampling.

**Sample Selection:**

**Inclusion Criteria:** Caregivers of age 18-60 years of either gender presenting with patients of learning disability (defined as a condition giving rise to difficulties in acquiring knowledge and skills to the level expected of those of the same age, especially when not associated with a physical handicap by using Wechsler Individual Achievement Test - second edition. Score<40 was considered as learning disability)

**Exclusion Criteria:** Caregivers with history of psychiatric disorder before being a caregiver, professional care giver (females or male nurse)

**Data Collection Procedure:** 100 caregivers fulfilled the selection criteria were enrolled in the study through OPD of Department of Psychiatry, Jinnah Hospital Lahore. Informed consent was obtained. The demographic data including name, age, sex, education level, socioeconomic status, relation with disable person and duration of taking care were noted. Then caregivers were assessed by using HADS scoring system by researcher himself. If HADS score was >11, then depression was labeled. The caregivers who found to have depression were given standard treatment as per hospital protocol. All this information was recorded through proforma (attached).

**Data Analysis:** Data was entered and analyzed through SPSS version 21. The quantitative variables like age, and duration of taking care were presented as mean and SD. The qualitative variables like gender, relation with disable person, education level of caregiver, socioeconomic status and depression were presented as frequency and percentage.

**RESULTS**

The mean age of caregivers was 38.99±11.31 years. There were 35 (35%) males and 65 (65%) females. The male-to-female ratio was 1:1.9. In the study, 41 (41%) caregivers belonged to low SES, 30 (30%) caregivers belonged to middle class while 29 (29%) caregivers belonged to high SES class. In the study, 31 (31%) caregivers were illiterate, 38 (38%) caregivers were matric pass or has less education while 31(31 %) caregivers were matric pass or has less education while 31(31 %) caregivers had education up to graduation or high. In this study, 10(10%) were father who were taking care of disable patient, 25 (25%) were mothers, 15 (15%) were son, 26 (26%) daughters, 14 (14%) were sisters and 10(10%) brothers who were taking care of disable patients. The mean duration of taking care was 6.65±4.63 years. In this study, the mean HADS score of caregivers was 14.19±5.60.

Table 1
There were 66 (66%) caregivers who had depression while 34 (34%) did not had depression as per HADS scoring system. Fig 1

**Table 1: Characteristics of Caregivers**

<table>
<thead>
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<tr>
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<td>Brother</td>
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<td>Duration (years)</td>
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<td></td>
</tr>
<tr>
<td>HADS score</td>
<td>14.19±5.60</td>
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</tbody>
</table>

In our study, the mean HADS score of caregivers was 14.19±5.60. There were 66 (66%) caregivers who had depression while 34 (34%) did not had depression as per HADS scoring system.

One study showed that frequency of depression among caregivers of patients with learning disability was found to be 56.7%. Another study showed that frequency of depression among caregivers of patients with learning disability was found to be 79%. Numerous studies have demonstrated that family caregivers of patients with a severe mental illness suffer from mental distress (especially depression, insomnia, anxiety, somatization, paranoia and obsessive behavior); and often receive inadequate assistance from mental health professionals. Research conducted in British (1992) reported that psychological distress (anxiety, depression, and insomnia) was twice as high as in the general population.

Other findings conducted in Latin America and KSA Arab country suggest that 40% of the caregivers compared to 13%-18% of general population and 23.33% of the caregivers group versus 3.33% of the control group met the criterion for being at risk of depression for the CES-D 10 scale as they got 10 or greater score respectively. Another study in Nigeria on caregivers of psychiatric out patients reveals almost half of the relatives had psychological distress (43.8%).

The literature consistently demonstrates that the mental distress of caregivers have been linked to objective burden, subjective burden, insufficient social support, age of patient, negative coping mechanism, real stigma, as well as secondary stressors such as finances and family conflict. Generally burden of family caregivers leads to negative consequences not only for themselves but also for patients, other family members, and health care systems. Their negative quality of life has impacted on poor caring, mistreatment or behaving violently to the patients which can cause patients relapse.

Burden of family caregivers also causes family conflict and financial problem in individual, family,
health care system, distorts the entire family functioning and the families under great stress would give up and reject the mentally ill individuals who would become outcasts socially. Furthermore, as conceptual models of care giving and health suggest that health effects should unfold in a cascading fashion. Caregivers first experience distress and depression, which are followed by physiologic changes and impaired health habits that ultimately lead to illness and possibly to death. However these impacts might be different among caregivers, as the level of burden is related to various factors.

CONCLUSION

Thus it has been concluded that the chances of depression is high among caregivers of patients having learning disability. In a developing country like Pakistan, the evidence regarding extent of depression among caregivers of patients with learning disability was missing. Now we have got the evidence to apply in local setting and screen caregivers of patients of learning disability. So that they may be screened earlier and can be counseled to relieve them from depression and they can be stable to take care of their disabled relative.

REFERENCES

Iron deficiency and iron deficiency anemia are the very common health related problems in all communities throughout world. Among children, iron deficiency anemia is 3-7% prevalent, with as high as mentioned upto 26%. In initial moments after birth, infant takes a significant blood volume from placenta. Delayed umbilical cord clamping steadily improves the blood indices and iron body stores of the neonate in contrast to early clamping of cord.

Objective: To compare mean hemoglobin and hematocrit in early and delayed umbilical cord clamping.

Subjects and Methods: Randomized control trial was done in Department of Obstetrics & Gynecology, Allied hospital. The total sample of 60 pregnant females of age between 25-35 years at term (gestational age 37-40 weeks) were enrolled in the study. All the females were haphazardly categorized into two groups. In group A of the neonates, early cord clamping (cord was clamped after 10 seconds of birth) and in group B delayed/late cord clamping (cord was clamped after 3 minutes of birth) were applied. After collection, all the data was entered on a pre-designed Performa. Data was analyzes using SPSS Version 21.0. Independent sample t-test was utilized to compare hemoglobin and hematocrit in both groups. The statistically significant p-values will be that were less than 0.05.

Results: Mean patient's age was 30.38±3.1 years. Mean hemoglobin level was 15.18±0.87g/dl in ECC and 17.05±0.9g/dl in DCC group (p-value=0.0001). Mean hematocrit level was 48.77±3.28 in ECC and 55.87±4.28 in DCC group (p-value=0.0001).

Conclusion: Delayed cord clamping is better than early clamping as it increases the hemoglobin and hematocrit level in neonates.

Key Words: Umbilical cord, hemoglobin, hematocrit, infant, placenta
delayed cord clamping has an inconsistent association with hyperbilirubinemia, polycythemia, and phototherapy requirements.\textsuperscript{4}

According to World Health Organization (WHO) findings, approximately 30.2\% of child-bane age women and 42.0\% of pregnant women are anemic. This condition is associated to the risk of low birth weight, fetal prematurity, inferior Apgar scores, low fetal ferritin concentrations and iron deficiency related anemia in childhood.\textsuperscript{5}

This contrasts with some earlier literature, as an example, Lanzkowsky and colleagues revealed in 1961 that maternal anemia has no effect on infant anemia.\textsuperscript{6}

A study performed on infants in USA, from their birth till 12 months proved that infants preserved their iron status over the time.\textsuperscript{7}

Miscellaneous studies have recognized that delaying clamping of cord at birth results more hemoglobin/hematocrit, which lasts up to four to six months of age.\textsuperscript{8} On average, hemoglobin gain was between 2–3 g/dl. In a second study, the serum ferritin concentrations persisted higher until 6 months in neonates of late clamping group: where mean gain was 11.8 µg/L with a range of 4.07 to 19.53µg/L.\textsuperscript{9}

In 1762 neonates meta-analysis, a considerably higher risk of neonatal jaundice and more phototherapy requirements were observed in group with delayed clamping of cord.\textsuperscript{10}

Rationale of my study is to may prove that delayed clamping of cord is beneficial to newborn in terms of increasing the hematocrit, hemoglobin, and iron levels in infants when compared to early clamping of cord. No local data is available.

**METHODS**

Randomized control trial was done in Department of Obstetrics & Gynecology, Allied hospital. The total sample of 60 pregnant females of age between 25-35 years at term (gestational age 37-40 weeks) were enrolled in the study. All the females were haphazardly categorized into two groups. In group A of the neonates, early cord clamping (cord was clamped after 10 seconds of birth) and in group B delayed/late cord clamping (cord was clamped after 3 minutes of birth) were applied. After collection, all the data was entered on a pre-designed Performa. Data was analyzes using SPSS Version 21.0. Independent sample t-test was utilized to compare hemoglobin and hematocrit in both groups. The statistically significant p-values will be that were less than 0.05.

**RESULTS**

60 pregnant females who were at term were involved in the study. Randomly 30 females were undergone early clamping of cord (Group A) and other 30 females were undergone delayed cord clamping (Group B).

Out of 60 patients, mean patient’s age was 30.38±3.1 years. And mean gestational age was 38.22±1.09 weeks. (Table # 1).

In group A, mean patient’s age was 30.53±3.13 years and mean gestational age was 38.33±1.18 weeks Similarly in group B, mean patient’s age was 30.23±3.11 years and mean gestational age was 38.1±0.99 weeks. (Table # 2).

In group A, mean hemoglobin was 15.18±0.87 g/dl and in group B, it was 17.05±0.9 g/dl. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. In group A, mean haematocrit was 48.77±3.28 and in group B, it was 55.87±4.28. There is a difference between two groups which is also statistically significant with p-value of 0.0001 (Table # 3).

Females having age < 30 years, in group A, mean hemoglobin was 14.87±0.78 g/dl and in group B, it was 17.05±0.9 g/dl. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. In group A, mean haematocrit was 48.77±3.28 and in group B, it was 55.87±4.28. There is a difference between two groups which is also statistically significant with p-value of 0.0001 (Table # 3).

In group A, mean hemoglobin was 15.18±0.87 g/dl and in group B, it was 17.05±0.9 g/dl. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. In group A, mean haematocrit was 47.63±2.7 and in group B, it was 55.99±3.96. There is a difference between two groups which is also statistically significant with a p-value of 0.0001 (Table # 4).

Females having age > 30 years, in group A,
mean hemoglobin was 15.44±0.88 g/dl and in group B, it was 16.93±0.92 g/dl. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. In group A, mean haematocrit was 49.76±3.5 and in group B, it was 55.71±4.8. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. (Table # 4).

Females having gestational age between 37-38 weeks, in group A, mean hemoglobin was 15.18±0.68 g/dl and in group B, it was 17.06±1.02 g/dl. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. In group A, mean haematocrit was 48.77±3.28 while in delayed clamping group, it was 17.05±0.9 g/dl (p-value = 0.0001). Similarly, in early clamping group, mean hematocrit was 47.63±2.7 and in delayed clamping group, it was 17.14±0.9 g/dl (p-value = 0.0001). (Table # 4).

Females having gestational age between 39-40 weeks, in group A, mean hemoglobin was 15.18±0.68 g/dl and in group B, it was 17.06±1.02 g/dl. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. In group A, mean haematocrit was 48.75±2.79 and in group B, it was 56.84±4.5. There is a difference between two groups which is also statistically significant with a p-value of 0.0001. (Table # 4).

**DISCUSSION**

Since a very long time ago, humans are using this modality called umbilical cord clamping. It is categorized into two types. One is early cord clamping (ECC) which means clamping of cord within 10 seconds after birth. Second is delayed cord clamping (DCC) which means clamping in 30-180 seconds after delivery.15

The results of my study revealed mean patient’s age was 30.38±3.1 years and mean gestational age was 38.22±1.09 weeks. In early cord clamping group, mean hemoglobin was 15.18±0.87 g/dl while in delayed clamping group, it was 17.05±0.9 g/dl (p-value = 0.0001). Similarly, in early clamping group, mean hematocrit was 48.77±3.28 while in delayed group, it was 55.78±4.28 (p-value = 0.0001).

A controlled randomized trial by Anderson was carried out on the impact of early versus delayed umbilical cord clamping on the iron levels and neonatal outcomes. According to his results average age was 31.6±4.2 years in ECC group and 30.9±4.7 years in DCC group. They observed mean hemoglobin level in ECC group was 175±19 g/L and in DCC group it was 189±17 g/L with p-value < 0.001. They concluded that delayed clamping of cord is better than early clamping by increasing the hemoglobin level which favors the results of my study.1

The effect of timing of cord clamp on serum iron levels of neonate and its association with type of

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<tr>
<th>Group</th>
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<th>Min.</th>
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<td>Gestational age in week</td>
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<td>37</td>
<td>40</td>
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Table 3: Comparison of Hb & Hct between Two Groups

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<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>15.18±0.87</td>
<td>17.05±0.9</td>
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<tr>
<td>Hematocrit</td>
<td>48.77±3.28</td>
<td>55.87±4.28</td>
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Table 4: Comparison of Hb & Hct between Two Groups in Relation to Age

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<td>&lt;30 years</td>
<td>Hemoglobin (g/dl)</td>
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<td>Hematocrit</td>
<td>47.63±2.7</td>
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<td>&gt;30 years</td>
<td>Hemoglobin (g/dl)</td>
<td>15.44±0.88</td>
<td>16.93±0.92</td>
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<td>Hematocrit</td>
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Table 5: Comparison of Hb & Hct between Two Groups in Relation to Gestational Age

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<td>37-38 weeks</td>
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<td>Hematocrit</td>
<td>48.75±2.79</td>
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MEAN HEMOGLOBIN AND HEMATOCRIT IN EARLY AND DELAYED UMBILICAL CORD CLAMPING.

delivery was studies by Shirvani and his colleagues. The results of their study showed that average hemoglobin was greater in delayed clamping group as compared to early group (16.08±1.9 g/dl vs 14.5±2.4 g/dl respectively). Average hematocrit level in DCC group was 47.6±5.6 and in ECC group was 42.8±7.1. They concluded that DCC is a simple, safe and low-cost delivery modality and increases the hemoglobin and hematocrit levels in neonates which are similar to the results of my study.

Saba K et al carried out a research on early versus delayed clamping of cordandnewborn’s anemia. The results of the study showed higher mean hemoglobin concentration (18.7±3.2 g/dl vs 16.5±2.1 g/dl with p-value = 0.007) and hematocrit level (61.3±7.1 vs 58.3±2.2 with p-value = 0.035) in DCC group than ECC group respectively. They conclude that delayed cord clamping method increases average neonatal hemoglobin levels and hematocrit within a physiologic range which favors the results of my study.

Emhamed MO et al conducted a study on the early effects of delayed cord clamping in term infants born to Libyan mothers. The results of the study showed higher hematocrit level in delayed clamp group than the early clamp group (52.9±6.3 vs 49.3±5.7, respectively). They observed that 24 hours after delivery, the mean neonatal hemoglobin concentration was significantly higher in the delayed cord clamping group than the early clamping group (18.5 g/dL versus 17.1 g/dL; p-value = 0.0005). They concluded that it is a simple, safe, and low cost intervention at birth time that should be integrated in practice intended at decreasing the iron deficiency anemia in newborns, especially in developing countries which favors the results of my study.

CONCLUSION

Delayed clamping of cord is better than the early clamping in terms of increasing the hematocrit and hemoglobin concentration in neonates. Delayed clamping of cord should be applied in the active management of labor for attaining better neonatal outcome in terms of hemoglobin and hematocrit as it is a safe and simple procedure of delivery.

REFERENCES

Coronary Artery Diseases (CAD) have emerged as the leading cause of death and disability. According to an estimate by the World Health Organization (WHO), by the year 2020, both Ischemic Heart Diseases that include Coronary Artery Diseases and depression will be the two major causes of disability-adjusted life years.¹

Depression is quickly becoming the leading cause of years of life lived with disability worldwide and has a particularly large impact on compromised health when co morbid with a chronic medical disorder. When MDD occurs with an individual who has also had a history of episodes of mania, this is called Bipolar Disorder (previously termed Manic-Depressive Illness). In this review, we will be focusing on MDD when it occurs without a history of mania, where it is often called Unipolar Depressive Disorder. Major Depressive Disorder (MDD) is the most commonly studied clinical diagnosis in relation to CAD. Several studies indicated that depression may have behavioural and direct pathophysiologic effects on CAD. Depression is associated with non-adherence to risk factor modification in many medical conditions,² such as smoking cessation, poor patient compliance, e.g. poor glycaemic control in diabetic patients and poor adherence to prescribed medication in general. In addition direct pathophysiologic effects linking depression to CAD have been postulated.

In a study done by Empana et al, he compared 2,228 patients with Depression to a control group of 4,164 patients. He found that presence and severity of clinical Depression in patients is associated with higher risk of cardiac arrest resulting in death and that clinically depressed patients had a higher odds ratio (OR) of a cardiac arrest (OR, 1.88; 95% CI, 1.59–2.23).³

Among patients with cardiac disease, Depression is common, persistent, and under recognized. The syndrome of Major Depression is present in...
approximately 15%\(^4\) of patients with cardiac disease, including those suffering ACS.\(3,24\). Such a rate is substantially higher than that seen in the general population (4% to 5%)\(25\) or primary care patients (8% to 10%). Though some cardiac illnesses may have associated impairments of appetite, concentration, sleep, and energy, true Depression (with persistent depressed mood or anhedonia) is not a normal consequence of cardiac disease.\(^4\)

In a local study done in Pakistan by Bokari et al for prevalence of Depression in patients with Coronary Artery Disease in a Tertiary Care Hospital in Pakistan, the prevalence of depression the sample was 37% (31.3% males and 53.8% females). Female sex, income level below Rs. 5000 per month, low education level, outpatient, single earning family member and hypertension were few variables associated positively with depression (\(p< 0.05\)). Only one patient was receiving treatment for depression by his cardiologist.\(^5\) The study is however more than 10 years old.

Kendler and colleagues\(^6\) have shown a major relation between depression and coronary artery disease, mainly in acute states. A high severity of depression within several weeks of admission to hospital for an acute coronary syndrome, or an inadequate treatment response in depression, can double cardiac mortality in 6-7 years of follow-up.\(^7\) Studies examining depression and anxiety as predictors of 2-year cardiac events in patients with stable coronary artery disease have shown a high likelihood of major adverse cardiac events in those with depression. These results have led to the recommendation that all patients with coronary artery disease be screened for depression; however, this recommendation is somewhat controversial.

Coronary artery disease (CAD) is the most common cause of mortality in the developed world. The term "coronary artery disease" encompasses a range of diseases that result from atheromatous change in coronary vessels. In the past, CAD was thought to be a simple, inexorable process of artery narrowing, eventually resulting in complete vessel blockage (and MI). However, in recent years the explanatory paradigm has changed because it was realized that a whole spectrum of coronary plaques exists—from stable (lipid-poor, thick fibrous cap) to unstable (lipid-rich, thin fibrous cap).

Data from 44 years of follow-up in the original Framingham Study cohort and 20 years of surveillance of their offspring has allowed ascertainment of the incidence of initial coronary events including both recognized and clinically unrecognized MI, angina pectoris, unstable angina, and sudden and non-sudden coronary deaths.\(8-10\) The following observations were noted: For persons aged 40 years, the lifetime risk of developing CHD is 49 percent in men and 32 percent in women. For those reaching age 70 years, the lifetime risk is 35 percent in men and 24 percent in women. For total coronary events, the incidence rises steeply with age, with women lagging behind men by 10 years. For the more serious manifestations of coronary disease, such as MI and sudden death, women lag behind men in incidence by 20 years, but the sex ratio for incidence narrows progressively with advancing age.\(^11\) The incidence at ages 65 to 94 compared to ages 35 to 64 more than doubles in men and triples in women. In premenopausal women, serious manifestations of coronary disease, such as MI and sudden death, are relatively rare. Beyond the menopause, the incidence and severity of coronary disease increases abruptly, with rates three times those of women the same age who remain premenopausal.\(^8\) Below 65 years of age, the annual incidence of all coronary events in men (12 per 1000) more than equals the rate of all the other atherosclerotic cardiovascular events combined (7 per 1000); in women, it equals the rate of the other events (5 per 1000). Beyond 65 years of age, coronary disease still predominates. Coronary events comprise 33 to 65 percent of atherosclerotic cardiovascular events in men and 28 to 58 percent in women. The male predominance of CHD is least striking for angina pectoris. Under 75 years of age, the initial presentation of coronary disease in women is more likely to be angina pectoris than MI.\(^12\)
Furthermore, angina in women is more likely to be uncomplicated (80 percent), while angina in men often occurs after a MI (66 percent). Infarction predominates at virtually all ages in men in whom only 20 percent of infarctions are preceded by long-standing angina; the percentage is even lower if the MI is silent or unrecognized.\(^8\)\(^9\)

Angina is caused by myocardial ischemia, which occurs whenever myocardial oxygen demand exceeds oxygen supply. Because oxygen delivery to the heart is closely coupled to coronary blood flow, a sudden cessation of regional perfusion following a thrombotic coronary occlusion quickly leads to the cessation of aerobic metabolism.

Major depression is a highly prevalent and disabling mental disorder that is under-diagnosed and undertreated.\(^12\) High rates of disease-related disability, and relapse or recurrence are common. Major depression is associated with as much physical and social dysfunction as many other common medical illnesses. Similarly, CAD is highly prevalent in western populations affecting men and women with increasing age.\(^13\)

The evidence that depression affects prognosis in patients with CAD, especially in patients after myocardial infarction is growing: reported relative risks for adverse outcome (mainly cardiac death) range from 2.5 to 5.7. In addition to the mortality risk associated with post-myocardial infarction depression, increased health care costs linked to both readmission and out-patient contact among depressed patients who survived the first year after infarction have been observed.

A higher prevalence of ventricular tachycardia during 24-h Holter monitoring among patients with CAD and depression than among CAD patients without depression has been noted which may contribute to the explanation of the increased risk for cardiac mortality in depressed patients with CAD. In patients with coronary artery bypass graft surgery, it has been shown that depression diagnosed before surgery was related to higher hospital re-admission rates and was an independent risk factor for cardiac events after surgery, suggesting that positive emotions may promote better recovery.

**OBJECTIVES:**

Determine the frequency of major depressive disorders among patients suffering from Ischemic heart disease

**Rationale:**

The rationale of the study Depression is an independent risk factor for Coronary Artery Disease and its complications. The patients who experience Depression after Myocardial Infarction attack, are at higher risk for sudden cardiac death. Early diagnosis and treatment of these patients will not only improve the quality of life of these patients but will also help us to reduce morbidity and mortality of patients with Coronary Artery Disease. This study will highlight the frequency and severity of Depression among Coronary Artery Disease patients in our population so that guidelines for management of these patients for their psychiatric disorders, which are usually neglected in our setting, can be established.

**METHOD**

**Research Design:**

The cross-sectional study design was used, as the study was conducted in one specific point of time, the cross-sectional design is the appropriate method to assess the co-relation among the selected variables of this study across different sections.

**Sampling Strategy:**

In present, study Non Probability / Consecutive Sampling technique was used to collect the data.

**Sample:**

The sample of 100 individuals within the age range of 35 to 65 years was included in the study. To estimate a proportion with Confidence level = 95% and acceptable difference = 0.08 with an expected percentage 15%\(^*\) of Depression among Coronary Artery Disease patients. The sample was collected from Department of CCU (both indoor and outdoor facilities), Jinnah Hospital Lahore. The date was collected from Diagnosed case of Coronary Artery Disease for at least 5 years.
FREQUENCY OF MAJOR DEPRESSIVE DISORDER IN KNOWN CORONARY ARTERY DISEASE PATIENTS.

Data collection Procedure:

100 subjects, those fulfilling the inclusion criteria, were included in our study after approval from ethical committee and an informed consent from subjects. A detailed demographic history and Coronary Artery Disease history assessment (angiography findings, duration of disease and current treatment) was also under taken. The patients were given Hospital Anxiety and Depression Scale's translated version in Urdu. Effect modifiers like duration of disease, age and gender were addressed by stratification of data. All the information was entered in a structured. (attached)

(i) Identification of the study variables
(ii) Methods for collection of data
(iii) Data collection tools (proforma/questionnaire)

Statistics:

The data was entered and analyzed on SPSS ver: 21.0 and following test were used.

Mean and standard deviation was calculated for numerical variables like age, duration of illness. Frequency and percentages were calculated for nominal variables like gender, depressive illness, and major depression disorder. Post- Stratification chi-square test was applied. P-value < 0.05 was considered significant.

RESULT

A total of 100 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the frequency of major depressive disorders among patients suffering from Ischemic heart disease.

Age Distribution:

Age distribution of the patients was done, it shows that 56 % (n=56) were between 35-50 years of age while 44 % (n=44) were between 51-65 years of age, mean+sd was calculated as 50.15+7.29 years. (Table No. 1)

Gender Distribution:

Patients were distributed according to gender, it shows that 57 % (n=57) were male and 43 % (n=43) were females. (Table No. 2)

Frequency of Major Depressive Disorder:

Frequency of major depressive disorders among patients suffering from ischemic heart disease was recorded in 21 %(n=21) while 79 % (n=79) had no findings of the morbidity. (Table No. 3)

Mean duration of illness:

Mean duration of illness (ischemic heart disease) was computed as 7.43+1.55 years. (Table No. 5)

Stratification:

The data was stratified for variables of interest like age, gender, and duration of Coronary Artery Disease. Post- Stratification chi-square test was applied. P-value < 0.05 was considered significant. (Table No. 5-7)

| Table 1: Age Distribution(n=100) |
| Age(in years) | No. of patients | % |
| 35-50 | 56 | 56 |
| 51-65 | 44 | 44 |
| Total | 100 | 100 |
| Mean+SD | 50.15+7.29 |

| Table 2: Gender Distribution (n=100) |
| Gender | No. of patients | % |
| Male | 57 | 57 |
| Female | 43 | 43 |
| Total | 100 | 100 |

| Table 3: Frequency of Major Depressive Disorders Among Patients Suffering from Ischemic Heart Disease (n=100) |
| Major depressive disorders | No. of patients | % |
| Yes | 21 | 21 |
| No | 79 | 79 |
| Total | 100 | 100 |

| Table 4: Mean Duration of Illness(n=100) |
| Duration of Illness (Ischemic heart disease) | Mean | SD |
| 7.43 | 1.55 |

| Table 5: Stratification for Frequency of Major Depressive Disorders among Patients Suffering from Ischemic Heart Disease with Regards to Age |
| Age (in years) | Major depressive disorders | P value |
| Yes | No |
| 35-50 | 9 | 47 | 0.17 |
| 51-65 | 12 | 32 |  |
The relationship between coronary heart disease (CHD) and major depressive disorder (MDD) has been investigated extensively over recent decades, as the prevalence of both conditions has risen around the world. Each condition remains a major contributor to the global burden of disease; CHD is the leading cause of death, while MDD (defined as the presence of severely depressed mood persisting for at least two weeks) is the top-ranking cause of disability.

We planned this study with the view that depression is an independent risk factor for Coronary Artery Disease and its complications. The patients who experience Depression after Myocardial Infarction attack, are at higher risk for sudden cardiac death.

In our study, 56%(n=56) were between 35-50 years of age while 44%(n=44) were between 51-65 years of age, mean+sd was calculated as 50.15+7.29 years, 57%(n=57) were male and 43%(n=43) were females, frequency of major depressive disorders among patients suffering from ischemic heart disease was recorded in 21%(n=21). In previous data, among patients with cardiac disease, including those suffering ACS. Such a rate is substantially higher than that seen in the general population (4% to 5%) or primary care patients (8% to 10%), these findings are in agreement with our results.

In a local study done in Pakistan by Bokari et al for prevalence of Depression in patients with Coronary Artery Disease in a Tertiary Care Hospital in Pakistan, the prevalence of depression the sample was 37% (31.3% males and 53.8% females). Female sex, income level below Rs. 5000 per month, low education level, outpatient, single earning family member and hypertension were few variables associated positively with depression (p< 0.05). Only one patient was receiving treatment for depression by his cardiologist. The study is however more than to 10 years old and they recorded prevalence of depression only and we evaluated the frequency of major depressive disorders in our study.

We are of the view that this co-morbidity is particularly problematic because CHD patients with depressive symptoms are more likely to experience poorer behavioural, psychological and clinical outcomes, including increased likelihood of morbidity and mortality, compared with those who are not depressed. In MI patients, a landmark study by Frasure-Smith, Lesperance, and Talajic revealed that the presence of depression was significantly related to 18-month cardiac mortality. This finding has since been corroborated; others have demonstrated that even mild to moderate depressive symptoms in post-MI populations are associated with decreased survival. While it may seem intuitive that individuals who have experienced a life threatening event would report negative emotions such as low mood in the ensuing recovery period, the relationship between cardiovascular disease (CVD) and depression is much more complex; the conditions may act bi-directionally rather than causally. Gaining a better understanding of the nature of these two conditions is of great importance; both in understanding the role of psychosocial factors in the relationship between CVD and depression and for

<table>
<thead>
<tr>
<th>Gender</th>
<th>Major depressive disorders</th>
<th>P value</th>
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</thead>
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<tr>
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<td>No</td>
</tr>
<tr>
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</tr>
<tr>
<td>Female</td>
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<td>35</td>
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</tbody>
</table>

<table>
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<th>Duration of illness (Coronary Artery Disease)</th>
<th>Major depressive disorders</th>
<th>P value</th>
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<tr>
<td>&gt;7</td>
<td>10</td>
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DISCUSSION

The relationship between coronary heart disease (CHD) and major depressive disorder (MDD) has been investigated extensively over recent decades, as the prevalence of both conditions has risen around the world. Each condition remains a major contributor to the global burden of disease; CHD is the leading cause of death, while MDD (defined as the presence of severely depressed mood persisting for at least two weeks) is the top-ranking cause of disability.

We planned this study with the view that depression is an independent risk factor for Coronary Artery Disease and its complications. The patients who experience Depression after Myocardial Infarction attack, are at higher risk for sudden cardiac death.

In our study, 56%(n=56) were between 35-50 years of age while 44%(n=44) were between 51-65 years of age, mean+sd was calculated as 50.15+7.29 years, 57%(n=57) were male and 43%(n=43) were females, frequency of major depressive disorders among patients suffering from ischemic heart disease was recorded in 21%(n=21). In previous data, among patients with cardiac disease, depression was common, persistent, and under recognized. The syndrome of Major Depression is present in approximately 15% of patients with cardiac
FREQUENCY OF MAJOR DEPRESSIVE DISORDER IN KNOWN CORONARY ARTERY DISEASE PATIENTS.

The development of appropriate treatment programs if they are to effectively impact on key components of HRQOL including mental, physical and related functioning outcomes.

The above finding reveal that early diagnosis and treatment of these patients may not only improve the quality of life of these patients but will also help us to reduce morbidity and mortality of patients with Coronary Artery Disease.

CONCLUSION

We concluded that the frequency of major depressive disorders is higher among patients suffering from Ischemic heart disease.

REFERENCES

Acute kidney injury in the setting of cirrhosis is a medical emergency characterized by significant morbidity and mortality. The purpose of the study is to determine the frequency of acute kidney injury in hospitalized patients with cirrhosis in a tertiary care hospital.

Methods: The study was conducted in Services Institute of Medical Sciences, Lahore. A total of 155 cases fulfilling the inclusion/exclusion criteria were enrolled from Medical and Ophthalmology outdoor department Services Institute of Medical Science, Lahore. An informed consent of the patients was taken from the patients to include their data in the study. Detailed history for cirrhosis and physical examination was done by the researcher. Baseline serum creatinine was recorded and repeated after 48 hours, the presence or absence of acute kidney injury was determined according to the operational definition.

Results: In our study, out of 155 cases, 22.58 % (n=35) cases were between 30-50 years of age while 77.42% (n=120) were between 51-80 years of age with mean age 55.17±8.27 years. 54.84% (n=85) were male while 45.16% (n=70) were females. Frequency of acute kidney injury in hospitalized patients with cirrhosis in a tertiary care hospital was recorded in 29.68% (n=46).

Conclusion: Frequency of Acute Kidney Injury is found to be high among patients with liver cirrhosis.

Keywords: Cirrhosis, Acute kidney injury, Frequency

Cirrhosis of liver is a serious disease which can lead to liver failure. Most common causes of liver cirrhosis include chronic viral hepatitis and alcoholic liver disease. In general population in Pakistan the prevalence of HCV and HBV infection was estimated at 3.6-18.66% and 4.25-7.13% respectively. Clinical features of cirrhosis or chronic liver disease (CLD) ranges from asymptomatic in one third of patients to full range of symptoms in two third of patients. Important symptoms are fatigue, weakness, development of ascites, gastrointestinal bleed and encephalopathy. Acute kidney injury (AKI) is a relatively frequent problem, occurring in approximately 20% of hospitalized patients with cirrhosis. Serum creatinine (S Cr) is the most commonly used method to determine AKI because of easy availability and low cost. AKI is defined as an abrupt rise in Serum Creatinine of 0.3 mg/dl or more; or an increase of 150% or more (1.5-fold) from baseline. The cause of AKI in cirrhosis is multifactorial and is unique in terms of pathogenesis. The most common causes of AKI in cirrhosis can be subdivided into either functional or structural.

A previous study recorded that the most common type of renal dysfunction in liver cirrhosis was AKI, present in 107 patients (70%) in hospitalized patients. Another study by Garcia-Tsao G and others reveal that approximately 20% of cirrhosis patients are suffering with acute kidney injury. Another study revealed that the prevalence of AKI has been reported to vary from 14–50% in patients with cirrhosis.

The study is conducted to find out the frequency of acute kidney injury in patients with cirrhosis as there is no local study available while the international studies are also showing a significant variation. The results of the study would also be helpful for timely management of the morbidity.

METHODS
Setting:

The study was conducted in Services Institute...
FREQUENCY OF ACUTE KIDNEY INJURY IN HOSPITALIZED PATIENTS WITH CIRRHOSIS

Study design:
   Cross sectional study

Sample technique:
   Non-probability: Consecutive Sampling Technique

Sample size: Sample size of 155 cases was calculated with 95% confidence level 6.5% margin of error and taking expected %age of acute kidney injury i.e. 20% in patients with cirrhosis.

Sample selection:
   Inclusion criteria
   • All diagnosed cases of cirrhosis (according to operational definition)
   • Age 30-80 years
   • Both genders

Exclusion criteria:
   • Already diagnosed cases and under treatment for acute kidney injury (on history and medical record)
   • Not willing to participate in the study

Data collection procedure:
   A total of 155 cases fulfilling the inclusion/exclusion criteria were enrolled from Outdoor department Services Institute of Medical Science, Lahore. An informed consent of the patients was taken from the patients to include their data in the study. Detailed history for cirrhosis and physical examination was done by the researcher. Baseline serum creatinine was recorded and repeated after 48 hours, the presence/absence of acute kidney injury was determined according to the operational definition on a predefined proforma.

Statistical analysis:
   The data was entered and analyzed in SPSS version for 16.0. Mean and standard deviation was calculated for quantitative variable like age, duration of cirrhosis. Frequencies and percentages were calculated for qualitative variables like gender and presence/absence of acute kidney injury in patients with cirrhosis. The data was stratified for age, gender and duration of cirrhosis to address the effect modifiers. Post stratification chi-square test was applied to see the significance. P value <0.05 was considered as significant.

RESULT
   Among patients enrolled in the study age distribution shows that 22.58% (n=35) cases were between 30-50 years of age while 77.42% (n=120) were between 51-80 years of age, mean+standard deviation of age was calculated as 55.17±8.27 years. Gender distribution shows that 54.84% (n=85) were male while 45.16% (n=70) were females.
   Frequency of acute kidney injury in hospitalized patients with cirrhosis in a tertiary care hospital was recorded in 29.68% (n=46) whereas 70.32% (n=109) had no findings of the morbidity. (Table No. 1) Stratification for frequency of AKI with regards to age shows that 7 out of 35 cases were between 30-50 years of age and 39 out of 81 cases were between 51-80 years of age had AKI, p value was 0.15. (Table No. 2) Stratification for frequency of AKI with regards to gender shows that 27 out of 85 cases were male and 19 out of 70 cases were females, p value was 0.53. (Table No. 3) Stratification for frequency of AKI in cirrhosis with regards to duration of cirrhosis shows that 17 out of 72 cases were between 1-3 years and 29 out of 83 cases had >3 years of age, p value was 0.12. (Table No. 4)

DISCUSSION
   In our study, out of 155 cases, 22.58% (n=35) cases were between 30-50 years of age while 77.42% (n=120) were between 51-80 years of age, mean+sd

Table 1: Frequency of Acute Kidney Injury in Hospitalized Patients with Cirrhosis in a Tertiary Care Hospital (n=155)

<table>
<thead>
<tr>
<th>AKI</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>46</td>
<td>29.68</td>
</tr>
<tr>
<td>No</td>
<td>109</td>
<td>70.32</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2: Stratification for Frequency of Aki in Cirrhosis with Regards to Age (n=155)

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>AKI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>30-50</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>51-80</td>
<td>39</td>
<td>81</td>
</tr>
</tbody>
</table>
Frequency of acute kidney injury in hospitalized patients with cirrhosis in a tertiary care hospital was recorded in 29.68% (n=46).

We compared these findings with previous study by Russ KB7 and others in which reported prevalence of AKI was 14-50% and thus our study is in agreement with that. The wide range in prevalence is likely due to different study populations and varying definitions of renal dysfunction. For example, in a prospective study of 206 cirrhotics (100 with sepsis), renal dysfunction as defined by serum creatinine >1.5 mg/dL was reported in 17% of cases and was higher among patients with sepsis (27% vs. 8%, p<0.0001). In another retrospective study, acute renal failure as defined by serum creatinine increase by >50% was reported in 23% of 82 decompensated Child-Turcotte-Pugh (CTP) stage C cirrhosis patients. Another study reported the prevalence of AKI as defined by increase in serum creatinine by >0.9 mg/dL in 25% of patients, with 93 cirrhosis patients with baseline creatinine <1.4 mg/dL.10In our study, we defined it as rise in serum creatinine of >50% from baseline or a rise of serum creatinine by >0.3 mg/dL in <48 hours (on lab investigations), which shows agreement with the above study. In summary, in our study, we focused only to determine the frequency of acute kidney injury in patients with cirrhosis as the international studies are showing a significant variation, however, our results clarified the variation and also recorded the exact frequency, the results of our study are helpful for timely management of the morbidity.

**CONCLUSION**

We concluded that the frequency of Acute Kidney Injury is high among cirrhotic cases. So, it is recommended that every patient who present with cirrhosis, should be sort out for acute kidney injury. However, it is also required that every setup should have their surveillance in order to know the frequency of the problem.

**REFERENCES**