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Editorial correspondence should be addressed to:

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CONTENTS

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EDITORIAL

CHALLENGES TO START A NEW BIOMEDICAL JOURNAL IN PAKISTAN

Iqbal Haider[1], Farooq Ahmad[2]

[1]Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

[2]Department of Medical Education, Khyber Medical College, Peshawar - Pakistan

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Start-up with creativity always leads to new learning opportunities with excellent outcomes in the biomedical field. However, starting a biomedical journal in Pakistan is a daunting task indeed. There is no doubt that Pakistan has a strong and growing scientific community but it will be unfair to negate that there are still many hurdles that must be overcome to create a journal that is truly successful and respected within the biomedical research community.

One of the biggest challenges to starting a biomedical journal in Pakistan is the lack of funding and human resources. Unlike more established journals, new journals must typically rely on the support of a small group of researchers who are willing to invest their time and resources into the journal. Another challenge is the lack of awareness and interest in scientific research in Pakistan. While there are certainly a number of researchers and institutions in Pakistan that are interested in biomedical research, there are still many who are not. This means that new journals may struggle to find a large enough audience to support their efforts.

Furthermore, starting a biomedical journal in Pakistan requires a significant amount of technical expertise and knowledge. It is not simply a matter of collecting research papers and publishing them online; journals must also adhere to a number of international standards and protocols like COPE and ICMJE to ensure the quality and integrity of their contents. This requires significant knowledge and experience in areas such as peer review, data management, research publication, and manuscript preparation.

Finally, there is the challenge of competition. There are already a number of established biomedical journals in Pakistan, as well as many international journals that are widely read and respected within the research community. This means that new journals must work hard to distinguish themselves from the competition and establish a strong reputation within the community.

Although starting a new biomedical journal is no doubt a challenging endeavor, however with careful planning and execution, such challenges can be overcome with the following strategies.

Secure funding and resources: One of the biggest challenges to starting a biomedical journal is the lack of funding and resources. The initial plan should be to arrange to fund a naïve biomedical journal for the upcoming two years at least. To overcome this challenge, the editorial board should consider seeking out funding from government agencies, private foundations, and other sources. They should also consider collaboration with universities, research institutions, and other organizations to provide technical expertise and support. The concept of charity donation in research should also be inculcated in Pakistan and entrepreneurs should come forward in this noble cause.

Build awareness and interest: To build awareness and interest in a new biomedical journal, editors should engage in outreach activities to promote the journal and its mission. This may be attending conferences and academic events, publishing articles and press releases, developing and utilizing social media links, and engaging with potential authors and reviewers.

Develop technical expertise: Starting a biomedical journal requires significant technical expertise and knowledge. To develop this expertise, editors should consider partnering with experienced journal editors and publishers, as well as participating in training programs and workshops. Physical and online certification courses in medical journalism will be of great help from this perspective.

Establish a strong reputation: To establish a strong reputation within the research community, newly established biomedical journals should strive to publish high-quality research that is rigorously reviewed and edit-

ed. They should also develop a strong brand identity and promote their journal through social media, email newsletters, and other channels. However, this is not an easy task as researchers are mostly reluctant to publish their articles in new journals mainly because these journals are not accredited with PMDC and HEC Pakistan. Both these regulatory bodies should devise strategies to support newly establishing journals in their accreditation process to maintain a high threshold for quality publications.

Differentiate from competitors: To differentiate from competitors, new biomedical journals should strive to offer unique and innovative features, such as open-access publishing, multimedia content, special sections like infographics, perspective, teaching and learning moments, or specialized focus areas. They should also focus on building strong relationships with authors and reviewers and providing excellent customer service to all stakeholders.

These strategies will help editors to overcome the challenges of starting a new biomedical journal and establish a successful and respected publication that contributes to the advancement of biomedical research.

The following execution plan will help the editorial board to accomplish its objectives:

Define the scope and mission of the journal: The first step in starting a new biomedical journal is to define the scope and mission of the journal. This includes deciding on the areas of focus, such as specific diseases or therapies, and the types of articles that will be published, such as original research, reviews, meta-analysis, clinical trials, or case studies.

Identify the target audience: Once the scope and mission of the journal have been defined, the next step is to identify a target audience. This includes determining the types of researchers, clinicians, and other healthcare professionals who are most likely to be interested in the journal.

Develop a business model for the journal: Starting a new biomedical journal requires a significant amount of funding and resources. To secure these resources, researchers must develop a comprehensive business model that outlines the costs associated with starting and running the journal, as well as potential sources of funding and revenue.

Build a team: Starting a biomedical journal requires a team of experts with a wide range of skills, including editorial, technical, computer, and business expertise. Editors and managerial teams should consider partnering with experienced journal editors, publishers, and technical staff to help develop and launch the journal.

Establish editorial policies and procedures: To ensure the quality and integrity of the content published in the journal, it is important to establish clear editorial policies and procedures. This includes developing guidelines for manuscript submission, peer review, and editorial decision-making. All these policies should be explicit and well-documented on the official website of the journal.

Build a submission and review platform: A key component of starting a new biomedical journal is building a submission and review platform that is easy to use for authors, reviewers, and editors. This can include utilizing existing publishing platforms or developing a custom platform specifically for the journal. Online Journal System (OJS) is offered by the Higher Education Commission of Pakistan to almost every journal for this purpose. All that editors need to train their human resources on OJS.

Approval and accreditation with media and print regulatory authorities to get International Standard Book Number (ISBN) or Online Standard Book Number.

Launch the journal: Once all of the necessary components have been developed and tested, it is time to launch the journal. This includes publishing the first issue of the journal, promoting it to potential authors and readers, and beginning the process of soliciting and reviewing manuscripts.

Monitor and evaluate: Finally, it is important to monitor and evaluate the success of the new biomedical journal. This includes tracking metrics such as submission and acceptance rates, citations, and reader engagement, and making adjustments to the journal's policies and procedures as needed to ensure continued success.

To get a digital object identifier (DOI) for the articles: This will enhance the visibility of articles globally.

Accreditation and Indexation for impact factors to augment the quality standards.

This execution plan will greatly boost the editorial team's efforts to launch and keep viable a new biomedical journal in Pakistan that contributes to the advancement of biomedical research and healthcare in the region.

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Dr. Farooq Ahmed
Chief Editor of JMS
Department of Medical Education, Khyber Medical College, Peshawar - Pakista
Cell: +92-313-3799901
Email: drfarooq.ahmed@kmc.edu.pk

ORIGINAL ARTICLE

BACTERIAL ISOLATES AND THEIR SENSITIVITY PATTERNS IN PATIENTS WITH DIABETIC FOOT ULCERS

Ghulam Abbas, Hamza Ali Khan, Salim Iqbal, Asif Nabi

Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To determine the frequency of common microorganisms (bacterial isolates) and their sensitivity and resistance patterns in patients with diabetic foot ulcers

Materials and Methods: This descriptive cross-sectional study was conducted in the Department of Medicine, Khyber Teaching Hospital Peshawar from June 2020 to June 2021. Two hundred and thirty-eight diabetic patients with foot ulcers were included in the study. Deep wound swabs were collected and sent to the microbiology laboratory for culture and sensitivity. The sensitivity patterns of different organisms were identified.

Results: One hundred and thirty-four out of 238 (56.3%) patients were male, and the remaining 104 (43.7%) were female. The mean age of the patients in our study was 57.12±9.58 (32-80) years. Cultures were positive in 216 out of 238 (91%). Gram-negative organisms were 175 (81%), while 41 (19%) were gram-positive bacteria. The common bacteria were Escherichia coli 99 (45.8%), Pseudomonas aeruginosa 49 (22.7%), Staphylococcus aureus including methicillin-resistant staphylococcus aureus (MRSA) 36 (16.6%). The most effective antibiotics against gram-negative organisms were Meropenem (Sensitivity 97%), Amikacin (96%), Piperacillin-Tazobactam (95%), and Cefoperazone-Sulbactam (94%). The most effective antibiotics against Gram-Positive organisms were Vancomycin (Sensitivity 100%), Teicoplanin (100%), and Linezolid (95%). Antibiotics with higher rates of resistance included Doxycycline (89%), Clarithromycin (80%), and Co-Trimoxazole (78.7%).

Conclusion: Diabetic foot ulcers are frequently infected with a variety of organisms. Escherichia coli, Pseudomonas, and staphylococcus aureus are the primary (predominant) organisms. Meropenem, Amikacin, Cefoperazone-Sulbactam, and Piperacillin-Tazobactam Are The most effective antibiotics against Gram-Negative Bacteria, while Vancomycin, Teicoplanin, and Linezolid are effective against gram-positive bacteria.

Keywords: Diabetes Mellitus, Foot Ulcer, Pus Culture, Bacteria, Antibiotic Sensitivity and Resistance

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INTRODUCTION

A diabetic foot ulcer is a major cause of disability, morbidity, and mortality for the diabetic population. It is associated with substantial economic loss and poor quality of life. About 7- 15% of people with diabetes develop a foot ulcer at some stage, and 1% end up with amputation. [1]

Contributing factors in diabetic foot ulcers include peripheral neuropathy, peripheral vascular disease, and increased susceptibility to infection. In DM, wound healing is impaired, leading to gangrene of the foot. [2] About 50 %of diabetic foot ulcers are affected by infection with resultant increased morbidity, limb amputations, and mortality. Common isolates from diabetic foot ulcers include Staphylococcus Aureus, E. coli, Pseudomonas, and Staphylococcus epidermidis. Though the isolates greatly vary from area to area. [3]

The emergence of bacterial resistance to single or multiple antibiotics is another issue leading to poor outcomes in diabetic foot ulcers. In a recent Indian study, it was found that 55-66% of isolates were resistant to commonly used antibiotics. There is also an increased tendency of multiple drug-resistant strains of bacteria, which poses a significant challenge in effectively treating diabetic foot ulcers. [4]

As the bacterial pathogens and their antibiotic sensitivities vary from place to place, this study aimed to determine the frequency of common bacterial isolates from diabetic foot ulcers and their sensitivity patterns to commonly used antibiotics in our local setup. This will help us formulate an empirical antibiotic regimen for diabetic foot ulcers.

MATERIALS AND METHODS

This descriptive cross-sectional study was con-

Correspondence
Dr. Hamza Ali Khan
Assistant Professor
Department of Medicine, Khyber Teaching Hospital,
Peshawar - Pakistan
Cell: +92-333-9333841
Email: hamzaalikhan48@yahoo.com
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ducted in the Out-patients department and wards of medical and surgical units of Khyber Teaching Hospital Peshawar from January 2019 to September 2020. A total of 238 patients were included using an online calculator for sample size calculation.

The research proposal was approved by the institutional ethical and review committee. Informed consent was taken from all the patients in the study. Patients older than 30 years with grade 1 to 5-foot ulcers with fasting blood glucose ≥ 126 mg/dl or random blood glucose ≥ 200 mg or HbA1c > 6.5 were included in the study. Non-diabetic patients with foot ulcers were excluded from the study. The patients were enrolled by non-probability convenient sampling.

After thoroughly cleansing the affected foot with normal saline, pus was collected through a special swab for culture. The samples were taken using a firm circular motion with the swab. One swab was used for gram staining and the other for culture. These swabs were sent to the hospital laboratory for gram staining and culture using a standard microbiological protocol. The samples were directly examined for gram staining while the inoculated plates were incubated at 37^{o}C overnight and the plates were examined for growth the next day. Once the initial growth was achieved, the microorganisms were tested for sensitivities and resistance to different antibiotics using the Kirby Bauer disk diffusion method on Mueller Hinton agar plates in the hospital microbiology laboratory. Standard operating procedures (SOPs) were used for specific purposes for all laboratory procedures. Quality control stains were used to confirm the results of antibiotics, and media. To assess the quality of the general laboratory procedure, the Quality of reagents, antibiotic disk, and media used were according to international guidelines.

Different tested antibiotics included Cefoperazone-Sulbactam, Piperacillin-Tazobactam, Meropenem, Amikacin, Aztreonam, Tigecycline, Doxycycline, Ceftazidime, Cefepime, Cefotaxime, Ceftriaxone, Co-Amoxiclav, Chloramphenicol, Co-Trimoxazole, Vancomycin, Teicoplanin, Linezolid, Flucloxacillin, Clarithromycin, Ciprofloxacin, Levofloxacin, and Colistin sulfate.

Data was collected through a specially designed proforma and analyzed with the SPSS version 25. Microorganisms found in cultures and their sensitivities and resistance to different antibiotics were recorded. Mean and standard deviations were calculated for numerical variables like age and ulcer duration. Frequencies were calculated for nominal variables like the growth of microorganisms and the sensitivity pattern of each antibiotic. Data was presented in pie charts, graphs, and tables.

RESULTS

The mean age of patients was 57±9.55 (32-80) years. The majority of patients were in the age range of 40-70 years. (89%). Out of 238, 134 (56.3%) were male, and 104 (44%) were female. 11 (4.6%) patients had grade 1 ulcers. 123 (51.7%) patients had grade 2, 98 (41%) patients had grade 3, and only 6 (2.5%) patients had grade 4 ulcers. Most patients presented in the second to fourth week after the onset of the ulcer. Among 216 positive cultures, 175 (81%) isolates were gram-positive, and 41 (19%) were gram-negative. Pus culture was positive in 215(91%) patients and negative in the remaining 23 (9%). The common bacterial pathogens are shown in table 1.

The effective antibiotics (high sensitivity and least resistance) included Cefoperazone-Sulbactam, Piperacillin-Tazobactam, Meropenem, and Amikacin. Doxycycline was the least effective antibiotic, with 89% resistance. (Figure 1). The sensitivity of MRSA to vancomycin and Teicoplanin was 100 % (N=21) and 95 % (N=20) for linezolid (See figure 4).

DISCUSSION

Diabetic foot ulcers occur in middle age people who are otherwise active. The mean age of patients in our study was 57±9.55 years. Many of the patients were in age groups that ranged from 40 to 70 years. These find-

Table 1: Common bacterial pathogens in diabetic foot ulcers

Bacteria	n=216	Percentage
E.coli	99	45.8
Pseudomonas aeruginosa	49	22.7
Proteus mirabilis	18	8.3
MRSA	21	9.7
Methicillin sensitive staphylococcus aureus	15	6.9
Acinetobacter	4	1.9
Klebsiella pneumoniae	1	.5
Proteus vulgaris	4	1.9
Strep faecalis	5	2.3

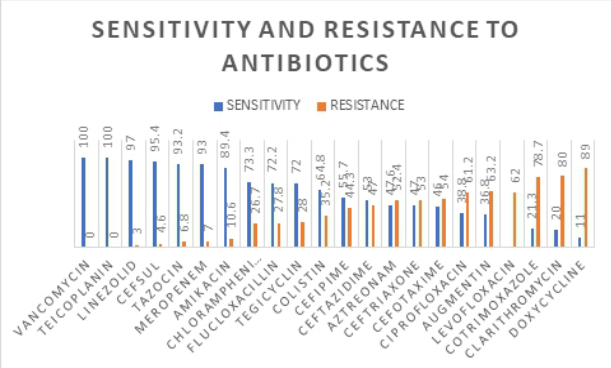

Fig 1: Sensitivity and resistance pattern of different antibiotics

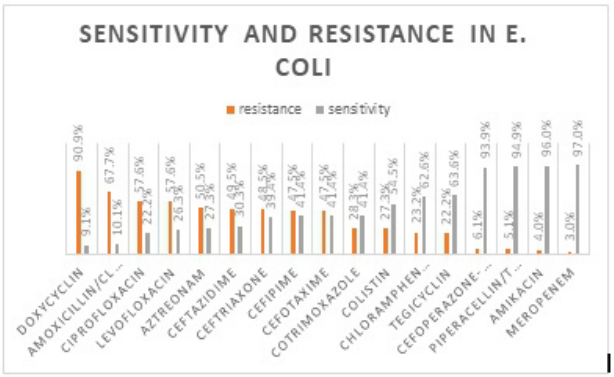

Fig 2: Sensitivity and resistance pattern of E.coli

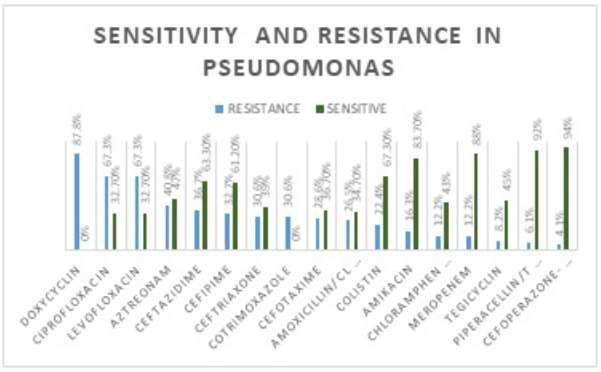

Fig 2: Sensitivity and resistance pattern of Pseudomonas aeruginosa

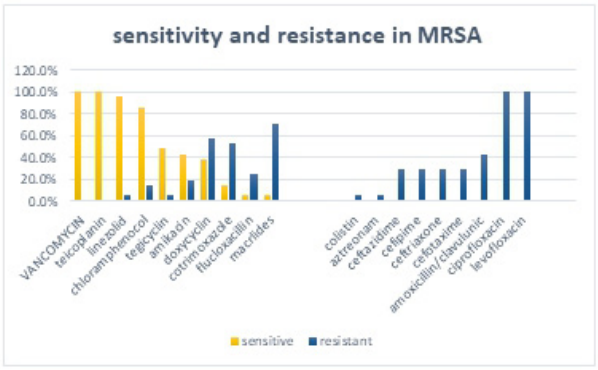

Fig 4: Sensitivity and resistance pattern of MRSA

ings are comparable to studies done worldwide. Since type 2 diabetes mellitus is usually a disease of adults and patients in this age group usually have other complications of diabetes as well, this may be a possible explanation for the higher frequency of diabetic foot ulcers in this age group. [5,6]

In our study, diabetic foot ulcers were more common in males than females. This is comparable to many local and international studies. [7,8] However, some studies have shown a higher frequency of diabetic foot ulcers in females. [9]

According to Wagner's classification, most of our patients had grade 2-3 foot ulcers. [10] This is because most patients ignore grade 1 ulcers or have poor knowledge about the early recognition of diabetic foot wounds. While patients with gangrene are usually referred to orthopedic surgeons for possible amputations. Similar results were found by Latif S et al. [11,12]

Many patients with diabetic foot ulcers have peripheral neuropathy. Initially, the patients may be unaware of the presence of the ulcer, or they underestimate the consequences of an initial ulcer. Therefore, more than 70% of our patients presented from the second to fifth week after the onset of the ulcer. [13,14]

The common isolates of the cultures from diabetic foot ulcers vary by location and setup. Most bacterial isolates in our study were gram-negative (81%) and gram-positive only 19%. The most familiar organisms in diabetic foot ulcers included staphylococcus aureus, Escherichia coli, and pseudomonas aeruginosa. According to Miyan Z et al., the most typical organism in descending order included staphylococcus aureus (20.67%), E. coli (15.72%), Klebsiella pneumonia (13.54%), Pseudomonas (13.54%) and Proteus mirabilis (12.81%). [15] Similar results were also shown in another local study by Amjad SS et al. [16]. According to that study, Staphylococcus aureus was identified in 46% of cases, E. coli in 28%, Pseudomonas in 6% and Klebsiella in 3.5%. According to the study of Saseedharan S et al. in India, the common isolates were Staphylococcus aureus (26.9%), Pseudomonas (20.9%), Enterococcus faecalis (12.7%), Escherichia coli 12%. [8] In our study, the predominant organism was Escherichia coli, followed by Pseudomonas aeruginosa and Staphylococcus aureus. These findings are supported by a similar study done in Iran by Hadadi A et al. [17,18,19]

In our study, E.coli isolates were more sensitive to Meropenem, Amikacin, Piperacillin-Tazobactam, And Cefoperazone-Sulbactam. These results are similar to the studies by Jain SK et al. [20] and Banashankari G et al. [21,] and Ozer B et al. [22]

E.coli showed high resistance to commonly used antibiotics like quinolones, Cephalosporins and Co-Amoxiclav. These results were supported by the study of Alvi et al.[23]Highest resistance was noted to doxycycline (91%). Due to this fact, Doxycycline is not recommended for gram-negative bacteria. [24]

Pseudomonas is an invasive bacterium and usually affects immunocompromised hosts. It is one of the most familiar bacteria responsible for a diabetic foot infection. In our study, Pseudomonas aeruginosa was the second most frequent organism isolated from pus culture. Very few antibiotics are effective against this organism. [25]

In our study, Pseudomonas isolates were more sensitive to Cefoperazone-Sulbactam, Piperacillin-Tazo-

bactam, Meropenem, and Amikacin. Higher sensitivity to these antibiotics was also noted in another local study by Ullah I et al. and Noor S et al. [14,26] In contrast to other studies, our study showed high rates of resistance to quinolones, ceftazidime, doxycycline, and aztreonam. [27,28] The increased resistance to these antibiotics is probably because of the unnecessary use of antibiotics and the emergence of resistant strains of pseudomonas species in diabetic foot ulcers. [29]

Methicillin-resistant Staphylococcus aureus is one of the leading causes of infection in diabetic foot ulcers. In our study, it was noted that 9.7% (n=21) of all the microorganisms and 58.3 % of all staphylococcus aureus cases. This rate is comparable to an international study by Akhi MT et al. and Dadashi M et al.[30,31] According to Nasiri M et al., in Iran, the prevalence of MRSA is 45%.

All isolates were sensitive to Vancomycin and Teicoplanin, while 95% (n=20) isolates were sensitive to Linezolid. According to Pai V et. al., all isolates were susceptible to vancomycin in India. Still, there was high resistance to quinolones, macrolides, aminoglycosides, and chloramphenicol.[32] Although there is widespread emergence of vancomycin resistance in methicillin-resistant staphylococcus aureus,[33] in our study, all isolates were susceptible to vancomycin. One important finding in our study was the high sensitivity of MRSA to the old antibiotic chloramphenicol. This fact has been mentioned in other well-validated studies. [34]

The isolates of Methicillin-sensitive staphylococcus aureus were 100% sensitive to vancomycin. They had higher sensitivity to antibiotics like chloramphenicol, co-amoxiclav, flucloxacillin, and ceftriaxone. Still, their sensitivity to other antibiotics like cefepime, linezolid, quinolones, tetracyclines, macrolides and co-trimoxazole was low. These antibiotics were associated with increased rates of resistance, as shown in a study done in Sri Lanka by Jayatilleke K et al.[35]

Proteus species frequently infect wounds. Proteus mirabilis infection was highly susceptible to cefoperazone-sulbactam, piperacillin-tazobactam, amikacin, quinolones and cefalosporins. At the same time, these isolates were resistant to penicillins, doxycycline, chloramphenicol, co-trimoxazole, and tigecycline.

An African study byMordi RM showed high sensitivity to ciprofloxacin and aminoglycosides but low sensitivity to tetracyclines, erythromycin, chloramphenicol, and penicillins. [36] Similar results were found in another study by Trojan R et al. in Indian Punjab.

In both these studies, proteus showed high sensitivity to ciprofloxacin and other quinolones, cephalosporins, meropenem, amikacins, and cefoperazone-sulbactam. [37]

Acinetobacter is a group of opportunistic microorganisms that usually affects hospitalized people. It is notorious for its widespread resistance to commonly used antibiotics. In our study, its isolates were sensitive only to cefoperazone-sulbactam and colistin. These findings are similar to another study in Iran by Ghaismian R et al., who conducted the study in ICU patients. [38] Similar results were also found in India by Islahi S et al. [39]

Most of the enterococcus faecalis isolates were sensitive to co-amoxiclav, linezolid, quinolones, carbapenems and piperacillin-tazobactam. But they were resistant to ceftriaxone, cefotaxime, doxycycline and co-trimoxazole. These results are similar to the results of a study by Anvarinejad et al. [40]

The majority of our patients lost to follow-ups. Therefore, we were unaware of the ultimate fate of their ulcers. In addition, many patients were already on antibiotics, which could change the culture and sensitivity results.

CONCLUSION

The majority of microorganisms in our set are gram-negative rod and staphylococcus aureus. The most effective antibiotics against gram-negative bacteria are cefoperazone-sulbactam, piperacillin-tazobactam, meropenem, and amikacin. In contrast, the most effective antibiotics against gram-positive organisms are vancomycin, linezolid, teicoplanin and chloramphenicol. Many patients use inappropriate antibiotics before they seek medical advice. This practice has increased the emergence of antibiotic-resistant strains of bacteria. Therefore, the combination of appropriate antibiotics should be started in diabetic foot ulcers before the results of culture reports are available. Appropriate empirical antibiotics can be recommended where pus culture facilities are not available.

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Following authors have made substantial contributions to the manuscript as under

Abbas G:	Conceiving the idea, data collection
Khan HA:	Literature search, writing and Statistical analysis
Iqbal S:	Data collection and review
Nabi A:	Literature search and review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

CLINICAL TEACHERS AS ROLE MODELS: PERCEPTION OF UNDERGRADUATE MEDICAL STUDENTS IN MEDICAL COLLEGES OF PAKISTAN USING ROLE MODEL APPERCEPTION TOOL

Maria Khan[1], Brekhna Jamil[2], Fatima Muhammad[3], Nazish Bilal[4], Bilqis Hasan[3]

[1]Department of Pathology, Peshawar Institute of Cardiology, Peshawar - Pakistan

[2]Institute of Health Profession Education & Research, Khyber Medical University, Peshawar - Pakistan

[3]Department of Medical Education, North West School of Medicine, Peshawar - Pakistan

[4]Department of Medical Education, Rehman Medical College, Peshawar - Pakistan

ABSTRACT

Objective: This study aimed to determine medical students' perceptions of their clinical teachers as role models during the clinical years of a medical program.

Materials and Methods: In this cross-sectional study, a pre-validated questionnaire, Role Modeling Apperception Tool was used and completed by Final year medical students selected from affiliated medical institutions of Khyber Medical University, Peshawar i.e. four graduating cohorts, comprising about 600 students. Participants were selected following universal sampling and data was analyzed for descriptive and inferential statistics.

Results: The response rate to Role Modeling Apperception Tool was 75.1% n=451. The total number of students participating in this study from Private sector medical colleges was 157 34.8% and Public Government was 294 65.2%. The mean age of the students was 23.71 years SD=0.77, Range=22-26. Male respondents comprised 42.4% n=191 and females were n=260 57.6% of the study sample. Altogether, 92.9% of students experienced positive role models while 72% had negative role models among academic staff in their medical colleges. Mostly, medical students perceived male clinical teachers as their role models in comparison to their female counterparts. Moreover, clinical teachers were more considered positive role models than basic sciences teachers. Private-sector medical college students rated their clinical teachers higher among all domains Clinical, Personal, and Teaching in comparison to Public sector medical college students. A strong positive correlation was noted among domains tested on Role Modeling Apperception Tool.

Conclusion: Clinical instructors are inveterately considered by students as their role models in medical colleges and significance are conferred on their position. Altogether, doctors with teaching roles must be cognizant of their responsibilities and their influence on the professional growth and performance of students. Eventually, components related to Personal, Clinical, and Teaching attributes were suggested as major traits perceived in role models.

Keywords: Clinical Teacher, Role model, Medical Student, Medical College

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INTRODUCTION

A considerable proportion of imminent doctors' training is devoted to erudition and teaching in a healthcare setting. [1] To shape the values, demeanors, and ethical behavior of scholars, William Osler suggested the approach of role modeling is the fundamental element. [2] Literature indicates that the transition to an excellent doctor role model entails creativity and commitment because it promotes the desire for the acquisition of knowledge, and the perfection of skills, as well as building directions for pursuing a specific field of medicine. [3] Role modeling correlates to the framework of social learning theory, and is depicted as a course during which "faculty members model and articulate expert thought processes, demonstrate clinical skills and exhibit positive professional attributes." [4, 5] Considerable literature exists on the clinical instructor as a role model[6], as well as research, has acknowledged its impact on medical students concerning future career choices, standards of professional attitudes, and their reputation among different subjects. [7] Usually, students learn by observation and imitation therefore us-

Correspondence
Dr. Maria Khan
Assistant Professor
Department of Pathology, Peshawar Institute of Cardiology, Peshawar - Pakistan
Cell: +92-331-9111986
Email: kmaria22@hotmail.com
Date Received: 16-09-2022
Date Revised: 06-02-2023
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ing the most powerful teaching strategy of role modeling, clinical teachers play a crucial part in shaping, mentoring, coaching, and assisting future clinicians. [8, 9] Whether, the on-the-job and formal teaching sessions in small discussion or lecture theatres, role modeling has been held as one of the twelve roles of clinical teachers, which directly impact students' professional learning. [10] As illustrated in one study, 90 percent of students choose a role model while still in medical college. [11] However, a significant dissimilarity had been observed between males and females in ranking for key role model attributions. [12]

Customarily, medical institutions in Pakistan are ensuing traditional curricula, formal links, and existent hierarchal schemes among teachers and students resulting in the mere acquisition of technical skills and medical knowledge in clinical training programs. [13, 14] The fundamental standards of medical professionalism linked to patient care are empathy, compassion, altruism, and honesty. Therefore, the Association of American Medical Colleges AAMC in 1999, demanded medical institutions instill attributes of professionalism in the core curriculum of medical education15. Likewise, the Royal College of Physicians and Surgeons, Canada CANMEDS established the core competencies for a medical professional, with role modeling being part of professionalism and care of self. [16] Importantly recognized characteristics by students in clinician role models were an expression of enthusiasm for specialty; profound clinical reasoning skills; establishing a close doctor-patient relationship; the skill of actively engaging students; incisive communication with students; as well as having personality, clinical competence, teaching ability, on the contrary, research achievements and academic title were of minimum significance. [17]

Generally, tools assessing the attributes of clinical educators are available but unevenly comprehend items on role modeling, as result lacking specificity to categorize key features of role models. 18 Notably, clinical educators as role models have infrequently been appraised in medical colleges outside the USA and the European continent. Nonetheless, limited data regarding students' perspectives on role model identification, and its impact on medical institutions across Pakistan is available, where cultural values and social configuration are in contrast to the Occident world. [19, 20] Hence, substantial influence of role models exists in a clinical and educational environment as well as their commendable influence on students' identity formation and professional, an attempt is undertaken to fill the gap using the Role Model Apperception Tool RoMAT, established and subsequently validated by Jochemsen-van der Leeuw et al. [21, 22] It consists of two components for evaluating the positive and negative role modeling behaviors in terms of Caring attitude and Effectiveness, eventually grading items such as teaching, personal and clinical attributes.

As evident, role models help in fostering the career of young doctors, therefore, it is imperative to recognize their characteristics. [23] The results of this research can be adopted; to implement a curriculum and its needs assessment by staff members; serve as a feedback tool to clinical tutors, appoint or promote a faculty member, or during the planning of staff development programs. [10, 24] Indeed little is known regarding the attributes of a clinician role model from the medical undergraduate's perspectives in a Pakistani context, therefore, the study aimed to assess the perspectives of undergraduate students regarding role model's attributes/characteristics both in the course of formal and informal teaching settings using a reliable and validated questionnaire.

MATERIALS AND METHODS

The study was a quantitative cross-sectional descriptive conducted among four graduating cohorts, i.e. 451 Final year medical students from a total of four medical colleges of Peshawar, which included two private and two public sector medical colleges during July-August 2021. While students were not willing to participate, not consenting and migrating students from other medical colleges were excluded. Ethical approval DIR/KMU-EB/MS/00113 & 08/06/2021 and data collection permission letters were obtained from the ethical committee of Khyber Medical University, Peshawar, as well as, individual institutions. RoMAT Role Model Apperception Tool[22] comprised of scoring each domain clinical, teaching, personal, caring attitude, and effectiveness on a five-point Likert scale was used. Moreover, students were asked to provide perceptions regarding experiencing Role models RMs in individual settings i.e. during formal clinical teaching or other circumstances, along with mentioning the hierarchal level, they belong to e.g. Trainee medical officers, Medical officers, Assistant Professors, Associate professors, and professors.

RESULTS

A total of 451 Final-year medical students, 191 42.4% males and 260 57.6% females with a response rate of 75.1% 451 were noted. Overall students from Private sector medical colleges were 157 34.8% and Public Government 294 65.2% with a mean age was 23.71 years, SD=0.77, Range= 22-26. In response to a question on the number of role models encountered by each student during undergraduate years, n=93 20.6% students selected "1", 98 21.7% students chose "2", 95 21.10% chose option "3", 89 19.70% mentioned, "more than 3", while n=76 16.90% students said to have encountered "none" no role models at all. In response to the presence of positive role models in each medical college, a total of 419 92.9% of students chose "Yes", while 32 7.1% replied "No". Next, about experiencing negative role models' students in their medical colleges, a total of 320 71% chose the option of

"Yes", while 131 29% replied "No". Using the Chi-square to compare two categorical variables type of medical college and encountering positive and negative role models. In table 1, a significant association was observed between the two variables ($p < 0.05$).

There was statistically no significant difference between the genders of students while experiencing positive and negative role models at their respective medical colleges. 174 (91.1%) male students and 245 (94.2%) females have experienced a positive role model, while 136 (71.2 %) males and 184 (70.8%) females have experienced a negative role model during the undergraduate years of MBBS. The majority of medical students 187 (41.5%) chose male clinical teachers as their role models (Table 2)

In response to perceptions of medical students regarding the location/site where role modeling usually occurs, the maximum number of students selected clinical wards n=209 (46.3%, $p<0.001$) as a primary site for experiencing role modeling; next 105 (23.3%) students chose Classrooms; while n=72 (16%) selected OPD and 65 (14.4%) selected the option of 'others'. In response to the appointment or designation of role models, the majority of medical students chose full Professors, n= 202 (44.8%), Assistant Professor= 146 (32.4%) Associate Professor= 80 (17.7%) trainee medical officer= 14 (3.1%), and Medical Officer=9 (2%).

According to study participants, the majority of positive role models were affiliated with the specialty of Medicine 218 (29.9%), Surgery 97 (13.3%), and Ophthalmology 81 (11.1%), respectively. In contrast, most of the negative role models belonged to the specialty of Gynecology n=107 (20.2%). The overall mean score obtained and standard deviation of each component of the Caring and Effectiveness domain of RoMAT are shown in Figure 1.

The majority of students (66.9%) in private medical colleges rated clinical teachers higher in Clinical components, whereas 51.7% of students in public medical colleges scored the average. For the teaching domain, 56.7% and 54.4% rated their clinical teachers as average in private and public medical colleges, respectively. Regarding personal attributes, 58% of students from private medical colleges and 51.7% of Public sector medical colleges rated their clinical teachers as average.

On the whole, for the Caring attitude domain, 61.8% of private medical college students rated their teachers higher, while 52.7% were rated as average in public medical colleges. On the whole, 57.3% of students in private medical colleges rated their clinical teachers as average on the effectiveness domain, whereas 43.5% of public medical colleges' students scored them as average and 25.9% rated them as low Table 3.

Almost all domains had a positive and strong correlation with each other. Total clinical score was more strongly correlated to the caring attitude domain, r 451 = 0.87, ($p<0.001$) than to personal scorer 451 = 0.73, ($p<0.001$), and teaching scorer 451 =0.75, ($p<0.001$). The results were statistically significant for teaching score i.e. strong positive correlation was noted r= 0.90, n=451, $p < 0.001$ with effectiveness domain and caring attitude r=0.82, $p < 0.001$.

Also, a strong positive correlation was observed between the personal domain and the effectiveness component r=0.88, $p < 0.001$. To evaluate the relationship between the overall Caring attitude and Effectiveness domain among medical colleges, the results were found to be statistically significant, i.e. strong positive correlation r= 0.6, n=451, $p < 0.001$ was noted in Table 4.

Table 1: Association between Percentage of Positive PRM and Negative Role Models NRM present in Medical College

Type of Medical College	Positive role model n %		Negative Role Model n %	
	Yes	No	Yes	No
Private	70 94.6%	4 5.4%	62 83.8%	12 16.2%
	69 83.1%	14 16.9%	34 41.0%	49 59.0%
Total	139 88.5%	18 11.5%	96 61.1%	61 38.9%
Public	206 94.9%	11 5.1%	169 77.9%	48 22.1%
	74 96.1%	3 3.9%	55 71.4%	22 28.6%
Total	280 95.2%	14 4.8%	224 76.2%	70 23.8%

Table 2: Choice of Gender Role Models among Medical Students

Final Year MBBS Students	Male Role Models n %	Female Role Models n %	Both Gender Role Models n %	Total n
Male Students	98 51.3%	14 7.3%	79 41.4%	191
Female Students	89 34.2%	38 14.6%	133 51.2%	260
Total Students	187 41.5%	52 11.5%	212 47%	451

Table 3: Mean Domain score comparison between Private and Public sector medical colleges

Domain	Type of Medical College	Total Score	Mean Score	Score					
				Low n %	Average n %	High n %	p value	Standard Deviation	Standard Error of Mean
Clinical	Private	30	23.04	1 0.6%	51 32.5%	105 66.9%	<0.001	3.11	.25
	Public		20.67	18 6.1%	152 51.7%	124 42.2%		4.39	.26
Teaching	Private	55	39.57	1 0.6%	89 56.7%	67 42.7%	<0.001	4.53	.36
	Public		35.26	41 13.9%	160 54.4%	93 31.6%		8.07	.47
Personal	Private	20	14.52	7 4.5%	91 58.0%	59 37.6%	<0.001	2.47	.19
	Public		12.81	64 21.8%	152 51.7%	78 26.5%		3.41	.19
Caring Attitude	Private	50	38.10	%1.9 3	%36.3 57	%61.8 97	<0.001	4.99	.39
	Public		34.86	%6.1 18	%52.7 155	%41.2 121		6.89	.40
Effectiveness	Private	55	39.03	%1.3 2	%57.3 90	%41.4 65	<0.001	5.34	.43
	Public		33.87	%25.9 76	%43.5 128	%30.6 90		9.33	.54

Table 4: Correlation of Scores achieved among different components of RoMAT

Pearson Correlation r	Total Clinical Score r p-value	Total Teaching Score r p-value	Total Personal Score r p-value	Total Score Caring Attitude r p-value	Total Score Effectiveness r p-value
Total Clinical Score	**1**	**0.001> 0.75**	**0.001> 0.735**	0.001> 0.871	0.001> 0.75
Total Teaching Score	0.75m<0.001	1	0.001> 0.78	0.001> 0.82	0.001> 0.90
Total Personal Score	0.001> 0.73	0.001> 0.78	1	0.001> 0.69	0.001> 0.88
Total Score Caring Attitude	0.001> 0.87	0.001> 0.82	0.001> 0.69	1	0.001> 0.63
Total Score Effectiveness	0.001> 0.75	0.001> 0.90	0.001> 0.88	0.001> 0.63	1

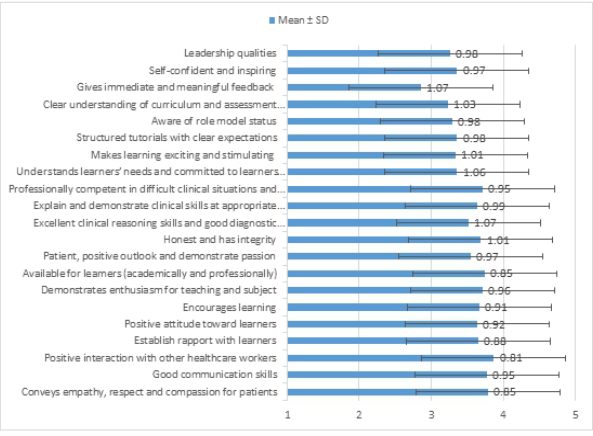

Fig 1: Mean ± SD scores for items in Effectiveness and the Caring Attitude components of RoMAT 1=Strongly disagree, 2=Disagree, 3=Neutral, 4=Agree, 5=Strongly agree

DISCUSSION

Based on the results obtained, medical students categorize the characteristics and roles of an admirable role model, which further support them in their future career lines because these role models have an impact both implicitly as well as explicitly. According to White et al., what students experienced throughout their preclinical years regarding patient-centered care was in contrast to what they truly experienced in their clinical years, as a result of this conflict, some level of compromise, transformation, and reinforcement might have changed their values. 25 Therefore, this research was conducted to observe whether undergraduate medical students, with a mean age of 23.71 years, experience PRM and NRMs during their medical education.

Provided that in one study, an average of 3.7 physicians were nominated as RMs by each medical student. [26] Contrarily, it was perceived that only 21.1% of students had three role models while 19.70% mentioned having more than three. In another study concerning the opinions of students about perceiving PRMs and NRMs, almost all students testified to having commonly witnessed both PRMSs as well as NRMs. Likewise, 92.9% of students have observed positive role models in their respective medical colleges. On the other hand, many graduating medical students did not find faculty members exhibiting skills, behaviors, and expertise that are perceived as attributes of PRMs. [27] Furthermore, earlier accounts from the 1990s in the USA, exposed the unprofessional and unethical conduct of teachers and supervisors with 90% of medical students and 92.5% of residents during training. [28] Similarly,

76.2% n=224 of students had agreed upon the presence of negative role models in their respective medical colleges. Moreover, findings from a study conducted among Japanese medical students reported a lesser proportion of medical students experiencing NRMs. Mostly due to cultural differences and social norms that made students compromise on professional values without being critical, or rarely any unprofessional teacher hired by Kagoshima University. [29]

Without a doubt, the majority of PRMs had an affiliation to major clinical specialties Medicine 29.9% and Surgery 13.3%. In contrast, the maximum number of NRMs 20.2% belonged to the specialty of Gynecology. Findings from a study on students of pharmacy and dentistry departments concerning role models indicated that respect towards colleagues, being knowledgeable, and having effective teaching abilities were considered essential traits. [30] By the same token, attributes that were scored higher by students were good communication skills and showing respect, empathy, and compassion towards patients.

Moreover, McGill University surveyed, the three most essential features for choosing a role model among residents of different specialties which included, personality, clinical expertise, and teaching aptitude [11] Likewise, the RoMAT questionnaire was used in the present study to test these three domains. Undoubtedly, two imperative traits documented by undergraduate students for clinician role models were interpersonal/communication skills, legal/ethical conduct, and ability of educational content delivery. Whereas interns ranked components of being knowledgeable and student support initiatives as the most significant qualities. [31] Presently, undergraduate students indicated teaching skills were ranking higher than the clinical and personal skills of a clinician role model. Another study by Reddy et al. reported more than 80% of students to get inadequate feedback from members of the faculty. [32] Particularly, giving meaningful and immediate feedback by the clinical teacher scored low among study participants, in the present study. Conversely, according to a majority of students, attributes concerning research abilities, professional status, and administrative services were categorized as least essential for clinician role models. [33] However, being honest, having integrity, as well positive interaction with other healthcare workers, were scored higher. Correspondingly, senior faculty members with the designation of Professor were mostly 44.8% considered as role models, while very few students chose junior doctors Medical Officers 2%.

According to students, most clinical teachers ranked lower during demonstrating clinical skills at the appropriate student level as well as most teachers were not aware of their role model status. Factually, more recent publications elaborated that empathy is to be taught and a role model at the same time. [34] Similarly, conveying empathy and compassion toward patients was considered an integral quality of a role model by study participants. Thereafter, we found that the majority of students provided higher scores to items on the 'Caring Attitude' element as opposed to the "Effectiveness" domain, these findings were comparable to a study in Amsterdam using RoMAT. [18]

Several factors may have contributed to achieving higher scores in all domains tested, as research has proved that in studies measuring questionnaire items or consisting of self-reporting methods, participants might give socially appropriate responses when inquired about sensitive topics. [35] Therefore, a tendency was shown by respondents towards selecting agree to the option, regardless of their opinion, when formulated questions have 'Agree/Disagree' options referring to the phenomenon of acquiescence bias. [36] On the other hand, comparatively homogeneous and higher scores may mirror the general satisfaction of students with the behavior of clinical teachers as role models. Probably, due to the robust emphasis on ongoing faculty development and clinical teaching skills exercises undertaken by clinical teachers currently in Peshawar, Pakistan. Our results showed significant correlations among components of personal attributes; it, therefore, raises the possibility that by strengthening and improving some traits other traits are habitually refined.

Primarily, the unanticipated outcome in most studies was the lack of provision of evidence on the gender bias among role models as perceived by students. [37] As evident and suggested from our findings, female clinician role models were rarely reported 11.5% and in addition, female students also reported male clinical teachers as their role models. Likewise, it seemed that the majority of the role models encountered by medical students were male clinical teachers, and only 7.3% of male students had a female clinical teacher as their role model. Partly, because medical faculty represents a less share of female members, as a result, females are less often perceived and pursued by students. Our outcomes as well confirmed that fewer role models were reported by female students as opposed to their male counterparts. In this sense, the dearth of female role models and professionals may prove as a significant obstacle to females' career development and accomplishments. [38]

Firstly, the likelihood that RoMAT may not have effective transferability to other institutions or educational settings due to distinctive cultures among organizations and a variable amount of contact time among teachers and students. Therefore, additional research is required to confirm the prominent elements tested in the present study that is reflected in other cultural groups, stages of medical education, and curriculum planners. Secondly, the study had a small sample size and medical colleges in one city. Therefore, research projects with large sample

sizes, involving multiple cities and countries will be essential to guarantee appropriate generalization of the study outcomes. Additionally, due to the use of a predetermined structured questionnaire in this study, it is recommended to further explore in-depth the roles, characteristics, and responsibilities of clinical teachers, Moreover, these limitations could be addressed through direct observation of role models. Further research is required to study the correlation between various aspects of role modeling to personality groups of students. Last but not least, it is suggested that research should emphasize upon identification of characteristics, and roles that clinical teachers perceive as significant for themselves.

CONCLUSION

On the whole, tools like RoMAT can be considered for reviewing the influence of training programs on clinical teachers. Even though participants had similar ethnic backgrounds and were studying the same curriculum, students in private medical colleges experience more positive role-modeling characteristics in comparison to public sector medical colleges. More male clinical teachers are perceived as role models than female clinical teachers by both male and female students. Students from private medical colleges had more positive perceptions regarding RMs compared to students from Public sector medical colleges. Although maximum students encountered both PRMs and NRMs during medical education, the results of this study revealed different numbers of both. Based on this study's findings, it is concluded that teachers ought to be more cautious of their professional and personal behavior because students expect role models who are accountable, punctual, and mindful regarding their authorized responsibilities.

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Following authors have made substantial contributions to the manuscript as under

Khan M: Concept, manuscript writing, data collection

Jamil B: Concept, Acquisition of data, critical review,

Muhammad F: Analysis and interpretation of data

Bilal N: Data collection, Statistical analysis

Hasan B: Bibliography and drafting of manuscript

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE PREVALENCE OF NEGLECTED RENAL STONE AMONG PATIENTS PRESENTED WITH ACUTE KIDNEY INJURY TO A TERTIARY CARE HOSPITAL

Humairia Bukhari, Muhammad Ikram, Shad Muhammad, Noor Mohammad, Muhammad Iqbal, Remon Ahmed, Sajidullah

Department of Nephrology, Lady Reading Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To determine the frequency of neglected renal calculi in patients with acute kidney injury.

Material and Methods: This was a descriptive study conducted at the division of nephrology, Lady Reading Hospital Peshawar, from 26/09/2021- 26/03/2022. Data was collected from 214 patients with acute kidney injury (AKI). Detailed clinical history was taken to confirm the patient did not know about the presence of previous stone disease. After confirming the acute kidney injury, bio-chemical investigations including serum urea, serum creatinine, serum calcium, urine analysis, and radiological investigation i.e. ultrasound KUB, X-ray KUB. When needed IUV and CT scan KUB was also done for the confirmation of the renal stones.

Results: In this study, the mean age was 52 years ± 13.81. Sixty-seven percent of patients were male, while 33% were female. Twelve percent of patients had neglected renal calculi, while 88% of patients didn't have neglected renal calculi.

Conclusion: Our study concluded that 12% of patients presented with Acute Kidney Injury at a tertiary care hospital had neglected renal stones.

Keywords: Neglected, renal calculi, Acute Kidney Injury.

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INTRODUCTION

A kidney stone is a solid mass formed due to the concentration of particles in the urine mostly due to metabolic abnormalities. Stone may stay in the renal parenchyma or travel down the urinary tract. [1] Kidney stone disease is more common in the general population i.e. almost affecting 1 in 11 individuals in the United States at some point in their lives and the numbers are still on the rise. [2] While in India, 12% of the population is estimated to have this disease and among them, 50% may get renal impairment at some stage of life. [3]

The incidence of calculus disease is on an increase worldwide affecting 12% of the population in Pakistan. Compared to the rising trend of this disease the treatment modalities for this disease fail to increase with the parallel speed leading to a discrepancy between the disease and the treatments. [4] Renal stone disease is more prevalent and an important cause of obstructive uropathy/nephropathy in our country and affects all age groups. [5] Unfortunately, above all the neglected renal calculi, has surfaced as another entity putting physicians and families in a mess along with the increasing misery to the patient and financial burden on the hospital resource because of late presentations of patients and complications related to it. [6]

These neglected renal stones remain a problem for countries like Pakistan as it increases the risk of renal impairments. Otherwise, uncomplicated stones can be easily managed with different noninterventional or interventional techniques. [7] Local studies show neglected and poor health infrastructure lead to acute kidney injury (AKI) in many cases. In another local study, among 278 patients, 12% were reported to have had AKI due to neglect or delay in diagnosis of renal stones and their first presentation was with AKI. Other reasons also contributed to the delay in presentation to a tertiary care unit as followed up with family physicians (19%), hakims, homeopaths, quacks (24%), and dentists (45%). Sometimes this delay has a high mortality of 10.4%, reflecting a loss of human life. [4]

Kidney stone disease is more common in men (10.6%) as compared to women (7.1%) while 8.8% of

Correspondence
Dr. Muhammad Ikram
Assistant Professor
Department of Nephrology, Lady Reading Hospital, Peshawar - Pakistan
Cell: +92-333-9354462
Email: mikramakhunzada@gmail.com
Date Received: 27-09-2021
Date Revised: 13-03-2023
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people in 20007-2010 had self-reported a kidney stone as mentioned in a recent National Health and Nutrition Examination Survey. [8]

From the review of the literature, it is evident that neglected renal calculi are one of the major causes of renal failure, particularly in developing and underdeveloped countries like Pakistan.

While the literature review also indicates the absence of such studies. The presence of such a gap provides a sound and logical rationale to conduct a study and provide data-based details about the frequency of neglected renal calculi leading to kidney injury in patients presenting to our institute and to also identify the factors contributing towards negligence of renal calculi leading to renal failure.

As research on the topic has not been conducted in our region yet, the outcome of the study will help to design better strategies to combat the problem. Furthermore, the findings of the studies will contribute to the body of literature and future courses about this disease.

MATERIAL AND METHODS

This study was carried out at the division of nephrology, Lady Reading Hospital Peshawar, from 26/09/2021- 26/03/2022, in an age group between 18-90 years of both genders. In this study, data was collected from 214 patients with acute kidney injury. Clinical history was taken to confirm the patient did not know about the presence of previous stone disease.

After confirming the acute kidney injury, biochemical investigations (including serum urea, serum creatinine, serum calcium, and urine analysis) and radiological investigation i.e ultrasound KUB, X-ray KUB, and when needed IUV and CT scan KUB were done. While patients with renal transplant (KT), end-stage renal disease (ESRD), and patients already diagnosed with kidney disease or known renal calculus disease without renal injury and admitted to the hospital for any other reason were excluded from this study. Patients with other causes of kidney injury e.g. liver diseases, urethral obstruction, vasculitis, gastroenteritis, glomerulonephritis (GN), pelvic malignancy, and lower urinary tract were excluded.

RESULTS

A total of 214 patients were included in this study. Among which 139 (65%) were in the age range 18-40 years, 58(27%) were in the age range 41-60 years, 17(8%) were in the age range 61-80 years, with a mean age of 52 years ± 13.81. While 143(67%) patients were male and 71(33%) were female.

Among 214 patients, 139(65%) had a weight ≤75 Kgs, while 75(35%) had a weight >75 Kgs and the mean weight was 75 Kgs ± 12.74. Regarding the history of previous treatment, 150(70%) patients had a history of previous treatment for renal stones, while 64(30%) patients didn't have a history of previous treatment for renal stones. Regarding the history of drug intake, 148 (69%) had a drug history, while 66 (31%) had no history of drug intake in the past for this disease (Table no.1).

Family history of a first-degree relative on dialysis or with KT among 214 patients was analyzed as 54(25%) had a family history of a first-degree relative on dialysis or with KT, while 160(75%) didn't have a family history of a first degree relative on dialysis or with KT. Neglected renal calculi among 214 patients, were analyzed (Table no.1).

Stratification of neglected renal calculi with age, weight, sex, past/present history of treatment, drug history, and family history is given (Table no. 2 and 3).

Table 1: Patients Demographics

	Age			Gender		Weight		History of treatment		History of Drug		Family History		Neglected Renal Calculi	
	18-40 Years	41-60 Years	61-80 Years	Male	Female	≤75 Kgs	>75 Kgs	Yes	No	Yes	No	Yes	No	Yes	No
Frequency	139	58	17	143	71	139	75	150	64	148	66	54	160	26	188
Percentage	65%	27%	8%	67%	33%	65%	35%	70%	30%	69%	31%	25%	75%	12%	88%

Table 2: Stratification of neglected renal calculi according to age, gender, weight

	Age						Gender				Weight			
	40-18 Years		60-41 Years		80-61 Years		Male		Female		≤75 Kgs		>75 Kgs	
Neglected Renal Calculi	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
	17	122	7	51	2	15	17	126	9	62	17	122	9	188
P Value	0.9982						0.8680				0.9607			

Table 3: Stratification of neglected renal calculi according to treatment, history of medications, first degree relative on dialysis

	Treatment of Renal Stones				History of Drug in take				First Degree Relative on dialysis / transplant			
	Yes		No		Yes		No		Yes		No	
Neglected Renal Calculi	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
	18	132	8	56	18	130	8	58	7	47	19	141
P Value												

DISCUSSION

The mean age of the patients in this study was 52 yrs ± 13.81. Sixty-seven percent were male while 33% were female. Moreover, the frequency of neglected renal calculi was 12% in patients with renal injury presenting to a tertiary care hospital in Peshawar.

As per international data of NHANES, the prevalence is more in men and the prevalence of self-reported kidney stones is more in the general population. [8] Similar results were observed in a study conducted by Mahmud HM et al, in which 152 patients with ureteric stones underwent a urological decompressive surgical procedure. AKI was present in 49 (32.2%) of patients with these neglected renal stones and those with AKI were found to be of higher age, increased weight, bilateral stones, lower ureteric stones, and with co-morbidities in comparison to those who were without AKI. For patients developing AKI, 89.7% recovered either partially (20.4 %) or completely (69.3%). The frequency of neglected renal calculi was 10% in renal injury. [9]

A study conducted by Ching YH et al reported a much different result that among adults only 1-2% of patients with kidney stones had AKI, although it may be totally different in children up to 30%. Obstructive uropathy remains the main factor of renal injury at presentation and a predictive marker for long-term prognosis and recovery. Obstructive uropathy is followed by crystalline nephropathy and has a worse outcome in regard to prognosis. Other factors such as oxalate crystals are key factors for AKI. Recently, several large cohort studies showed an association between kidney stones with CKD and ESRD. The frequency of neglected renal calculi was 8.2% in renal injury. Urological diseases, urinary tract infections, and shared underlying risk factors (e.g., diabetes, hypertension) all impact renal stones-associated CKD risk. [10]

In a study by Tang X et al, out of 1919 patients with upper urinary tract stones (UTI), with an average age of 54 ± 13.8yrs, male to female ratio of 2.59: 1, with the stone composition of calcium-containing stones 1736 (90.5%) calcium oxalate mixed with calcium phosphate stones, calcium oxalate stones 579 (30.2%), 204 (10.6%) calcium phosphate stones, and 182 (9.5%) non-calcium-containing stones, of which 21 (1.1%) were struvite stones 161 (8.4%) were uric acid stones. In this study by Tang X et al, the frequency of neglected renal calculi was 8.2% in renal injury. Calcium stones with oxalate mixed with phosphate followed by uric acid and struvite stones remained the predominant calcium stones in different studies. When renal functions were analyzed in regard to the stone composition it was obvious that calcium oxalate mixed with calcium phosphate had the highest eGFR: 73.4 ± 22.6 mL/min/1.73 m^2 in contrast to patients with uric acid stones who had the lowest eGFR: 54.1 ± 17.1 mL/min/1.73 m^2. The eGFR values were 67.0 ± 23.7 mL/min/1.73 m^2, 70.3 ± 21.5 mL/min/1.73 m^2, and 54.9 ± 18.6 mL/min/1.73 m^2 in patients with calcium phosphate, calcium oxalate, and struvite stones, respectively. It is clearly shown that the patients with calcium-containing stones (calcium phosphate and calcium oxalate) had significantly better renal function compared with those with non-calcium-containing stones (struvite and uric acid, $p < 0.01$). [11]

Due to a small sample size and single-center study, the results of this study may not be reflecting the true prevalence of this condition. Multicentre epidemiological studies of this kind may be conducted to determine the true prevalence of neglected renal stones in our population.

CONCLUSION

Our study concludes that the frequency of neglected renal calculi was 12% in patients with renal injury presenting to a tertiary care hospital in Peshawar.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Bukhari H:	Idea and writing of the manuscript.
Ikram M:	Data analysis and statistical analysis.
Muhammad S:	Data collection
Muhammad N:	Supervision of the study and data collection.
Iqbal M:	Assistance in manuscript writing
Ahmed R:	Correction and re-writing corrections.
Sajidullah:	Data collection and compilation

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE IMPACT OF COVID-19 ON THE EDUCATION OF MEDICAL STUDENTS OF FEDERAL MEDICAL COLLEGE, ISLAMABAD, PAKISTAN

Gul Mehar Javaid Bukhari[1], Hareem Binte Saleem[1], Javeria Saleem[2], Munazza Batool[2], Fatima Majeed[2], Hania Batool[1]

[1]Department of Community Medicine, Federal Medical College, Islamabad - Pakistan

[2]Department of Public health, University of Punjab, Lahore - Pakistan

ABSTRACT

Objective: The objective of this study was to assess the impact of covid-19 on the learning of medical students of Federal Medical College, Islamabad.

Materials and Methods: This descriptive cross-sectional study was conducted on 215 medical students of Federal Medical College, Islamabad from October to December 2021. A pretested validated tool was used to collect primary data from medical students via random sampling. SPSS version 25 was used for data analysis. The chi-square test was used to see the association between various variables.

Results: This study included 54.9% (118) females and 45.1% (97) males. 188 (87.4%) students reported that they were taking online classes. Most of the students, 181 (84.2%) thought that COVID-19 affected their study durations. The pandemic has caused wastage of time was reported by 155 (72.1%) students and 60 (27.9%) stated pandemic had given them extra time to clear their concepts. More than 2/3rd of the students (78.6%) were concerned about their professional examinations due to the present situation of the pandemic. Among all the respondents, 177 (82.3%) were not satisfied with this method of learning and also 184 (85.6%) students have lost interest in their studies. Most of the students 173 (80.5%) were facing difficulty in establishing the boundary between their work and home and 180 (83.7%) were missing classroom engagement.

Conclusion: Covid 19 has severely affected medical education. E-learning is not suitable for medical students as most of their learning involves practical performance and interaction with patients.

Keywords: Covid-19, medical students, medical education, online learning

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INTRODUCTION

The covid-19 outbreak was declared a pandemic by the world health organization on 11th march 2020. This deadly disease not only took the lives of millions of people globally but also disrupted the social, economic, and healthcare functioning worldwide. Worldwide lockdown and social restrictions brought unprecedented change in our lives, especially with the closure of educational institutions. To continue the educational process, learning was shifted to the online system. Traditional Medical education and clerkship were also subjected to this change in a desperate time. A US study on the impact of Covid 19 on medical education showed that the majority 74.7% of students believed that their study was adversely affected by the pandemic. Similarly, a Pakistani study conducted in various medical colleges indicated that 75.4% of students agreed that the pandemic caused time wastage in terms of their education. 76% of medical students were having online classes in a study conducted in Karachi. Delay and uncertainty of examination and clinical rotation/residency was significant stressor for medical students during this time. Clinical exposure was suspended for almost all medical undergraduates across the globe to minimize exposure to the deadly covid-19.[3] The majority (59%) of the medical students were willing to serve in the hospitals in the wake of this pandemic in a KAP study conducted in Libya. Half of the medical undergraduates agreed to volunteer for clinical service during the pandemic in an Indonesian study. 59.7% of students were satisfied with the e-learning mode and considered it as a substitute for on-campus learning since it was less time-consuming. On the other hand, most medical students didn't find e-learning much effective since it lacked teacher-student interaction.[3] Most of the medical students discouraged the idea

Correspondence
Dr. Gul Mehar Javaid Bukhari
Assistant Professor
Department of Community Medicine, Federal Medical College, Islamabad - Pakistan
Cell: +92-333-6481505
Email: drgulmehar@gmail.com
Date Received: 05-06-2022
Date Revised: 09-03-2023
Date Accepted: 18-03-20223

of the online examination and preferred to stick to the traditional pattern (62.8%).[1] About 73.6 % of students were unable to continue online classes smoothly due to technical glitches making it unfeasible for students coming from rural areas. Connectivity issue was a major hurdle faced by medical students (70%) of Rawalpindi medical university during e-learning. Internet issue was a major problem for medical students during online classes in a Pakistani study. Some students (36.4%) were worried about the distracting environment at home during online learning. A study assessing anxiety levels of medical students during covid 19 showed a higher score among those with a covid positive friend or relative. A Japanese study conducted on the same lines showed that 58.1% students were apprehensive about covid 19. A study conducted by students of Rawalpindi medical college showed that students (46.67%) from low-income family backgrounds were more likely to develop mental health issues which can be linked to the economic crisis faced during the pandemic. The objective of this study was to assess the impact of covid-19 on the learning of medical students of Federal Medical College, Islamabad.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted on medical students who were studying at a Federal Medical College in Islamabad. The sample size was 215 (calculated by the WHO calculator with a confidence level of 95%) and the study duration was three months (from October to December 2021). The sample was selected through simple random sampling (drawing lots). A pretested validated tool was used in the study. The objectives of the research were explained to each participant. The Structured questionnaires were handed over to each participant and the same was collected on the next day. Ethical approval for the study was granted by the Ethical Review Board of Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad. Informed consent was taken from all the participants and the anonymity of all the participants was ensured by not collecting any personal information. Data were secured by the Principal Investigator. SPSS version 25 was used for data analysis. In Descriptive Statistics, frequencies and percentages were computed and in Inferential Statistics, the Chi-square test was used to see the association between various variables.

RESULTS

The study constitutes 215 students of the federal medical college with equal representation of 43 each from 1st to 5th year. There were 54.9% (118) females and 45.1% (97) males. Most of the students 175 (81.4%) were from urban areas and the remaining 40 (18.6%) were representing rural areas.

Overall, most of the students, 181 (84.2%) thought that COVID-19 affected their study durations. The pandemic has caused wastage of time reported by 155 (72.1%) students and 60 (27.9%) stated pandemic had given them extra time to clear their concepts. More than 2/3rd of the students 169 (78.6%) were concerned about their professional examinations due to the present situation during the pandemic. The clinical work also suffered due to no ward rotations severely reported by 83 (38.6%) students followed by 69 (32.1%) who reported moderate effect, 31 (14.4%) said mild effect and 32 (14.9%) respondents who said clinical work had not suffered at all. There were 141 (65.6%) students who said that they should do clinical service in this situation. Most of the students 179 (83.3%) thought clinical service would impact their medical education. The information about the disease was adequately given by teachers to 106 (49.3%) students. Among all the respondents, 177 (82.3%) were not satisfied with this method of learning and also 184 (85.6%) students have lost interest in their studies.

The transition increased social media usage and so affected studies among 187 (87%) students and 165 (76.7%) students thought e-learning was not a real substitute; physical examinations could not be replaced by online as reported by 190 (88.4%) students and 192 (89.3%) concerned about future performance in the clinical rotations. Most of the students 173 (80.5%) were facing difficulty in establishing a boundary between their work and home and 180 (83.7%) were missing classroom engagement. E-learning was suitable for rural areas among only 42 (19.5%) students. The human connection with your instructors was missed by 184 (85.6%) students. Various fears by students like burnout due to overabundance of information were reported by 61 (28.4%) students, deterioration of psychological state due to negative news and events by 60 (27.9%) students, 74 (34.4%) students had difficulty studying at home in the current situation, fear of getting sick or passing on the disease to others was feared by 60 (27.9%) students. Only 05 (2.3%) students feared losing scholarships or funding, 15 (7%) students feared losing the support from their parents and 40 (18.6%) students feared losing their loved ones living abroad due to the closure of borders.

DISCUSSION

Our study showed that Covid 19 massively impacted the education (84.2%) of medical students at Federal medical college. This finding is similar to the results of a study conducted in the USA which showed 74.7% of students' medical education was affected by the pandemic.[3] Majority 87.4 % of students reported that they were taking online classes as the learning shifted from physical to online globally during the pandemic [3,4,5]. 72 % of students in this study believed that covid 19 pandemic caused a waste of time in line with the findings of a similar Pakistani study (75.4%).[4] More than 2/3rd of the students were worried about their professional exams and clinical rotation

Table 1: Association of various factors affecting Education with the gender of the students (n=215)

		Male (%)	Female (%)	Chi/p-value
Concerned about Professional Exams	Yes	70 (72.2)	99 (83.9)	4.358/0.037*
	No	27 (27.8)	19 (16.1)	
The pandemic has affected clinical work due to no ward rotations	Severe	36 (37.1)	47 (39.8)	0.047/7.995*
	Moderate	24 (24.7)	45 (38.1)	
	Mild	19 (19.6)	12 (10.2)	
	No Affect	18 (18.6)	14 (11.9)	
Online Classes	Yes	92 (94.8)	96 (81.4)	0.003/8.882*
	No	05 (5.2)	22 (18.6)	
Satisfied with E-Learning	Yes	24 (24.7)	14 (11.9)	0.014/6.068*
	No	73 (75.3)	104 (88.1)	
Students Interest in Studies	More Interested	20 (20.6)	11 (9.3)	0.019/5.506*
	Lost Interest	77 (79.4)	107 (90.7)	
E-Learning would be real substitute	Yes	33 (34)	17 (14.4)	0.001/11.475*
	No	64 (66)	101 (85.6)	
Feasible for Rural Area Students	Yes	27 (27.8)	15 (12.7)	0.005/7.746*
	No	70 (72.2)	103 (87.3)	
Difficulty of Studying at Home in current Situation	Yes	26 (26.8)	48 (40.7)	0.033/4.54*
	No	71 (73.2)	70 (59.3)	
Total		97 (100)	118 (100)	

*p-value<0.05

Table 2: Association of various factors according to the Studying Class of the students (n=215)

		1st (%)	2nd (%)	3rd (%)	4th (%)	5th (%)	Chi/p-value
Concerned about Professional Exams	Yes	37 (86)	35 (81.4)	35 (81.4)	36 (83.7)	26 (60.5)	10.857/0.028*
	No	06 (14)	08 (18.6)	08 (18.6)	07 (16.3)	17 (39.5)	
The pandemic has Effected clinical work due to no ward rotations	Severe	17 (39.5)	11 (25.6)	16 (37.2)	19 (44.2)	20 (46.5)	26.945/0.008*
	Moderate	12 (27.9)	10 (23.3)	14 (32.6)	15 (34.9)	18 (41.9)	
	Mild	05 (11.6)	08 (18.6)	06 (14.0)	08 (18.6)	04 (9.3)	
	No Effect	09 (20.9)	14 (32.6)	07 (16.3)	01 (2.3)	01 (2.3)	
Online Classes	Yes	38 (88.4)	39 (90.7)	41 (95.3)	41 (95.3)	29 (67.4)	21.009/<0.001*
	No	05 (11.6)	04 (9.3)	02 (4.7)	02 (4.7)	14 (32.6)	
Effective is the E-Learning	Quite a Lot	03 (7)	03 (7)	0	02 (4.7)	0	18.673/0.017*
	Somehow Effective	23 (53.5)	24 (55.8)	15 (34.9)	15 (34.9)	13 (30.2)	
	Not Effective at all	17 (39.5)	16 (37.2)	28 (65.1)	26 (60.5)	30 (69.8)	
Transition increased use of social media affected study	Yes	41 (95.3)	36 (83.7)	37 (86.0)	41 (95.3)	32 (74.4)	11.744/0.019*
	No	02 (4.7)	07 (16.3)	06 (14)	02 (4.7)	11 (25.6)	
E-Learning would be real substitute	Yes	13 (30.2)	14 (32.6)	11 (25.6)	09 (20.9)	03 (07)	9.903/0.042*
	No	30 (69.8)	29 (67.4)	32 (74.4)	34 (79.1)	40 (93)	
Total		43 (100)	43 (100)	43 (100)	43 (100)	43 (100)	

*p-value<0.05

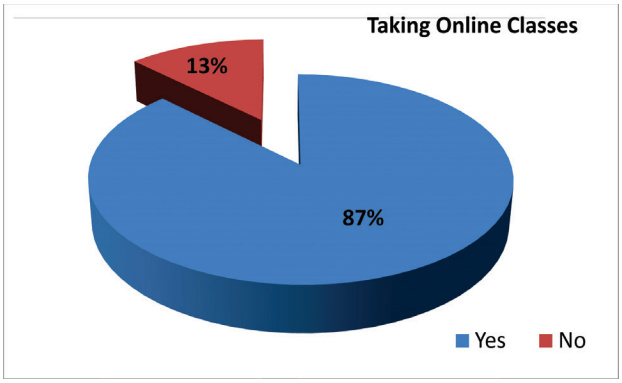

Fig 1: Frequency of students taking Online Classes

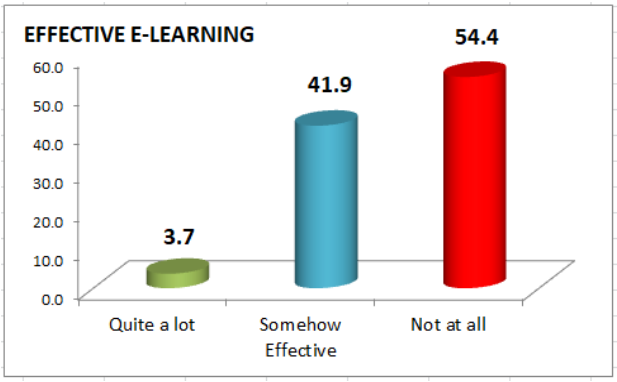

Fig 2: Perception of Effectiveness of E-Learning among Students (%)

which increased anxiety about Covid 19 in medical students similar to the conclusions of a study conducted at the University of South Carolina.[5] Majority 85.1 % of the students especially of clinical years had no clinical rotations which were similar to the situation of medical students worldwide.[7,8] 82.3%students were not satisfied with e-learning and 76.7% of students didn't consider it as a possible mode of learning in future contrary to 59 % students who believed e-learning was less time-consuming and efficient in a survey conducted in a medical university in Saudi Arabia.[10] Our findings are similar to the results of a study carried out on UK medical students which did not approve of e-learning as it lacked teacher-student interaction.[11] 81% of students considered online learning ineffective for students belonging to rural areas, this can be attributed to technical glitches and internet connectivity issues making it unfeasible to study online.[161718] 34.4% of students had difficulty in maintaining a studying atmosphere at home in accordance with 36.4% of medical students experiencing the same distraction in a research conducted in Jordan1[8]. A great number of students (87%) believed they were wasting more time on social media amidst covid pandemic hence affecting their studies, similar to the results (90.5%) of a study conducted in multiple medical colleges in Punjab. [22] 60% of the students wear fearful of catching covid or transmitting it to their friends/ family which corresponds to the findings on the psychological impact of covid 19 on medical students in various studies.[202219]Fear of income loss, scholarship, and funding were also causing stress among the students relatable to the results of Rawalpindi Medical University study.[21]

This indicates that the pandemic adversely impacted the mental health of students due to uncertainty and fear of the deadly disease itself. 83.7% of students missed classroom interaction and 85.6% missed human connection with their teachers in line with 80.7% and 82.7% findings respectively of a study conducted recently.[22] Pakistani students had a huge transition in terms of the mode of learning because online learning was very uncommon until Covid 19 was declared a pandemic.

CONCLUSION

The educational system shifting to online learning in the wake of covid 19 pandemic has posed a challenge for all levels of learning especially medical/clinical education which relies hugely on practical demonstrations and patient interaction. Alternative methods should be devised to continue medical education in times of pandemic, especially in third-world countries like Pakistan where there is a scarcity of resources and technology. The quality of medical education should not be compromised in any situation due to the delicacy of their profession.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Bukhari GMJ:	Conceptualization of study design, literature search, data analysis, data interpretation, write up, proof reading
Saleem HB:	Literature search, collection of data, drafting of the article
Saleem J:	Data analysis and interpretation
Batool M:	Data analysis and interpretation
Majeed F:	Drafting of the article, critical revision of the article
Batool H:	Collection of data, drafting of the article

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

PERSONAL, PROFESSIONAL, AND EDUCATIONAL CHALLENGES FACED BY THE POSTGRADUATE RESIDENTS OF GYNECOLOGY AND OBSTETRICS IN PESHAWAR DURING COVID-19 PANDEMIC

Fauzia Afridi[1], Ayesha Afridi[2], Arzoo Gul Bangash[1], Jamila Mehnaz Naib[1], Romana Bibi[1]

[1]Department of Gynaecology and Obstetrics, Khyber Teaching Hospital, Peshawar - Pakistan

[2]Department of Radiology, Polyclinic Hospital, Islamabad - Pakistan

ABSTRACT

Objectives: To find out the personal, professional, and educational challenges in training by the post-graduate residents of Obstetrics and Gynecology in the three tertiary care hospitals of Peshawar during the Covid-19 Pandemic.

Methods: This was a web-based cross-sectional study conducted among the postgraduate residents of Gynecology and Obstetrics in the three main teaching hospitals of Peshawar, from 1st April 2020 to 31st July 2020. A structured survey using Google forms was distributed among 98 postgraduate residents through emails and social media platforms. The challenges faced and their severity was assessed using the Likert Scale. Results were analyzed in Microsoft Excel.

Results: Total number of participants was 98, with 99% being female. The mean age was 28.3±1.8 years. Their worst fear was of the family getting infected (86.7%). Their greatest challenge was the inability to practice social distancing due to the nature of their work (85%) amidst a lack of PPEs (51%). Their training suffered due to inadequate opportunities for elective surgeries (78%).

Conclusion: Post-graduate residents in Gynaecology/Obstetrics faced substantial personal, professional, and educational challenges while training during the covid-19 pandemic.

Keywords: training, challenges, Covid-19, postgraduate residents, Obstetrics and Gynecology

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INTRODUCTION

Covid-19 has rightly been named as a 'Once-in-a-century pandemic'[1]. Worldwide, there have been more than 600 million confirmed cases and more than six million deaths, to date[2]. Pakistan has been severely affected by this pandemic too, with 1.57 million confirmed cases and more than 30,000 deaths due to covid[2,3].

When a new pandemic erupts, there is a lot of uncertainty regarding its transmissibility, severity, and prevention. Also, there is a lack of protective equipment due to the sudden, unexpected nature of a pandemic. Their impact is more pronounced on healthcare professionals who are exposed to stress, stigma, and burnout. They are at risk of infection while trying to save patients[4]. They have to modify and limit the standard of care they routinely provide to cater to the additional healthcare needs imposed by the pandemic[5,6].

Postgraduate medical/ surgical residents face an extra challenge, not only have personal challenges and professional obligations but they are also faced with the dilemma of inadequate post-graduate training opportunities in the face of lockdowns, lack of patient exposure, curtailed elective surgeries, canceled educational conferences/ training workshops, postponed specialty exams etc[7,8].

It is important to assess the personal and professional challenges, as well as challenges in training, faced by these postgraduate residents, so that timely adaptive strategies may be devised amid such crises.

MATERIAL AND METHODS

This was a web-based cross-sectional descriptive study. The period of the study was from 1st April 2020 to 31st July 2020. All the postgraduate residents of Gynecology and Obstetrics in the three main teaching hospitals of Khyber Pakhtunkhwa i.e., Khyber Teaching Hospital, Hayatabad Medical Complex Peshawar, and Lady Reading

Correspondence
Dr. Arzoo Gul Bangash
Assistant Professor,
Department of Gynaecology and Obstetrics, MTI, Khyber Teaching Hospital, Peshawar - Pakistan
Cell: +92-333-9165875
Email: arzoobangash@gmail.com
Date Received: 25-11-2022
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Date Accepted: 17-03-20223

Hospital Peshawar were included in the study. Trainees who were on maternity leave or clinical rotation in another specialty at the time of the study were excluded. Ethical approval was taken from the Institution's ethical review board (No.919/ADR/KMC). A questionnaire aimed at postgraduate residents (PGRs) of Obstetrics/Gynaecology (ObGyn) was designed on google forms and consisted of questions related to four components; demography, personal challenges, professional challenges, and educational challenges.

The questionnaire was internally and externally validated by two experts and was pilot-tested on 20 participants before being finalized. It was distributed among the postgraduate residents through social media platforms.

PGRs from the three selected hospitals and different residency years were asked to circulate them in their respective unit's WhatsApp groups(snowballing). Informed consent was taken from the participants at the start of the survey.

The sample size was 98 and the sampling technique was convenient sampling. The challenges faced and their severity was assessed using the Likert Scale. Results were analyzed in Microsoft Excel and presented as bar graphs and pie charts.

RESULTS

The total number of participants was 98. The mean age of participants was 28.3+/_1.8 years. 99% were female, 54% were married, 39%had kids, and 10% were pregnant at the time of the survey. 41% lived in a nuclear family, 31% in a joint family, and 22% lived in a hostel. The percentage of trainees in residency years 1, 2, 3, and 4 were 19.4%, 26.6% 22.4%and 26.5% respectively.

The biggest personal fear stated by most (86.7%) participants was that of the family getting infected (figure 1). Seventy-five percent claimed that the time and energy spent cleaning up after returning from work affected their personal life immensely.

This was followed by the inability to mingle with kids and family (40.8%), lack of domestic help (15%), and closure of child-care facilities/ schools (11%) (figure 2). The greatest hurdles in practicing precautionary measures against Covid-19 at the workplace were difficulty in practicing social distancing due to the practical nature of work (85%), PPE either not being available regularly (51%), or intolerable to wear due to hot weather (52%).

Half of the PGRs reported that working as healthcare workers affected their mental health significantly (figure 3) and 54% felt that they were unable to do justice with patient care due to fear of getting infected (figure 4).

Regarding educational challenges, 82% thought that their training lagged due to the covid crisis. Forty-two percent of gynae PGRs were slightly apprehensive, 18% were very apprehensive, and 25% were extremely apprehensive about their clinical/surgical skills being inadequate as compared to their predecessors. Other fears included the inability to collect data for the dissertation, the delay in the national residency exam schedule, and the possibility of an extension in the training period.

The aspects of residency affected during the covid 19 pandemic are highlighted in figure 5. Forty-three percent of PGRs felt that online teaching resources were not reasonable alternatives to pre-covid traditional teaching resources.

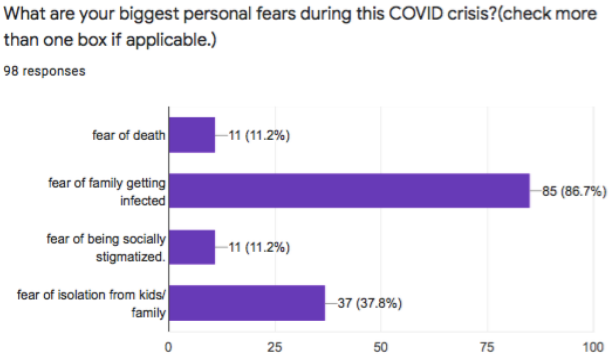

Fig 1: Personal fears during the Covid-19 crisis

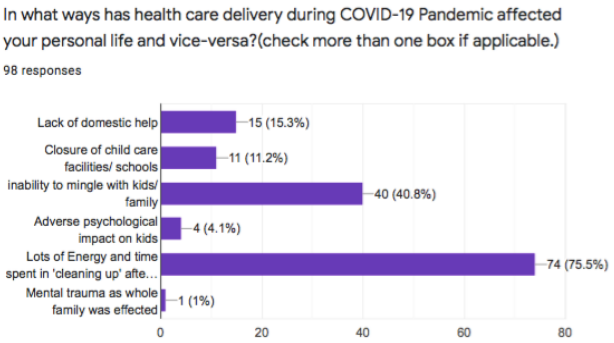

Fig 2: Impact of COVID-19 on personal life

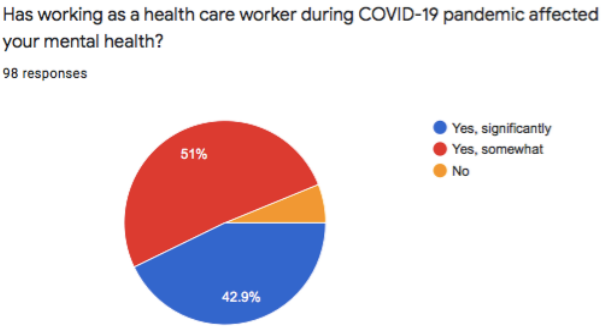

Fig 3: Impact on mental health

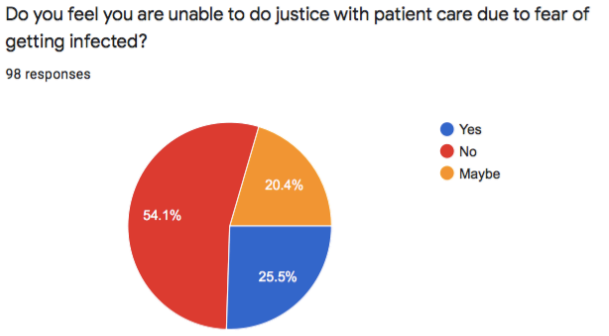

Fig 4: Impact on patient care

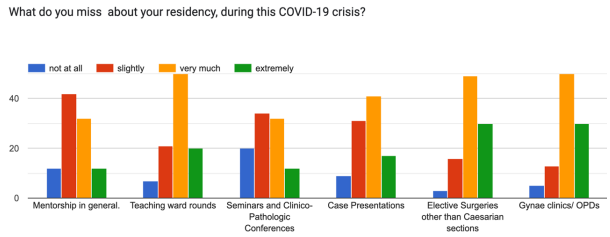

Fig 5: Impact on residency

DISCUSSION

This study highlights the impact of Covid 19 on personal and professional lives as well as challenges in training faced by the Gynae post-graduate residents (PGRs). In our study, 99% of the participants were female. This is consistent with the 98.5% proportion of females in a study conducted by Sultana R AND 86% in a study conducted in India, but in contrast with that by Gudu et al, in which 85% were male residents. [9-11]

The biggest personal fear stated by most (86.7%) participants in our study was that of the family getting infected. This is consistent with another study that has been done country-wide on healthcare workers in Pakistan[12]. Similar results were obtained in a study conducted in Southwest Ethiopia according to which the demotivating factors in working as health care workers during covid included fear of transmission to family (35%), transmission to self (28%), transmission to other patients from self (21%) and, death (13%)[13].

Our study revealed that the greatest hurdles in practicing precautionary measures against Covid-19 at the workplace were difficulty in practicing social distancing due to the practical nature of work (85%), PPE either not being available regularly (51%) or intolerable to wear due to hot weather (52%). A similar study conducted on healthcare workers in Pakistan showed that quarantine facilities and full PPEs were available in only 55% and 40% of cases, respectively, and 70% were not formally trained on the proper use of PPE[12]. A study conducted by Diego Delgado et al. in Latin America reports that 95% of the health care professionals were having access to hand sanitizer, 91% to disposable gloves, 67.3% to disposable gowns, disposable surgical face masks (83.9%), N95 face mask (56.1%), protective face shield (32%). [14] Our study reported that 85% of trainees felt that social distancing was not possible due to the nature of work. This is in contrast to a study in Turkey in which 67% of trainees reported that it was possible. [15]

In our study, 51% PGRs reported that working as healthcare workers affected their mental health significantly. In a study conducted by Sultana R, out of 268 gynecology and obstetrics residents, 66% of respondents had depression,71.6% had anxiety and 56% had stress during the COVID-19 pandemic. [9] Similar results were obtained in studies conducted in Peshawar and Italy. [16, 17]

Working as HCWs in covid crisis was daunting as 54% of respondents in our study felt that they could not do justice with patient care due to fear of getting infected. Such circumstances usually lead to complex emotional trauma and moral injury. This is consistent with the results of a study in JAMA, in which healthcare professionals expressed their experiences of moral injury during the Covid pandemic. [18]

In addition to personal and professional challenges, the gynae residents enrolled in our study also mentioned various challenges faced in their post-graduate training due to Covid 19 pandemic. In our study, 85%% were apprehensive that their clinical/ surgical skills would suffer due to the lockdown. Similar results were obtained in a study done in Peshawar on PGRs of Surgery and Allied specialties, which revealed statistically significant reductions in opportunities to observe, assist and perform surgeries. [19] Our study revealed that the aspects of training missed by Gynae PGRs included gynecological surgeries, Gynae clinics, and teaching ward rounds. A study conducted by Abdul Hafiz et al in Nigeria reported that the PGRs in surgery reported a decrease in the number of patients in the out-patient clinics (83.6%), as well as in the number of elective procedures (90.8%). [20]

In our study, 82% of residents thought that their training lagged due to the covid crisis. A similar study conducted by Ferry Boekhorst et al in Europe reported a negative impact on their training due to the COVID-19 pandemic 95% of trainees. [21]

Our study revealed that online teaching platforms were considered an inadequate alternative to pre-covid, traditional learning methodologies by 43% of residents. A similar study in India revealed that 91% of Gynae residents think that online teaching was not very useful due to problems in internet connectivity, and the inability to cater to practical training. [10]

The strength of the study lies in the fact that this is the first study with a holistic overview of the challenges faced by the gynae postgraduate residents of the three major government-sector, tertiary care hospitals of Peshawar. It was done during the peak of the pandemic when most of the private obstetric setups had curtailed/ stopped altogether maternity services, but obstetric emergency services continued in these hospitals, exposing the trainees to several challenges of unprecedented nature. Limitations of the study include its small sample size and convenient sampling technique. Also, this study was done during the initial days of covid 19 pandemic, when online learning platforms were not fully established. Much progress has been made in this regard; therefore, further studies should be done to assess whether the gap has been filled. Also, with the advent of effective covid vaccines, such studies should be duplicated in the current times to re-evaluate the impact of covid 19 on postgraduate residents.

CONCLUSION

Gynae trainees faced significant personal and professional challenges while working during the Covid-19 pandemic. Their worst fear was that of the family being infected. Their training had a considerable impact, with the highest impact on their surgical/ clinical skills.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Afridi F:	Concept, design, writing
Afridi A:	Analysis and review
Bangash AG:	Concept, critical review
Naib JM:	critical review
Bibi R:	Data collection, bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ASSESSMENT OF IMMEDIATE PERINEAL COMPLICATIONS OF NORMAL VAGINAL DELIVERY VERSUS VAGINAL DELIVERY WITH EPISIOTOMY IN TERM PREGNANCY IN A TERTIARY CARE HOSPITAL

Samdana Wahab[1], Qudsia Kamran[2], Rukhsana Karim[3], Rabia Khan[2], Maria Pervaiz[2]

[1]Department of Obstetrics and Gynecology, Peshawar Medical College / Mercy Teaching Hospital, Peshawar - Pakistan

[2]Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar - Pakistan

[3]Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar - Pakistan

ABSTRACT

Objective: To assess immediate intra and postpartum perineal complications following normal vaginal delivery versus vaginal delivery with episiotomy in term pregnancy.

Material and methods: This Cross-sectional study, was conducted in Peshawar, Lady Reading Hospital, Gynae ward from 1st November 2019 to 31st January 2020 after approval from Institutional Research Board. A total of 250 patients (125 in each group), 120 in group A with normal vaginal delivery, 115 in group B (vaginal delivery with an episiotomy), and 15 patients were excluded due to different modes of delivery (instrumental delivery/cesarean section). All patients with full-term pregnancies were included. Patients who refused to give consent or had bleeding disorders and indications for instrumental delivery or cesarean section were excluded. Non-probable convenience sampling technique, P-value <0.05, 95% confidence interval, and Chi-square test used for statistical analysis

Results: In the group, A mean age of 22 years, primigravida (PG) 84 (70%) multigravida (MG) 36 (30%) mean period of gestation (POG) 38 weeks, 96(80%) spontaneous, 24 (20%) induced labor. In group B the mean age was 21.8 years, PG 77 (66%), MG 38(33%), mean POG 41 weeks, 97 (84%) spontaneous, and 18 (15%) induced labor. Group A vaginal tears 6 (5%), cervical tears 4 (3%), mixed tears 9 (7.5%), para-urethral tears 2 (1.6%), and perineal tears 9(7.5%). Group B vaginal tears 3 (2.6%), cervical tears 3 (2.6%), mixed tears 2 (1.7%). No significant post-natal pain difference was observed in the groups.

CONCLUSION: Routine practice of episiotomy should be discouraged as no significant difference was observed in both groups.

KEYWORDS: Episiotomy, Term pregnancy, Vaginal delivery.

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INTRODUCTION

Episiotomy is defined as a minor surgical procedure to enlarge the introitus and facilitate the delivery of a baby in the second stage of labor.[1] It is a commonly performed surgical procedure practiced for a long time, although its beneficial role is controversial, still, healthcare practitioners have increased its application more to reduce maternal and baby complications. The World Health Organization (WHO) recommends an episiotomy rate of 10% and discourages its routine application.[2] According to the American College of Obstetricians and Gynecologists (ACOG), "based on the existent evidence, there is no specific situation in which episiotomy is essential, and the decision to perform this procedure should be based on clinical considerations".[3] The incidence in many European countries is approximately 10% and very high in Asia, South America, and Africa.[4]

Research studies showed that despite the recommendations for its restrictive use, still, the prevalence varies in different countries. In Romania, the incidence was 62.1%, Pasc A, et al[5] and a study conducted at Saint Paul's Hospital Millennium Medical College in Addis Ababa, also reported a very high prevalence of episiotomy, which was 65.4%, Tefera T et al.[6]

The routine practice of episiotomy is very common

Correspondence
Dr. Qudsia Kamran
Assistant Professor
Department of Obstetrics and gynecology, Lady Reading Hospital, Peshawar - Pakistan.
Cell: +92-336-0096618
Email: qudsiakamran@gmail.com
Date Received: 9-08-2022
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in developing countries as compared to developed countries. The valid reason for increasing its need is because of antenatal counseling for women to deliver their babies in hospitals. In addition, multiple factors include certain maternal and fetal indications, gestation period, labor duration, increased pelvic floor resistance, fetal birth weight, fetal distress, and expected complications like perineal tears and lacerations. Mixed tears are lacerations, that can occur spontaneously or iatrogenically, as with an episiotomy, on the perineum, cervix, vagina, and vulva.[7]

According to the Cochrane Database of Systematic Reviews 2017, an episiotomy may lead to intra and post-delivery complications such as postnatal pain and discomfort, postpartum hemorrhage, infection, prolonged hospital stay, and may cause urinary incontinence for a long period. [8] It is necessary to change the practice, especially in developing countries for unnecessary obstetrical intervention, birth attendants should be properly trained and motivated for its application, where indicated.

This study was conducted to assess the complications associated with normal vaginal delivery and vaginal delivery with episiotomy and restrict the routine practice of episiotomy in deliveries to reduce intra and postnatal maternal complications.

MATERIALS AND METHODS

This observational cross-sectional study was conducted in Peshawar, Lady Reading Hospital, Gynae B labor ward from 1st November 2019 to 31st January 2020 after approval from Institutional Ethical Research Board (IREB). The women after giving consent with term pregnancy irrespective of parity were included. Those women, who refused to give consent, had bleeding disorders, mal-presentation, instrumental delivery, or an indication for cesarean section were excluded.

The sample size was 250 patients with a 78%[2] prevalence of episiotomy, calculated by using WHO sample size calculator version 2.0, the margin of error was 5.14% along with 95% CI. There were two groups (125 patients in each group). Non- probability convenience sampling technique was used. After taking the informed written consent, a structured proforma was filled immediately after delivery by the patients admitted to the labor room irrespective of their age and parity. For the patients who refused to fill proforma because of discomfort or pain, the period was extended till their discharge from the labor ward.

The patients were equally divided into two groups. Group A underwent normal vaginal delivery without episiotomy. While group B, the decision for mediolateral episiotomy on crowning to facilitate vaginal delivery, in a woman with any parity was taken to avoid immediate complications like perineal trauma, post-operative pain, and hematoma formation. Post-natal pain was assessed by using the nominal scale instead of the Visual Analog Scale (VAS) charts.[9]

For statistical data analysis, the statistical package of Social Sciences (SPSS) version 20 was used, and the results were presented as frequencies and percentages for qualitative variables such as parity status and complications. Mean and standard deviation was used for continuous variables like age, period of gestation, etc. Chi-square was used for categorical variables and the t-test for numerical variables with a P-value < 0.05 was considered statistically significant.

RESULTS

Out of the total of 250 patients (125 patients in each group), in Group A 120 patients, out of which 5 patients were excluded (2 patients developed fetal distress, 3 had labor dystocia) While in Group B total of 115 patients, out of which 10 patients were excluded (7 patients had cesarean due to labor dystocia and fetal distress while 3 had instrumental delivery). A total of 235 patients were assessed in the study.

as shown in table 1a and 1b no significant difference was observed in both groups. In group A, 96(80%) had spontaneous labor and 24(20%) induced, in group B, 97(84%) patients had spontaneous labor, and the rest were induced.

There was no significant difference in both groups regarding the para-urethral, vaginal, and cervical tears. There were significant differences in both groups regarding perineal tears and mixed tears, (combination of perineal, vaginal, or cervical tears) in group A there were just a few patients, perineal tears, and more mixed tears were observed (table2).

The maternal outcomes regarding post-delivery hematoma formation and prolonged stay in the hospital were not significantly different in both groups. Regarding post-delivery pain, the discomfort was observed in the few patients in the group A but the difference in outcome was not significant (table3).

DISCUSSION

The routine practice of episiotomy should be restricted in our population and only its application should be encouraged, where indicated. The results of our study demonstrate no sufficient notable difference regarding intra and post-operative immediate complications in both groups.

While comparing the mean difference in the maternal age, period of gestation, and pattern of labor between the two groups, no statistically significant difference in outcome was noted. In group 1, 96(0.80%) had spontaneous labor, and the rest were induced, while in group 2, 97(0.84%) patients had spontaneous labor and the rest

Table 1a: Quantitative Demographic Data (N = 235)

Features	Groups		t-test	P-value (%95 CI for difference)
	A	B		
	Mean ± SD	Mean ± SD		
Age in years	3.58 ± 22.04	3.7 ± 21.89	0.316	1.08-0.78-) 0.7524)
	1.01 ± 38	1.10 ± 41	0.000	0.7288-1.2712-) 7.264)

Table 1b: Qualitative Demographic Data (N = 235)

Features	Group		X^2 (1)	P-value
	A	B		
Parity				
Primigravida	84 (70)	77 (66)	0.252	0.616
>than p1	36 (30)	38 (33)		
Labor				
Spontaneous	96 (80)	97 (84)	0.756	0.400
Induced	24 (20)	18 (15)		

Table 2: Frequency of Different Tears in both Groups

Complications	Group		X^2 (1)	P-value
	A	B		
	n (%)	n (%)		
Para-urethral tear	Yes	2 (100)	0 (0)	0.164
	No	118 (50.6)	115 (49.4)	
Vaginal tears	Yes	6 (66.7)	3 (33.3)	0.340
	No	114 (50.4)	112 (49.6)	
Cervical tears	Yes	4 (57.4)	3 (42.9)	0.744
	No	116 (50.9)	112 (49.1)	
Perineal tears	Yes	9 (100)	0 (0)	0.003
	No	111 (49.1)	115 (50.9)	
Mixed tears	Yes	9 (81.8)	2 (18.2)	0.037
	No	111 (49.6)	113 (50.4)	

Table 3: Maternal outcome in terms of Hematoma formation, post-natal pain, and hospital stay in group A and B

Complications		Group		X^2 (1)	P-value
		A	B		
		n (%)	n (%)		
Post-delivery pain and discomfort	Yes	21 (17)	27 (23)	1.291	0.263
	No	99 (83)	88 (77)		
Hematoma formation: Prolong hospital stay (more than 24 hours)	Yes	8 (4.3)	5 (6.6)	0.604	0.571
	No	112 (95)	110 (93)		

were induced. A study conducted by Räisänen, S et al.[10] mentioned the common practice of episiotomy among primigravida (55% versus 12%, p≤0.001) and especially those, who were induced as compared to multigravida and with spontaneous labor (66% versus 53%, p=0.036).

Regarding the frequency of vaginal, cervical, and perineal tears, there was the least non-significant difference observed. The Argentine Episiotomy Trial Collaborative Group reported severe perineal trauma that was uncommon in both groups and was slightly less frequent in the restrictive group (1.2% vs. 1.5%). Although the frequency of perineal trauma was more in the restrictive group the complications like other perineal tears, post-delivery pain, and infection were less in the same group. Therefore, they strongly recommend the avoidance of routine use of episiotomy.[11]

The review published by Matern J[12] showed no significant differences in women sustaining perineal tears in two groups (6.1 % (7/115) in episiotomy versus 3.7% (9/243) in those not receiving episiotomy, p = 0.308.

Singh S, T. Thakur et al [13] also reported first-degree perineal tears (n=4805, 3.9%), second-degree perineal tears (n=1082, 0.9%), third and fourth-degree perineal tears (n=186, 0.2%) and cervical tear 0.08 percent in their study which is consistent with the results of our study. They also concluded that the risk of vaginal, cervical, and para-urethral tears was also approximately the same in both the routine and selective groups, except they reported an increase in the anterior tears (n=490, 0.4%) in the selective group[13]. In our study, the rate of vaginal, cervical, para-urethral, and mixed tears, were observed less frequently in women who received episiotomy. However, Vieira F et al [14] also mentioned that avoiding routine episiotomy favored the decreased chances of immediate and late complications, and the common practice of episiotomy does not prevent vaginal and perineal tearing.

Regarding post-delivery pain and hematoma formation, no significant difference was noted in both groups. While Homsi et al [15] observed the complications like increased blood loss, post-natal pain, edema, sometimes hematoma formation, infection, and dehiscence with the episiotomy is more as compared to those with the restricted group. Aziken ME et al[16] also mentioned increased post-natal perineal pain, damage to the Bartholin gland, and delayed wound healing in their study. It needs close attention to reduce the common practice of episiotomy and thus decrease the maternal morbidities

The benefits of avoiding the routine practice of episiotomy in also mentioned by Carroli G et al [17] who documented the decreased risk of less blood loss, perineal trauma, low frequency of postpartum perineal pain, hematoma formation, and the chance of infection.

While Baker et al in their study mentioned that routine episiotomy should be avoided to reduce the chance of unnecessary maternal and fetal complications[18]. The same findings were observed in a study done by Gun I et al[19] who reported that routine episiotomy application did not reduce the complications rates of urinary incontinence, perineal pain, and sexual dysfunction, and has no benefit to the newborn. However, the analysis of different studies did not demonstrate a clear difference between the perinatal outcome, duration of stay in the hospital, and maternal satisfaction level in both groups.

This study helped in understanding the patient's complications associated with the application of episiotomy which will help in conducting interventional studies. The limitation of this study was that it was a single-center study with a small sample size.

CONCLUSION

Based on the results of this study, it is concluded that episiotomy should be carried out, only when considered to be essential or when anticipating the chances of pelvic floor damage and its consequences like vaginal, para-urethral, and perineal tears. In our study, there was no significant difference in the outcome of patients in both groups. Moreover, the data regarding the routine practice of episiotomy in preventing complications is also unclear and needs further studies.

The routine practice of episiotomy should be discouraged to improve the well-being and quality of life of a woman. There should be proper antenatal counseling regarding the intra and post-natal complications with and without episiotomy. Training awareness programs can be frequently arranged regarding the benefits of normal vaginal delivery versus vaginal delivery with routine practice of episiotomy and its complications, especially for traditional birth attendants and healthcare workers and its routine practice should be strongly discouraged.

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Following authors have made substantial contributions to the manuscript as under

Wahab S:	Concept, Design, and drafting of initial manuscript
Kamran Q:	Acquisition and critical review
Karim R:	Analysis and interpretation of data
Khan R:	Data collection
Pervaiz M:	Bibliography and proofreading

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

CAN OUT-PATIENT DEPARTMENT OF A TERTIARY CARE HOSPITAL PROVIDE AN INSIGHT INTO THE PREVALENCE OF COMMONEST DERMATOSES?

Abdur Rahim Khan[1], Sara Riaz Khan[1], Fahad Faizullah[1], Durdana Jalal[1]

[1]Department of Dermatology, Hayatabad Medical Complex, Peshawar - Pakistan

ABSTRACT

Objective: To determine the frequency of five commonest dermatoses among patients presenting to the Dermatology outpatient department (OPD) of a tertiary care hospital.

Meterials and Methods: This cross-sectional study was conducted in the department of Dermatology Hayatabad Medical Complex (HMC), Peshawar, KP, from January 1st, 2021 to 31st December 2021. Non-probability consecutive sampling technique was used. Ethical approval was taken from the hospital's ethical committee. Patients of either gender or age were included in this study. The diagnosis was classified according to the International Classification of Diseases (ICD-10). Statistical analysis was performed using SPSS version 22.0.

Results: A total of 4807 patients were registered for this study. Male patients outnumbered females. The maximum number of patients were 20 to 29 years old. Eczema was the commonest disease, followed by acne. Three hundred eighteen patients, whose diagnosis could not be ascertained in out-patient department, were admitted for establishing a diagnosis or further investigations.

Conclusion: An outpatient department of a tertiary care hospital can provide first-hand insight into the prevalence of various dermatological conditions.

Keywords: Outpatient department, Skin diseases, Tertiary care hospital

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INTRODUCTION

Skin diseases are an important disease group in almost all communities of the world, and are influenced by both internal and external factors.[1] The commonest external factors are socioeconomic status, personal habits, geographic location, and climate.[2] Internal factors influencing skin disease are age, gender, and heredity. These factors are usually responsible for the difference in the prevalence of skin diseases among various regions.[2]

Data regarding the prevalence of any disease, including skin diseases, is essential for planning both preventive and therapeutic healthcare services. Population-based studies are useful in this context. This present study was performed in a tertiary care hospital in Peshawar, Khyber Pakhtunkhwa (KP), Pakistan, with a population of 4.26 million.[3] However Afghan refugees also live in KP in sizeable numbers and many come to Peshawar from Afghanistan for treatment purposes. If these diseases are not diagnosed timely they can be a cause of significant morbidity and have economic implications for our province.

There is limited information on the frequency of various skin diseases in our country. Therefore this particular study was designed to estimate the frequency of various skin diseases in KP. The objective of this study was to identify five dermatoses that can be most commonly seen among patients presenting to the Dermatology outpatient department (OPD) of a tertiary care hospital. The results of this study will be shared with health authorities for a large-scale study on this subject and planning prevention strategies if some preventable skin diseases were identified.

MATERIAL & METHODS

This cross-sectional study was conducted in the department of Dermatology Hayatabad Medical Complex (HMC), Peshawar, KP, from January 1st, 2021 to 31st December 2021. Ethical approval was taken from the hospital ethical committee (Ref No: 367/HEC/B&PSC/2020). A nonprobability consecutive sampling technique was used for this study. Patients of both gender and age coming

Correspondence
Dr. Abdur Rahim Khan
Associate Professor
Department of Dermatology, Hayatabad Medical Complex, Peshawar - Pakistan
Cell: +92-307-4085922
Email: dermatology_98@yahoo.com
Date Received: 17-09-2022
Date Revised: 11-12-2022
Date Accepted: 23-12-2022

to the outpatient department of the Dermatology Unit of HMC were included in this study. These patients were diagnosed by a senior consultant Dermatologist having at least five years of experience as a consultant. Where needed appropriate laboratory tests, wood's lamp examination, dermoscopy, and histopathological examinations were done for confirmation of diagnosis. The dermatoses were classified according to the International Classification of Diseases (ICD-10). Statistical analysis was performed using SPSS version 22.0

RESULTS

A total of 4807 patients were registered from only one consultation desk of the Dermatology outpatient department of the Hayat Abad medical complex. Male patients outnumbered females by 1.28:1 (Fig 1). The maximum numbers of patients were in the age range of 20 to 29 years (27.81%), while the minimum numbers of patients were in the age range of 40 to 49 years (8.94%) (Table 1). Eczema was the commonest disease seen among the enrolled patients, followed by acne, seen in 642 and 543 patients respectively (Table 2). The third most commonest dermatosis was fungal infection seen in 525 patients. Various types of bacterial infections were seen in 346 patients. It was followed by scabies which were seen in 327 patients (Table 2). Three hundred eighteen patients were seen whose diagnosis could not be ascertained in the outpatient department. Therefore these patients were either admitted for establishing a diagnosis or further investigations were advised for this purpose. Various other dermatoses seen are shown in table 2.

Table 1: Age of enrolled patients

Age range (years) N (%)	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
0-9	87	124	120	85	93	87	34	59	36	52	44	24	845 (17.57)
10-19	137	167	167	76	97	70	61	51	61	45	45	29	1007 (20.94)
20-29	126	174	201	140	168	83	78	62	82	91	85	47	1337 (27.81)
30-39	89	98	100	89	71	53	43	41	40	35	50	29	738 (15.35)
40-49	70	67	63	53	34	16	27	20	22	27	22	09	430 (8.94)
≥ 50	57	60	71	52	52	34	18	21	26	19	25	15	450 (9.36)
Total	566	691	722	495	515	343	261	254	267	269	271	153	4807 (100)

Table 2: List of diseases

	Disease	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
1	Eczema	59	100	100	84	84	42	22	23	36	45	32	13	642
2	Acne	64	74	66	58	57	38	40	20	35	37	30	23	542
3	Tinea	58	72	54	42	48	27	22	22	15	14	15	06	395
4	Candida	9	9	14	4	11	3	2	3	4	2	5	1	67
5	Versicolor	6	5	4	4	8	6	8	5	5	6	4	2	63
6	Scabies	50	51	62	22	26	24	28	13	11	14	15	11	327
7	Folliculitis	10	10	08	09	07	05	06	13	08	06	02	04	88
8	Ecthyma	2	2	2	1	2	2	0	2	1	0	3	1	18
9	Furunculosis	10	12	15	07	6	9	3	14	8	4	7	2	97
10	Sycosis	1	2	1	1	0	0	0	0	0	0	0	0	05
11	Abscess	3	6	5	1	2	0	0	3	0	0	1	0	17
12	Impetigo	5	12	7	5	7	11	5	13	10	10	2	3	90
13	Erysipelas	2	5	3	6	7	4	0	1	1	0	1	1	31

14	Viral. Ex	1	2	3	1	7	5	0	1	0	1	3	0	24
15	Warts	14	28	21	19	8	6	8	0	6	6	8	0	124
22	Chicken pox	11	03	13	04	13	15	06	01	01	02	01	01	71
23	Herpes Zoster	7	6	6	5	8	3	2	1	3	3	4	0	48
24	Herpes Simplex	2	2	5	1	0	4	0	0	2	0	2	0	18
25	Molluscum Contagiosum	1	4	6	6	2	1	1	0	1	0	0	1	23
26	Lupus Vulgaris	1	2	2	0	0	0	0	0	0	0	3	0	08
27	Melasma	10	26	40	35	33	14	14	12	17	15	09	04	229
28	Psoriasis	10	12	11	10	9	8	1	2	3	8	2	4	80
29	Seborrhoeic Dermatitis	32	38	21	19	08	06	08	00	06	06	08	00	152
30	Alopecia Areata	11	12	09	10	02	04	02	03	06	02	06	00	67
31	Diffuse Hair loss	16	21	15	11	11	05	15	04	09	10	02	05	124
32	Androgenic Alopecia	4	5	5	2	2	1	0	4	5	2	2	0	32
33	Miscellaneous	28	48	39	26	35	29	15	25	10	18	36	09	318
34	Ulcers	1	3	2	2	4	3	0	0	1	1	0	0	17
35	Peri anal fistula	1	0	0	0	0	0	0	0	0	0	0	0	1
36	Pityrosporum Folliculitis	3	1	1	2	2	1	0	0	1	0	0	1	12
37	SLE	1	3	0	1	1	1	0	0	1	0	3	1	12
38	Diabetic Dermopathy	1	0	0	0	0	0	0	1	0	1	0	0	03
39	Acute Urticaria	10	15	30	19	17	11	3	7	3	4	3	3	125
40	Chronic Urticaria	8	3	11	6	8	3	1	6	1	3	3	1	54
41	Cholinergic Urticaria	8	4	4	1	0	0	0	0	1	0	2	0	20
42	Aquagenic Urticaria	1	0	1	1	0	1	0	0	0	0	0	0	04
43	Paronychia	6	8	4	1	3	3	2	4	3	1	2	0	37
44	Infertility	6	2	12	1	4	0	0	0	1	0	2	0	28
45	Post Herpetic Neuralgia	3	0	2	5	2	1	0	1	0	0	0	0	14
46	Sex Problems	4	7	11	2	5	1	1	2	4	2	1	3	43
47	Pemphigus vulgaris	3	0	0	4	2	2	0	1	1	0	2	0	15

48	Nodular Prurigo	3	1	1	2	1	1	0	1	0	2	0	0	12
49	Pityriasis Rosea	3	2	4	0	0	3	0	1	0	0	0	2	15
50	Pediculosis capitis	3	1	5	1	1	3	1	0	0	2	0	2	19
51	Xerosis	6	6	19	3	5	3	1	0	6	0	6	3	58
52	Callus	1	2	3	0	0	0	0	0	0	0	0	0	6
53	Keloid/Hypertrophic scar	4	1	6	1	1	1	1	3	1	2	2	0	23
54	Gen. pruritus	4	7	2	3	6	2	4	0	2	1	2	0	33
55	Diabetic bullae	1	0	1	0	0	0	0	0	0	0	0	0	2
56	Fixed Drug Eruption	1	3	0	2	1	1	1	1	1	0	3	0	14
57	EM/SJS/TEN	1	1	3	0	0	0	0	2	1	2	0	0	10
58	Lichenoid drug rash	1	0	0	0	0	0	0	0	0	0	0	0	01
59	Perniosis	29	8	1	0	0	0	0	0	0	0	3	0	41
60	Dermatosis Papulosa Nigra	1	0	0	0	0	0	0	0	0	0	0	0	01
61	Cutaneous Leishmaniasis	7	9	6	3	9	1	4	1	1	3	5	3	62
62	Sebaceous Cyst	1	1	0	0	0	0	0	0	0	0	0	0	02
63	Inect Bite Reaction	3	4	6	7	7	5	2	5	5	4	1	0	49
64	Leucocytoclastic Vasculitis	1	0	0	0	0	0	0	0	0	0	0	0	01
65	Striae	1	0	3	1	0	1	0	0	0	1	0	0	07
66	Amyloidosis	3	5	5	3	4	0	0	0	1	2	0	0	23
67	Nail dystrophy	1	0	0	0	0	3	2	3	1	2	3	3	18
68	Vitiligo	2	3	7	3	7	2	1	4	6	3	1	1	40
69	Lichen Planus	8	8	20	12	07	4	4	3	6	7	7	6	92
70	Colloid Milium	2	0	0	0	0	0	0	0	0	0	0	0	2
71	Milia	0	5	2	1	2	2	0	0	0	0	1	0	13
72	Chronic granulomatous diseases	3	3	1	3	2	0	0	0	2	0	1	0	15
73	Schamb.disease	1	0	1	0	0	0	0	0	0	0	0	0	2
74	Burns	1	1	1	3	0	1	1	1	1	1	1	0	12
75	Erythema ab igne	1	0	0	0	0	0	0	0	0	00	0	0	01

76	BCC	1	2	1	2	1	1	0	1	0	1	0	2	12
77	Keratosis Pilaris	1	1	2	3	0	1	0	1	0	2	2	0	13
78	Pemphigus Herpetiformis	1	0	1	0	0	0	0	0	1	1	0	0	04
79	Hyperhydrosis	1	0	1	2	0	0	1	0	0	0	0	0	05
80	HSP	1	0	1	0	0	0	0	0	0	0	2	0	04
81	Ichthyosis	1	3	0	2	0	0	0	0	0	2	1	1	10
82	Miliaria	0	0	0	0	4	8	5	23	4	1	0	0	35
83	Erythroderma	1	0	0	0	0	0	0	0	0	1	2	0	04
84	Malanoc.naevi	2	6	1	0	5	1	0	3	1	1	1	1	22
85	Pyoderma Gagrenosum	1	0	1	0	0	0	0	0	0	0	0	0	02
86	Linear morphea	1	1	0	0	0	0	1	0	0	1	0	0	04
87	PEPregnancy	1	1	0	0	1	0	0	0	1	0	0	1	05
88	Maculopapular drug rash	1	4	7	2	2	1	0	1	1	3	4	0	28

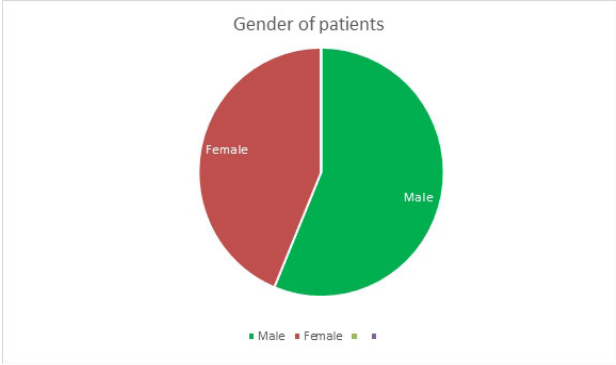

Fig 1: Gender of patients

DISCUSSION

This study was conducted in the outpatient department of HMC, Peshawar, to document the prevalence of various skin diseases in the population visiting this hospital. HMC is a tertiary care hospital in Peshawar, Khyber Pakhtunkhwa Province. Patients from all over the province visit this hospital for the treatment of various ailments. Hence statistics from this hospital give an approximate guide to the prevalence of diseases in the entire province.

Among enrolled patients, male patients were more as compared to females. Singhal and his colleagues from India reported a similar trend.[1] The plausible reason for this could be that as per the population consensus of 2017, the number of males in KP is more than females.[3] Hence there are more chances of disease burden among the male population. The second reason could be that the predominant dermatosis noticed was eczema. Since the male population of our province is mostly responsible for earning livelihood for their families hence the chances of sensitization leading to eczema are more in the male population. This fact was highlighted by Bonamonte and Kanton and their colleagues who stated that occupation along with environmental factors, socio-economic status, literacy, and age of the patients was responsible for various dermatological diseases.[4'5] So the number of male patients visiting our outpatient department was more as compared to females. Also in KP male dominance is more as compared to other provinces. Females can't seek treatment without a male accompanying them. Since males are mostly out of their homes for earning a livelihood therefore many females don't go to the hospital despite suffering from various skin diseases.

Almost 50% of the patients suffering from various skin diseases were in the third and second decades of their lives respectively (Table 1). In an International study, it was reported that the majority of their patients were in the second and fourth decades of their lives.[6] The reason for similar observation of having more patients in the second to fourth decade of their lives could be due to the reason that most of the patients in the two studies were working-class suffering from eczema. Hence more patients

were in the second and third decades of their lives because our working class mostly belongs to this age group.

Eczema was the commonest dermatosis among enrolled patients (Table 2). Earlier Asian studies also reported eczema to be the commonest skin disease.[7] The reason for higher local as well as global burden of eczema as compared to other dermatoses in Asian countries is due to a higher number of patients having allergic contact dermatitis.[7] The reason for high percentage of eczema among our patients could be that they are exposed to various occupational allergens and chemicals but they do not indulge in protective measures. Moreover, use of artificial jewelry in females and footwear allergy in both genders owing to hot and humid climate are contributing factors as well.[8] Similarly females in our province have more chances of allergic sensitization as they are responsible for cooking, washing and other house hold activities.[9] Thus females have more chances of allergic as well irritant contact dermatitis.[9]

Second commonest skin disease noted was acne (Table 2). We are aware of the fact that acne is more commonly seen in teenage and third decade. In our study majority of our enrolled patients were in the second and third decades of their lives. Hence we observed a sizeable number of patients having acne. According to study conducted by Alshammrie, acne is the commonest disease and the highest cause of disability-adjusted life year in developed countries.

It is particularly prevalent during the late adolescent period, which many sources regard as being between the ages of 15 and 18 years, most likely initiated by the onset of puberty.[10] Reason for acne in teenage is that the cellular mechanisms at play during this time frame mostly involve an increase in androgens capable of stimulating an intra-nuclear receptor and activating the proliferation of cells within the pilosebaceous unit.[11] Also diet including meats, dairy, and high glycemic index foods, can also influence this same pathway by inactivating the regulator of the androgen receptor.[12]

The 3rd most frequently seen disease was fungal infection including superficial fungal infections like pityriasis versicolor, candida, and tinea. In a Nigerian study a prevalence of superficial fungal infection was seen in a much higher percentage of their enrolled patients while it was 10.2% in our study. [13] It has been suggested that differences in the prevalence of superficial fungal infection in different regions may be due to variation in climatic and environmental conditions of the areas being studied. There was no case of tinea pedis found in this Nigerian study, unlike our study which had tinea pedis being the commonest fungal infection. This is probably due to the age group that was being studied. Tinea pedis has been found more in older age groups as documented by Khudadadi.[14]

Bacterial infections were the fourth most common disease category encountered in our outpatient department (table 2). These were localized mostly in lower limbs and a possible reason could be the presence of Staphylococcus aureus and/or beta-hemolytic streptococcus in toe webs, leg erosions or ulcers, and/or prior splenectomy. These factors independently correlate with the development of skin and soft tissue infections of the lower leg.[15] Among bacterial infections commonest was furunculosis (table 2), the reason for it could be the frequent presence of its risk factors in our community which is anemia, previous antibiotic therapy, diabetes mellitus, and poor personal hygiene.[16]

Scabies was 5th commonest disease seen in our out-patient (table 2). Nocturnal itching was the presenting complaint in almost every patient. Similarly, in a study conducted by Chandler nocturnal itching was the most frequently cited element in the patient history.[17] Frequency of scabies in our study was 6.8% which is almost equal to a study conducted by Pasha and his colleagues that showed the frequency of scabies as 7%.[18] Reason for this similarity could be the same living and environmental conditions in both regions. A study conducted by Alberfikani in Iraq showed a prevalence of 45% which is higher than our frequency through their time period and the sample of the study was smaller but a reason could be that it was conducted in a rural area where poverty could be a contributory factor.[19] Secondly this study also included quite a higher number of internally displaced persons which could be another reason for a higher prevalence.[19]

The health department should conduct workshops for doctors working in rural areas for educating those doctors so that they can treat or refer these patients to tertiary care hospitals for timely treatment of these patients.

Being a single center is the main limitation of this study. Large multicenter trials are required for the generalization of the findings.

CONCLUSION

Out-patient departments of our tertiary care hospitals can help us identify commonest dermatoses in our province. Communication of this data to our health department can help in educating our masses about prevention of these diseases through electronic and print media.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan AR: Conceiving the data, data collection

Khan SR: Literature search writting up the article, & statistical analysis

Faizullah F: Literature search

Jalal D: Bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ASSOCIATION OF SERUM VITAMIN D WITH GLYCOSYLATED HEMOGLOBIN LEVELS AND DURATION OF DISEASE IN TYPE-II DIABETES MELLITUS PATIENTS

Afsheen Mahmood[1], Naveed Afzal Khan[2], Shahzad Ahmad[3], Shahida Naz[4], Farida Ahmed[1], Abdul Jalil Khan[5]

[1]Department of Physiology, Khyber Girls Medical College, Peshawar - Pakistan

[2]Department of Medical Education, Khyber Girls Medical College, Peshawar - Pakistan

[3]Department of Medicine, North West General Hospital, Peshawar - Pakistan

[4]Department of Dermatology, Pak International Medical College, Peshawar - Pakistan

[5]Department of Family Medicine, Khyber Medical University, Peshawar - Pakistan

ABSTRACT

Objective: To find a possible association between levels of vitamin D and glycosylated hemoglobin levels in patients with type II diabetes mellitus.

Material and Methods: A cross-sectional study was conducted at a tertiary care hospital in Peshawar over six months. Diagnosed cases of Type-II diabetes mellitus were recruited through non-probability consecutive sampling. The levels of glycosylated hemoglobin and serum vitamin D levels were assessed in 219 selected patients enrolled in the study through Cobas Integra 800 and Enzyme-Linked Immunosorbent Assay respectively. Patients were divided into three categories based on increasing levels of glycosylated hemoglobin. The trend in the levels of vitamin D levels in these categories of increasing HbA1c was identified.

Results: Out of 219 Type II diabetic patients, 30.1% (66) were men while 69.9% (153) were women. The mean age was 59.48 ± 9.29 years. Similarly, HbA1c and serum vitamin D, were 9.47 ± 2.88 and 18.63 ± 16.54, respectively. Overall, 59% of the patients were Vitamin D deficient. The decrease in Vitamin D levels was associated with an increase in glycosylated hemoglobin levels (p-value 0.002).

CONCLUSION: Vitamin D deficiency in Type-II diabetes mellitus patients increases with increasing levels of glycosylated hemoglobin.

Keywords: Diabetes Mellitus, Type II Diabetes, HBA1c, Vitamin D.

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INTRODUCTION

Type-II Diabetes mellitus (DM) has been reported to be the most widely spread epidemic throughout the world in this century.[1] World Health Organization (WHO) projections reveal that the number of patients suffering from diabetes would escalate to 366 million in 2030. [2]

The economy of a country is highly affected by DM. Dealing with such a chronic condition takes a lot of time and resources from the healthcare system of the country. It is also of a great financial burden to the health system through medical bills. The work hours lost to the morbidity of DM means a decrease in the working force of the country as a whole. By 2045, 7.7% of the world's population would be debilitated by DM and its associated complications.[3] The greatest increase in the prevalence of DM is to be recorded in developing countries where healthcare resources are already scarce.[4]

These strains on the economy and medical resources caused by DM are also reflected in the population of Pakistan. A study conducted in Pakistan concluded that 9.5% rural population and 9.4% urban population in Pakistan is suffering from DM in 2007.[5] A Meta-analysis has revealed that the increased risk of T2M and GDM is associated with worsening deficiency of Vitamin D levels.[6] Vitamin D receptor activation enhances the insulin sensitivity, and secretion of insulin and protects the βcell against cy-

Correspondence
Dr. Naveed Afzal Khan
Assistant Professor
Department of Medical Education, Khyber Girls Medical College, Peshawar - Pakistan
Cell: +92-334-9085561
Email: dr.naveed@live.com
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tokines delaying the βcell maturation.[7]

Over the recent years, many studies have been conducted on the relationship of vitamin D deficiency with the duration and glycemic control of DM, however, most of the data accumulated in this regard have some level of contradiction. This inconsistency in the reported data has led to an emphasis on conducting further studies to assess the association of the levels of vitamin D in patients with DM and the factors affecting it. This study explores the possible association between levels of vitamin D and glycosylated hemoglobin levels in patients with type II diabetes mellitus.

MATERIAL AND METHODS

This cross-sectional research project was undertaken in the admitted patients and out-patient Departments (OPD) of Endocrinology and Medicine, Hayatabad Medical Complex, Peshawar 6 months after the approval of the synopsis by KMU-ASRB.

We included in the study patients suffering from type-II diabetes mellitus, older than 30 years of age presenting to the department of Endocrinology, Hayatabad Medical Complex, Peshawar.

According to the "International Osteoporosis Foundation current guidelines 2010" vitamin D Insufficiency is defined as "A serum 25-hydroxyvitamin D level from 21-29 ng/ml", vitamin D deficiency defined as "A serum 25-hydroxyvitamin D levels < 20 ng/ml" whereas, vitamin D Optimal / Healthy Level are defined as "Serum 25-hydroxyvitamin D > 30 ng/ml". [8]

The study participants included Patients who were already confirmed as type-II Diabetics or patients having fasting blood glucose levels of ≥126 mg/dl after 8 hours of fasting or patients having plasma glucose levels of ≥ 200mg/dl after 2 hours of a glucose load of 75-g anhydrous glucose load dissolved in water or, Random plasma glucose level of ≥ 200mg/dl in a patient with classic symptoms of hyperglycemia.[9] Sample size was 216 calculated by the WHO formula through Goldberg's Equation.[10] Non-probability convenient sampling technique was employed in this study.

All patients meeting the inclusion criteria and consenting to the study were approached for participation in the study. Those type-II Diabetics who were on vitamin D & calcium supplements, steroids, chemotherapeutic agents, anti-epileptics, Bisphosphonates & Orlistat were excluded. Patients having chronic kidney diseases (eGFR< 60 ml/min), chronic liver diseases, history of Rickets/Osteomalacia or received treatment for it, malabsorption syndrome, thyroid disorders (Hypo & Hyperthyroidism), parathyroid disorders (Hypo & Hyperthyroidism), diabetics who were started on Insulin from the beginning, diabetics who were diagnosed with Ketoacidosis at the time of presentation and diabetics having BMI of < than 18 were not included in the study.

A questionnaire about the patient's demographics, disease duration, and treatment record was recorded. After an informed verbal & written consent, 5ml venous blood was withdrawn with 5ml disposable syringes from the vein of the subjects under aseptic conditions. Three milliliters of the blood was used for 25 Hydroxy-vitamin D levels & 1 ml was used for creatinine estimation.

Data were analyzed using SPSS 20. Categorical variables are expressed as percentages and continuous variables are expressed in means and standard deviations.

The 25-Hydroxyvitamin D was categorized into vitamin D deficient, insufficient, and optimum/ healthy levels. HbA1c was categorized as good control (6-6.67), fair control (6.8-7.65) and poor control (>7.65).[11] The chi-square test was used to evaluate the association between categorical variables HbA1c levels and vitamin D levels. P-value of < 0.05 was considered statistically significant.

RESULTS

The study included 219 Type II diabetic patients. The mean age of the study participants was 59.48 ± 9.29 years as shown in figure 1. We reported 30.1% (66) of the patients were male while 69.9% (153) were females (table 1).

Overall 59% of the patients were Vitamin D deficient. 31% patients were severe vitamin D deficient while 28% of patients had Vitamin D Insufficiency. 41% of the total patients have optimal vitamin D levels as shown in figure 2.

In order to find out whether the effect of HBA1c on levels of vitamin D, levels of vitamin D were compared with HbA1c, Analysis revealed that vitamin D levels decrease with an increase in HbA1c levels with a p-value of 0.002 (Table 2)

DISCUSSION

Type-II DM has been reported to be the most widely spread epidemic throughout the world in this century It has grown from 30 million in 1985 to 135 million adults in 1995, soaring up to 173 million in 2002 World Health Organization projections reveal that it would reach 366 million in 2030. [5]

The European Prospective Investigation into Cancer (EPIC)-Norfolk study after conducting a meta-analysis shows that irrespective of gender, duration, sample size, and the diagnostic criterion for T2DM, low levels of vitamin D levels are associated with T2DM while some studies associate different factors like age, gender, socioeconomic status, lifestyle, BMI, dietary intake and duration of T2DM.

Table 1: Descriptive statistics of the study population

Variables	Sub group	Frequency (N)	Percent (%)
Gender	Male	66	30.1
	Female	153	69.9
Vitamin D Status	Vitamin D deficiency	89	40.6
	Vitamin D Insufficiency	61	27.9
	Vitamin D Optimal level	69	31.5
Age group	40 - 30 years	5	2.3
	60 - 41 years	99	45.2
	above 60 years	115	52.5

Table 2: Association of vitamin D levels with diabetic control

Vitamin D status	HbA1c control			p-value
	Good control	Fair control	Poor control	0.002
Vitamin D deficiency	21	21	47	
Vitamin D Insufficiency	8	25	28	
Vitamin D Optimal level	23	8	38	
Total	52	54	113	

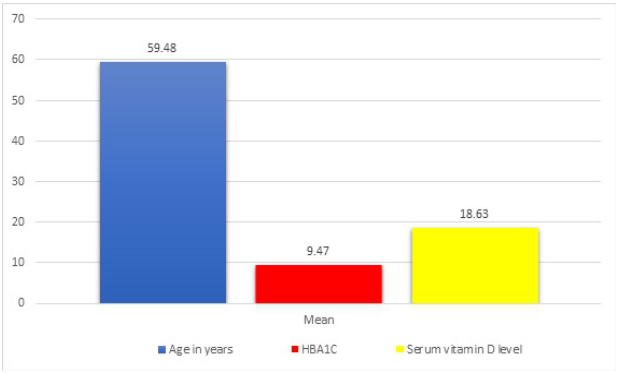

Fig 1: Demographic data of the Diabetic patients

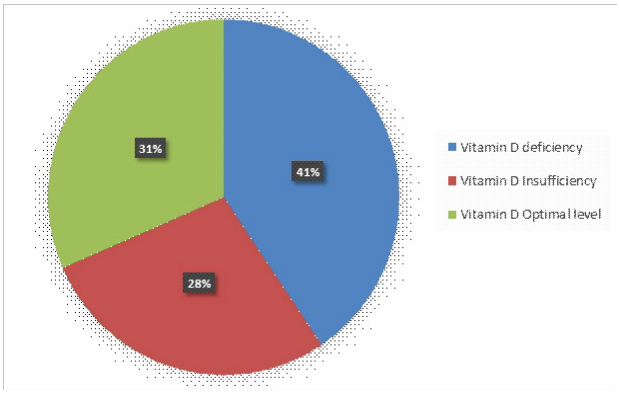

Fig 2: Vitamin D levels of study population

In our study, we have covered most of these factors and measured their significance in confounding the effect of diabetes in lowering serum vitamin D levels.[12]

In our study, we found that vitamin D deficiency is associated with T2DM. The association of vitamin D deficiency with T2DM has been found to be impacted upon by several factors. [13] We have found that vitamin D deficiency in T2DM is associated with an increase in age. We reported in our findings that vitamin D deficiency is less common in the age group of 30-40. As the age of the patients in our study increases, there is a progressive decrease in vitamin D levels (p-value 0.03). The decrease in vitamin D levels with increasing age has been depicted by several other studies.[14,15]

Our statistical analysis shows that higher levels of HBA1c have been found to be associated with a decrease in the levels of vitamin D. This association was displayed in the form of an inverse trend, the greater the levels of HBA1c, the lower the values of vitamin D were associated with it with a significant p-value of 0.002. Patients with optimum control of their sugar levels showed a normal range of serum vitamin D levels.[16,17]

CONCLUSION

Vitamin D deficiency is associated with T2DM. Vitamin D deficiency in T2DM increases with increase in age and increases with poor glycemic control showed by an increase in HBA1c. This needs to be taken into consideration in the management of T2DM patients.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Mahmood A:	Conceiving the idea, data collection
Khan NA:	Literature search writing up the article and Statistical analysis
Ahmad S:	Data collection
Naz S:	Literature search
Ahmed F:	Bibliography
Khan J:	Data collection

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

FREQUENCY OF HYPERTENSION, DIABETES MELLITUS, AND CIGARETTE SMOKING IN PATIENTS PRESENTING WITH ST-ELEVATION ACUTE MYOCARDIAL INFARCTION

Saleem Iqbal[1], Badar Mahmood[1], Hamza Ali Khan[1], Muhammad Darwesh Iqbal[1]

[1]Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objectives: The objectives of our study are to determine the frequency of hypertension, diabetes mellitus, and cigarette smoking in patients presenting with ST-elevation acute MI.

Material and methods: A descriptive cross-sectional study, was carried out in the Department of Medicine and Cardiology, Khyber Teaching Hospital, Peshawar, from June to December 2019, after proper approval from IREB, keeping a 95% confidence interval and 6% margin of error under WHO sample size calculator. The data so recorded, was analyzed in SPSS version 23. Mean ± Standard deviation was calculated for continuous variables like age. The modifiable risk factors (diabetic mellitus, hypertension, and smoking), were stratified among age and gender to see the effect modifications. Post-stratification Chi-square test was applied in which p-value ≤0.05 was considered significant.

Results: Out of 243 patients, 57% were males and the rest 43% were females. The mean age of patients was 64 years with SD ±10.69. Hypertension was recorded in 69%, cigarette smoking in 43%, and diabetic mellitus in 37% of patients presenting with acute ST-elevation myocardial infarction.

Conclusion: The frequency of modifiable risk factors i.e. hypertension, smoking, and diabetic mellitus, was quite significant, in patients presenting with acute ST-elevation myocardial infarction.

Keywords: Acute ST-elevation myocardial infarction, diabetic mellitus, hypertension, cigarette smoking.

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INTRODUCTION

Worldwide acute myocardial infarction (MI) is the leading cause of death. Its annual incidence in the United States is estimated to be 600000 new cases and 320000 recurrent attacks. Every fifth middle-aged Pakistani adult has been reported to have coronary artery disease (CAD).[1,2] Acute myocardial infarction (MI) occurs due to irreversible necrosis of cardiac muscle due to prolonged ischemia. Myocardial ischemia may present as acute coronary syndromes (ACSs), which include unstable angina (USA), ST-elevation MI (STEMI), or non–ST-elevation MI (NSTEMI). Most of the patients with ST-segment elevation MI will develop Q waves. Patients without ST-elevation myocardial ischemia will be diagnosed as unstable angina or NSTEMI depending upon the normal or elevated serum cardiac enzymes.[3,4]

Correspondence
Dr. Hamza Ali Khan
Assistant Professor
Department of Medicine, Khyber Teaching Hospital,
Peshawar - Pakistan
Cell: +92-333-9333841
Email: hamzaalikhan48.com
Date Received: 02-09-2022
Date Revised: 03-10-2022
Date Accepted: 07-03-2023

Identification of individuals at high risk of STEMI and its consequences by risk stratification remains a significant issue in the prevention and management of Acute STEMI.[5] About nine most common risk factors for obesity are diet, alcohol consumption, reduced physical activity, smoking, hypertension, diabetes mellitus, dyslipidemia, and psychosocial factors, that account for over 90% of the patients who have suffered from acute MI.[6] The INTERHEART investigators have reported that almost all people, regardless of race or ethnic group they belong, throughout the world have some of the combinations of the above risk factors. Some of these risk factors are interlinked with each other and may predispose to the development or worsening of other factors, for example, the risk of developing T2DM, increases with increasing age,[7,8]obesity,[8,9] and lack of physical activity.[8,10]

Diabetes mellitus is a component of metabolic syndrome, the other components of which include abdominal obesity, hypertension, hypertriglyceridemia, and low serum HDL cholesterol.[11] The risk of acute MI has been reported to increase by 40% by cigarette smoking 1-5 cigarettes per day.[12,13] Unfortunately, it has been observed that cigarette smoking is gradually increasing among young people and ladies in some of the many low and middle-income countries.[14] The risk of coronary events diminishes by fifty percent at one year of cessation of smoking. Hypertension is also a well-established risk factor for adverse

cardiovascular outcomes.[6,15] A study conducted in Karachi on STEMI patients revealed that 45% had hypertension, 41% had smoking, 35% had diabetes mellitus& 33% had dyslipiemia[16]. Abstaining from smoking, and controlling blood glucose, hypertension, and dyslipidemia reduces the risk.

The rationale of our study is to determine the frequency of hypertension, cigarette smoking, and diabetes mellitus in our patients presenting with acute STEMI. This will help us to make a policy for launching an effective awareness program for the prevention and long-term management of ischemic heart disease.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted in the Department of Medicine and Cardiology Khyber Teaching Hospital, Peshawar, after approval from the hospital research and ethical committee from Jan. to December 2019. We enrolled 243 consecutive patients, keeping a confidence interval of 95% and a 6% margin of error as per the WHO sample size calculator[13].

The Inclusion Criteria were all the diagnosed cases of Acute STEMI, of either gender after written informed consent. The patients who declined consent or suffered from other and multiple comorbid conditions for example chronic renal failure or chronic liver disease were excluded from our study to avoid confounders and bias in the results.

After detailed history and meticulous clinical examination, the modifiable risk factors (diabetic mellitus, hypertension, and cigarette smoking) thus recorded, were analyzed in SPSS 23. Because we had no financial grants available so we have not included other risk factors in our study. Mean ± standard deviation was calculated for continuous variables like age. Percentages and Frequencies were calculated for categorical variables like gender and modifiable risk factors.

Modifiable risk factors were stratified amongst age and gender, a post-stratification chi-square test was applied, and a p-value of ≤0.05 was considered significant.

Table 1: Age Distribution

Age	Frequency	Percentage
30-50 years	73	30%
51-60 years	80	33%
61-70 years	90	37%
Total	243	100%

RESULTS

The mean age of our patients was 64 years with SD ±10.69 (table1), 57% of patients were males while 43% were females, Diabetic mellitus was found in 90(37%), hypertension in 198(69%), and cigarette smoking in105(43%) of patients presenting with acute STEMI. Table 2,3

Table 2: Stratification of Modifiable risk factors with age (n=243)

Modifiable Risk Factors		30-50 years	51-60 years	61-70 years	Total	P value
Diabetes Mellitus	Yes	27	30	33	90	0.9937
	No	46	50	57	153	
Total		73	80	90	243	
Hypertension	Yes	50	55	63	168	0.9747
	No	23	25	27	75	
Total		73	80	90	243	
Smoking	Yes	31	35	39	105	0.9868
	No	42	45	51	138	
Total		73	80	90	243	

Table 3: Stratification of Modifiable risk Factors with gender (n=243)

Modifiable Risk Factors		Male	Female	Total	P value
Diabetes Mellitus	Yes	51	39	90	0.8971
	No	88	65	153	
Total		139	104	243	
Hypertension	Yes	96	72	168	0.9778
	No	43	32	75	
Total		139	104	243	
Smoking	Yes	105	0	105	6.1534
	No	34	104	138	
Total		139	104	243	

DISCUSSION

We included 243 patients, of ages varying from 30-70 years, the mean age of whom was 64 years with SD ±10.69. In another study which was conducted in 2013, the mean age of the patients presenting with STEMI was 53 years[13].

There is a quite significant difference in the mean ages of the patients, though both studies were done in the same country, the study was conducted seven years ago. People have become more health conscious and have changed their lifestyle and that is why seven years ago mean age of onset of ST-elevation AMI was 53 years and now has gone to 64 years, showing quite a significant improvement. In our study 139 (57%) patients were males while 104 (43%) patients were females, but the study conducted by Saleh U and Ali SS has shown that males were 81% as compared to only 19% females[13].

This may be because, over time, males have changed their lifestyle, but the sedentary lifestyle of our female population has increased in their proportion. In our study 168(69%) patients had hypertension, which is quite significantly higher than the value of 45% as reported by Saleh U and Ali SS as compared to 70.4% as reported by Adam AM et al[17].

As in 95% of cases of Hypertension, the underlying cause may be familial, so it may be possible that the patients of Saleh U and Ali SS may genetically have higher blood pressure. In our study 105 (43%) patients were smokers, which is very close to the figure of 41% reported by another local study[13] but quite high as compared to the figure of 29.2%, by Adam et al[17].

In our study, Diabetes mellitus was present in 90 (37%) patients, this figure is quite close to a figure of 35% reported by another study[13] but is significantly lower than the figure of 51.2% as reported by Adam AM et al[17]. Cigarette smoking was comparatively more common in males, while hypertension and Diabetes mellitus were more common in females. A study was conducted on 337 female patients only, with a mean age of 53 years ± 8 years, who presented with Acute Coronary Syndrome by Ashraf A et al[18].

History of cigarette smoking was present in 43 (12.7%), while diabetes mellitus was present in 63.7% and hypertension in 76.5% besides other risk factors. One can see that history of cigarette smoking was quite low in the female population of our province as compared to other risk factors.

In a study conducted in another city of the same province of Pakistan by Ahmad et al on 250 adult patients presenting with the acute coronary syndrome (ACS), 161 (64.4%) males and 89 (34.6%) females, the overall frequency of diabetes mellitus was 31.6%, 16.4% males and 15.2% females[19]. Another study from another province of Pakistan which was conducted on 605 patients having ischemic heart disease by Hussain, et al[20] reported the frequency of DM in these patients as 36.85%. The frequency of DM was 16.69% in men and 20.16% in women.

CONCLUSION

The frequency of modifiable risk factors i.e. diabetic mellitus in 37%, hypertension in 69%, and cigarette smoking in 43% in patients presenting with acute ST-elevation myocardial infarction, is quite significant. By having mass public awareness programs at various levels, these risk factors can be reduced and thus the prevalence of ischemic heart diseases can also be reduced.

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Following authors have made substantial contributions to the manuscript as under

Iqbal S:	Concept, Design, and drafting of initial manuscript
Khan HA:	Acquisition and critical review
Mahmood B:	Analysis and interpretation of data
Iqbal MD:	Data collection, Bibliography, and proofreading

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE FREQUENCY OF HYPOMAGNESAEMIA IN PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROME

Zahoor Ahmad Khan, Farman Ullah, Hameed Ullah, Salman Ahmad, Yasir Hakeem

Department of Cardiology, Hayat Abad Medical Complex, Peshawar - Pakistan

ABSTRACT

Objectives: To determine the frequency of hypomagnesemia in patients presenting with Acute Coronary Syndrome. **Materials and Methods:** A descriptive cross-sectional study was carried out at the department of cardiology, Hayat Abad medical complex, Peshawar from 07 March 2021 to 20 September 2021 after approval from the Institutional ethical board. All patients (a total of 185) admitted to the CCU with Acute Coronary Syndrome were included in the study. After informed consent, using an aseptic 3cc BD syringe, 5ml of blood was drawn and was sent for assessment of magnesium level using an automated analyzer machine. All the information, along with the patient's demographics, was recorded in the proforma attached.

Results: The maximum number of patients were in the age group 51-70 years i.e. 77.83% (144) patients. About 22.16% (41) of patients were recorded in the 35-50 years age group. Mean and SDs for age were 62+7.11 years and BMI was 27.2+1.56 kg/m2. Mean and SDs for the magnesium level was 0.79+0.04 mmoles, 44 (23.78%) patients had unstable angina, 124 (67.02%) patients had NSTEMI, and 17 (9.18%) patients had STEMI. Fifteen (8.10%) patients were found to have hypomagnesemia.

Conclusion: A significant number of patients with Acute Coronary Syndrome were found to have hypomagnesemia and this should be screened while treating such patients. Hypomagnesemia may result in deadly consequences such as coronary artery spasms, ventricular arrhythmia, and sudden death.

Keyword: Hypomagnesaemia, Parathyroid Hormone, Acute Coronary Syndrome

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INTRODUCTION

Acute coronary syndrome (ACS) refers to a group of myocardial ischemia states that include unstable angina, non-ST-elevated myocardial infarction (MI), and ST-elevated MI. ACS is associated with significant morbidity and death, as well as a significant financial load on the healthcare system. [1]

The data regarding the accurate burden of acute coronary syndrome in 3rd world countries are not available up till today. [2] The traditional modifiable risk factors of acute coronary syndrome is smoking, hypertension, dyslipidemia, diabetes mellitus, and obesity. [3] Contrary to hyponatremia, hypokalemia, and hypocalcemia, hypomagnesemia has received comparatively little attention in the medical literature despite being the body's second and fourth-most common intracellular and extracellular cations, respectively. [4]

Correspondence
Dr. Farman Ullah
Department of Cardiology, Hayat Abad Medical Complex, Peshawar - Pakistan
Cell: +92-333-9889443
Email: drfarmanullahpmc@gmail.com
Date Received: 06-10-2022
Date Revised: 18/03-2023
Date Accepted: 18-03-2023

It is essential for numerous processes that regulate cardiovascular function, including controlling vascular tone, endothelial function, and myocardial excitability. It also controls glucose and insulin metabolism. [5]

Magnesium (Mg) is necessary for life and is important for a number of biochemical and physiological activities in the body. Hospitalized patients (7–11%) frequently have hypomagnesemia, and those who also have other electrolyte disorders tend to have it more frequently. Hypomagnesemia may result in deadly consequences such as coronary artery spasms, ventricular arrhythmia, and sudden death. [6]

It also associates with increased mortality and prolonged hospitalization. [7] Anjum et al. in 2014 reported the frequency of hypomagnesemia as 8.2% in patients presenting with ACS. [8] Maciejewskiet al. 2014 reported the frequency of hypomagnesemia to be 22 % in acute coronary syndrome patients. [9]

Alzamani et al. (2006) observed the frequency of hypomagnesemia to be 12.5% of STEMI among Malaysian patients with the acute coronary syndrome. [10] However, Mir Mohammadi et al. in 2013 reported a much higher frequency of hypomagnesemia to 24.7% among Iranian patients with ACS. [11]

However, Mir Mohammadi et al. in 2013 reported a much higher frequency of hypomagnesemia to 24.7% among Iranian patients with ACS. [11]

The goal of this study is to determine how frequently hypomagnesemia occurs in ACS patients. Literature has shown that the frequency of hypomagnesemia was low (8.2%)[8] in ACS patients but controversial evidence has also been observed in the literature showing high frequency (24.7%) of hypomagnesemia in ACS patients. [11] Therefore, we aim to carry out this study to confirm the severity of the issue in the local community.

MATERIALS AND METHODS

A descriptive cross-sectional study was carried out at the department of cardiology, Hayat Abad medical complex, Peshawar from 07 March 2021 to 20 September 2021 after approval from the Institutional ethical board. All patients (a total of 185) admitted to the CCU with Acute Coronary Syndrome were included in the study. After informed consent, 5ml of blood was drawn and was sent for assessment of magnesium level using an aseptic 3cc BD syringe. All the information including ages, gender, type of acute coronary syndrome, and the levels of Mg was recorded in the proforma attached.

RESULTS

The Mean and SDs for age were 62+7.11 and BMI was 27.2+1.56. Mean and SDs for the magnesium level was 0.79+0.04. (Table No. 1). Forty-one (22.16%) patients were in the 35-50 years' age group, and 144 (77.83%) patients were in the range 51-70 years. 136 (73.51%) patients were males whereas 49 (26.48%) patients were female patients. 44 (23.78%) patients had unstable angina, 124 (67.02%) patients had NSTEMI, and 17 (9.18%) patients had STEMI. (Table No. 2). Fifteen (8.10%) patients were recorded with hypomagnesemia. Stratification of hypomagnesemia with gender, age, and type of ACS is recorded in Table 3 and Table 4. the mean age of participants was 62 years with a mean BMI of 27.2 km/m^2 and the mean S. Mg levels were 0.79 mmol/l. the frequencies of different types of Acute coronary syndrome are shown in table-1. Hypomagnesemia was seen in 15 patients (8.1%), the stratification of which has been shown in table 2 among different genders.

Table 1: The frequency and percentages for types of ACS

Type of ACS	Frequency	Percentage
Unstable	44	23.78%
NSTEMI	124	67.02%
STEMI	17	9.18%
Total	185	100%

Table 2: The stratification of Hypomagnesemia with gender

Gender	Hypomagnesaemia	Frequency	Percentage	P value
male	Yes	12	6.48%	0.552
	No	124	67.02%	
female	Yes	03	1.62%	
	No	46	24.86%	

Table 4: Stratification of hypomagnesemia with gender (n=185)

Gender	Hypomagnesaemia	Frequency	Percentage	P value
male	Yes	12	6.48%	0.552
	No	124	67.02%	
Female	Yes	03	1.62%	
	No	46	24.86%	

Table 3: Hypomagnesaemia (n=185)

Hypomagnesaemia	Frequency	Percentage
YES	15	8.10%
NO	170	91.89%
TOTAL	185	100%

DISCUSSION

Anjum et al. 2014 reported the frequency of hypomagnesemia as 8.2% in patients presenting with ACS [8]. Maciejewskiet al. 2014 reported the frequency of hypomagnesemia to be 22 % in acute coronary syndrome patients Hypomagnesaemia. [9]

Alzamani et al. (2006) observed the frequency of hypomagnesemia to be 12.5% of STEMI among Malaysian patients with acute coronary syndrome. [10] However, Mirmohammadi et al. in 2013 reported a much higher frequency of hypomagnesemia to be 24.7% among Iranian patients with ACS. [11] In the study, 44 (23.78%) patients had unstable angina, 124 (67.02%) patients had NSTEMI, and 17 (9.18%) patients had STEMI.

Fifteen (8.10%) patients were recorded with hypomagnesemia. Atherosclerosis is accelerated by magnesium shortage because it increases vascular endothelial injury, low-density lipoprotein concentration, and oxidative modification. [12, 13] It also influences myocardial infarction risk factors like blood pressure, lipid levels, and glucose metabolism. [14,15]

In my study, 44 (23.78%) patients had unstable angina, 124 (67.02%) patients had NSTEMI, and 17 (9.18%) patients had STEMI while 15 (8.10%) patients were recorded with hypomagnesemia. Moreover, prolonged magnesium deficit may be proarrhythmic, whereas magnesium has antiarrhythmic properties. [16]

Recent researchers have attributed low blood magnesium levels to a higher risk of atrial fibrillation and sudden cardiac death. [17, 18] Our findings confirmed this hypothesis by identifying an inverse relationship between serum Mg level and MACEs in patients having DES implantation for acute myocardial infarction, with a median follow-up of 24 months for ACS patients.

The physiological Ca antagonist is Mg, and in healthy humans, its blood content is remarkably stable. Endothelial function is adversely affected by low Mg levels which trigger the Ca excess that follows reperfusion. [19, 20]. Mg was revealed to be negatively associated with platelet aggregation and adenosine triphosphate release and to be implicated in platelet-dependent thrombosis. [21, 22]. Mg supplementation has been proven to reduce acute platelet-dependent thrombosis in clinical trials. [21]

Additionally, Mg can inhibit the growth of smooth muscle cells and promote the growth of endothelial cells, which may have a positive impact in the case of vascular damage brought on by stents. [23]

These might be possible explanations for the lower MACEs seen in the patients who had low magnesium levels. In my study, 44 (23.78%) patients had unstable angina, 124 (67.02%) patients had NSTEMI, and 17 (9.18%) patients had STEMI.

It still needs to be determined why the relationship was only observed in patients suffering from acute myocardial infarction and not unstable angina. The primary limitation is that the majority of the endpoints required PCI repeatedly. Second, the sample size was limited. Further studies of this kind are needed in an older population and with a high sample size in multiple centers.

CONCLUSION

A significant number of patients (up to one in 10 patients) with Acute Coronary Syndrome were found to have hypomagnesemia and this should be screened while treating such patients. Hypomagnesemia may result in deadly consequences such as coronary artery spasms, ventricular arrhythmia, and sudden death.

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Khan ZA: Concept, Design, and drafting of initial manuscript

Ullah F: Acquisition and critical review

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Hakeem Y: Data Collection

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ORIGINAL ARTICLE

WILL PHYSICAL DISTANCING BE THE NEW PERCEIVED WAY OF LIFE IN THE POST-COVID-19 PANDEMIC ERA?

Soban Qadir Khan[1], Imran Alam Moheet[2], Faraz Ahmed Farooqi[1], Nazeer Khan[3], Sara Wahab[4], Iqbal Haider[5], Noorah Al-Shayea[6], Saqib Ali[6]

[1]Department of Dental Education College of Dentistry, Imam Abdulrahman Bin Faisal University, Dammam - Saudi Arabia

[2]Department of Science of Dental Materials, Ziauddin College of Dentistry, Ziauddin University, Karachi - Pakistan

[3]Office of Research, Innovation, and Commercialization, Shifa Tameer-e-Millat University, Islamabad - Pakistan

[4]Department of Research, Jinnah Sindh Medical University, Karachi - Pakistan

[5]Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

[6]Department of Biomedical Dental Sciences, College of Dentistry, Imam Abdulrahman Bin Faisal University, Dammam - Saudi Arabia

ABSTRACT

Objective: The current study was conducted to determine whether people will keep practicing physical distancing behavior as part of their daily lives after the end of the COVID-19 pandemic.

Materials and Methods: A structured questionnaire was prepared online using "Question Pro" software for surveys, and the study was conducted electronically. The questionnaire for the study had two components, the first was related to the participant's demographics, and the other was about physical distancing questions. There were 16 questions in total.

Results: Women were more fearful/careful and would want to limit socializing than men. The religious aspect is one primary reason people will be willing to avoid physical distancing. Physical distancing was more acceptable to people with higher education levels. This physical distancing trend might affect the public transportation and tourism industry.

Conclusion: This study showed that the female gender and population with higher education are willing to follow better adherence to SOPs of the COVID-19 pandemic.

Keywords: Post-pandemic, physical distancing, lifestyle, behaviour, Pakistan

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INTRODUCTION

A Pandemic is a large-scale outbreak of infectious disease or natural disaster that spreads over a large geographical area, causing significant morbidity and mortality. The likelihood of pandemics has increased over the last century because of increased global travel, urbanization, and greater environmental exploitation[1]. Pandemics have multifaceted consequences, affecting global health, socioeconomic conditions, and political implications[2]. In the early 19th century, one-third of the world population was affected by Spanish influenza, and approximately 50 million people died due to it. A direct comparison of the current pandemic due to the Coronavirus Disease of 2019 (COVID-19) can be made to the pandemic of the previous century, Spanish influenza[3,4]. Novel Coronaviruses (n-CoV) belongs to the same family of coronaviruses that includes the Middle East Respiratory Syndrome Virus (MERS-CoV) and Severe Acute Respiratory Syndrome coronavirus (SARS-CoV)[5]. The viruses for both pandemics are pretty different. The combined effects during both pandemics are significantly similar[3,4].

Epidemiological and virologic studies reported that the primary source of transmission of COVID-19 could be transmitted through respiratory droplets, direct contact with infected people, or contact with contaminated surfaces and objects[6-10]. Pre-symptomatic transmission is the second kind of transmission in which a virus is transmitted before having any symptoms to another person[11,12]. Globally, measures to prevent the spread of COVID-19 include increasing handwashing, reducing face touching, wearing masks in public, and physical distance[13]. Countries take various measures to practice physical distancing. These measures include avoiding handshakes or physical con-

Correspondence
Dr Iqbal Haider
Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan
Cell: +92-313-9696102
Email: driqbalhaiderkth@gmail.com
Date Received: 01-11-2023
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tact, avoiding social gatherings or visiting family or friends, wearing masks and gloves, closing public and tourist places, etc[14]. Furthermore, governmental authorities ensured the availability of necessary medical supplies for health care practitioners, the general population, and patients by imposing restrictions on exporting those goods or items[15]. Hence, the government of Pakistan took steps to cut the spread of this virus. Apart from imposing physical distancing, actions were taken to stop mass gatherings by closing schools, colleges, universities, malls, and marriage halls during the pandemic[16]. Furthermore, political and non-political gatherings were also called off[17]. To the authors' best knowledge, minimal literature is available on the topic which assessed the physical distancing behavior in the post-pandemic era. However, one study published in Saudi Arabia evaluated the same idea and reported that people were keen to follow some physical distancing behaviors[18]. In addition, the study also reported that males showed less agreement to stop complying with physical distancing measures than females, even after the ease of the restrictions[18].

The current study population comprised Pakistanis, and Pakistani society can be classified as a "high-context culture" [19]. People rely heavily on nonverbal communication, such as shaking hands and hugging, as a greeting or welcome and as a sign of respect[20]. In addition, the majority of the population is Muslim, where praying five times at the Mosque is obligatory; therefore, people may avoid going outside for a walk or just moving around, but they cannot stop themselves to not go for obligatory prayers at mosque[21]. Keeping homo-sapiens socially apart is against human nature[22]. However, regular repetition of behavior results in a habitual or programmed way of life[23]. Furthermore, due to the secondary reinforcement gained, people are becoming accustomed to limited socialization and taking preventive measures. Hence, the current study's purpose was to determine whether people will keep practicing physical distancing behavior as part of their daily lives after the end of the COVID-19 pandemic or if they will return to the old ways of life.

MATERIALS AND METHODS

This cross-sectional study was conducted in Karachi, Pakistan. The period of the study was from October to December 2020. Ethical approval was obtained from the Institutional Review Board (IRB) of Jinnah Sindh Medical University (JSMU) (Ref. #: JSMU/IRB/2020/-361). Inclusion criteria were: (1) Males and females aged 18-80 years residing in Karachi, Pakistan. Exclusion criteria were: (1) those who could not read Urdu or English, (2) people who were unwilling to participate or did not provide consent. Formal ethical approval was obtained from the Institutional Review Board (IRB) of Jinnah Sindh Medical University (Ref. #: JSMU/IRB/2020/-361), per the Declaration of Helsinki.

Rao soft software was used to calculate the study sample size. With a response distribution of 50%, a margin of error of 3%, and a 95% confidence level, the required sample size for the study was calculated to be 1066. Lower than the customary margin of error of 5% was taken to increase the study's strength.

The questionnaire for the study had two components, the first was related to the participant's demographics, and the other was about physical distancing questions. Questions related to physical distancing were derived from the preventive measures provided by WHO/CDC guidelines. The questionnaire was designed in English and was translated into Urdu, and the translation person of JSMU did reverse translation to validate the translation procedure. Following the development of the questionnaire, the validity of the questionnaire was determined by conducting a pilot study. This pilot study was conducted in Karachi, and 40 responses were collected. Results from the Kappa statistic (0.79) provided acceptable results; hence no change in the questionnaire was required.

A structured questionnaire was prepared online by using "QuestionPro" software for surveys. The study was conducted electronically. There were 16 questions in total. A cover page and a summary of the study's purpose and consent were attached to the questionnaire. The participant had the option to click on "I Agree' or 'I Disagree" at the end of the consent on the cover page. The questionnaire will not proceed to the next section if the participant clicks on the "I Disagree" button. Response options for each question related to physical distancing behavior were recorded on Likert Scale (1. Never, 2. Seldom, 3. Sometimes, 4. Frequently, 5. Always). The survey link was sent to all the study's authors' WhatsApp contacts. The authors also asked their contacts to spread the link further. The submission of the completed anonymous survey implied consent.

Electronically collected data was initially entered into the Excel program and then transferred and coded in Statistical Package for Social Sciences (IBM SPSS V. 23, Chicago, USA) for analysis. Frequency distributions and bar diagrams were used for the descriptive presentation of the data. The Shapiro-Wilk test was used to look for the normality of data. Insignificant results from this test proved that the data were normally distributed. Hence, parametric tests were used for inferential data analysis. A comparison between participants' demographics with their responses to questions related to physical distancing was made by using the chi-square test. The level of significance was set as 0.05.

RESULTS

The survey link was sent to 1319 individuals, of which 910 completed and submitted the questionnaire. Hence the response rate was 69%. The mean age of the participants was 27.68 ± 8.734 (range: 18 – 80) years. The total number of female participants was 511(56%), out of

which 72 (8%) were housewives. Many study participants lived in houses with 4 to 6 adults; 407 (45%) and 1 or 2 children 357 (39%). Based on the level of education, 39 percent (349) participants belonged to undergraduate school, followed by graduate school students, 290 (33%), 225 (25%) postgraduate, and 23(3%) belonged to high school or lesser grades level. The majority of the population (based on professional status) who participated in the current study were students 411 (45%), followed by other professions 315 (35%) (e.g. accountant, pharmacist, private workers, IT professional, Banker, etc.). Doctors 50 (5%), Teachers 48 (5%), businessmen 47 (5%), and Engineers 38 (4%) constituted the remaining of the sample population. The overall percentages of agree, disagree, and neutral responses of participants are given in Figure 1. Disagreement was on the higher side in questions regarding going out for picnic/shopping, etc., using public transport, and attending public gatherings (100%, 60%, and 43%, respectively). On the contrary, the highest percentage of agreement was recorded for attending congregational prayer in Masjid/Church/Temple (56%), followed by hanging out with family/friends or relatives (50%). Hosting a gathering at home and shaking hands with family and friends had 44% agreement, respectively. Table 1 (A & B) and Table 2 (A & B) show the comparisons of the demographical characteristics of participants with their perceptions about the post-COVID lifestyle concerning friends/family interactions and outdoor activities, respectively. Overall, a significantly high proportion of males showed their agreement as compared to women about attending religious practice outside (64% vs 49%, $p < 0.0001$), handshaking with friends/colleagues (51% vs 40%, $p= 0.001$), greeting friends by hugging them (41% vs 30%, $p= 0.003$), hanging out with family/friends (57% vs 44%, $p= 0.001$) and attending a gathering of families and relatives (40% vs 32%, $p= 0.04$). Female participants' disagreement was significantly higher regarding traveling in public transport (65% vs 54%, $p =0.003$) than men.

Participants' level of education was found to be significantly associated with their perception regarding attending gatherings of family/friends or other relatives ($p= 0.001$). Level of education was also significantly associated with the usage of public transportation, fear of attending public gatherings and attending regular appointments (p – values of 0.017, 0.043 & 0.011, respectively). It was found that an increase in education reduced the fear of attending public gatherings ($p= 0.017$). Participants living with nine or more adults were significantly more likely (60%) to shake hands than those living with fewer adults in their houses ($p =0.047$). Disagreement level was found to be significantly high among the families, irrespective of the number of adults and children in the family regarding public transport (p-value = 0.023, 0.014 respectively). Almost 100% of participants disagreed with going out for entertainment (picnic, shopping mall, sports etc.).

Table 1A: Participants' demographics' association with self-perception

		I would feel normal/safe shaking hands with my family, friends, and colleagues			I would feel normal/safe greeting my family, friends, and colleagues by giving a hug			I would feel normal/safe hanging out with fami-ly/friends		
		Disagree	Neutral	Agree	Disagree	Neutral	Agree	Disagree	Neutral	Agree
		Disagree	Neutral	Agree	Disagree	Neutral	Agree	Disagree	Neutral	Agree
Gender	Male	81(20)	116(29)	202(51)	104(26)	132(33)	163(41)	71(18)	100(25)	228(57)
	Female	108(21)	201(39)	202(40)**	184(36)	172(34)	155(30)**	93(18)	192(38)	225(44)**
Education	Postgraduate	59(26)	77(34)	89(40)	80(36)	74(33)	71(32)	46(20)	71(32)	108(48)
	Graduate	64(22)	104(36)	122(42)	90(31)	110(38)	90(31)	53(18)	102(35)	134(46)
	Undergraduate	62(18)	123(35)	164(47)	106(30)	107(31)	136(39)	60(78)	107(31)	182(52)
	High school or less	3(13)	6(26)	14(61)	5(22)	6(26)	12(52)	3(13)	8(35)	12(52)
Number of Adults	1-3	74(24)	121(39)	118(38)	106(34)	103(33)	104(33)	65(21)	97(31)	150(48)
	4-6	76(19)	134(33)	197(48)	115(28)	148(36)	144(35)	62(15)	134(33)	211(52)
	7-9	26(23)	37(33)	50(44)	44(39)	30(27)	39(34)	21(19)	41(36)	51(45)
	9+	6(14)	11(26)	25(60)*	13(31)	11(26)	18(43)	8(19)	9(21)	25(60)
Number of Children	1-2	73(20)	139(39)	145(41)	119(33)	120(34)	118(33)	76(21)	112(31)	169(47)
	3-4	36(25)	42(29)	66(46)	53(37)	47(33)	44(31)	26(18)	47(33)	70(49)
	5-6	13(23)	14(25)	29(52)	18(32)	12(21)	26(46)	9(16)	17(.30)	30(54)
	6+	6(21)	9(31)	14(48)	7(24)	10(34)	12(41)	6(20)	9(31)	14(48)

* statistically significant at 0.05 level of significance

** statistically significant at 0.01 level of significance

Table 1B: Participants' demographics' association with self-perception

		I would feel normal/safe to attend gatherings of family/friends/ other rela-tives			I would feel safe hosting a friend/family gathering at my home		
		Disagree	Neutral	Agree	Disagree	Neutral	Agree
Gender	Male	117(29)	122(31)	160(40)	98(25)	129(32)	172(43)
	Female	164(32)	183(36)	164(32)*	124(24)	154(30)	233(46)
Education	Postgraduate	88(39)	67(30)	70(31)	70(31)	61(27)	94(42)
	Graduate	89(31)	110(38)	91(31)	65(22)	100(34)	125(43)
	Undergraduate	97(28)	111(32)	141(40)	79(23)	110(32)	160(46)
	High school or less	2(9)	7(30)	14(61)**	3(13)	7(30)	13(57)
Number of Adults	1-3	112(36)	101(32)	100(32)	86(27)	104(33)	123(39)
	4-6	121(30)	128(31)	158(39)	97(24)	116(29)	194(48)
	7-9	30(27)	43(38)	40(35)	22(19)	39(34)	52(64)
	9+	11(26)	17(40)	14(33)	10(24)	11(26)	21(50)
Number of Children	1-2	126(36)	114(32)	117(33)	92(26)	112(31)	153(43)
	3-4	44(31)	52(36)	48(33)	33(23)	53(36)	58(40)
	5-6	14(25)	14(25)	28(50)	12(21)	10(18)	34(60)
	6+	8(26)	11(38)	10(34)	6(21)	10(34)	13(45)

* statistically significant at 0.05 level of significance

** statistically significant at 0.01 level of significance

Table 2A: Participants' demographics' association with their perception of social activities

		I would feel normal/safe using public transportation with strangers around			I would be fearful of attending a public gathering like welcoming house parties			I would feel normal/safe to tend at my regular appointments at hospital/healthcare centres		
		Disagree	Neutral	Agree	Disagree	Neutral	Agree	Disagree	Neutral	Agree
Gender	Male	218(54)	96(24)	85(21)	100(25)	113(28)	186(46)	131(33)	129(32)	139(35)
	Female	332(65)	105(20)	73(15)**	151(30)	153(30)	207(40)	179(35)	173(34)	159(31)
Education	Postgraduate	140(63)	48(21)	36(16)	66(29)	50(22)	109(48)	83(37)	66(29)	76(34)
	Graduate	197(68)	56(19)	37(13)	79(27)	97(33)	114(39)	105(36)	108(37)	77(27)
	Undergraduate	189(54)	84(24)	76(22)	95(27)	106(30)	148(42)	110(32)	119(34)	120(34)
	High school or less	12(52)	7(30)	4(17)*	2(9)	10(43)	11(48)*	6(26)	3(13)	14(61)*
Number of Adults	1-3	197(63)	67(21)	49(16)	75(24)	88(28)	150(48)	112(36)	98(31)	103(33)
	4-6	235(58)	99(24)	72(18)	113(28)	117(29)	177(43)	133(33)	144(35)	130(32)
	7-9	79(70)	17(15)	17(15)	38(34)	30(27)	45(40)	42(37)	34(30)	37(33)
	9+	22(52)	6(14)	14(33)*	13(31)	17(40)	12(29)	13(31)	11(26)	18(43)
Number of Chil-dren	1-2	227(64)	76(21)	53(15)	95(27)	99(27)	163(46)	119(33)	129(36)	109(31)
	3-4	94(65)	30(21)	20(14)	40(28)	38(26)	66(46)	51(35)	40(28)	53(37)
	5-6	25(45)	12(21)	19(34)	24(43)	9(16)	23(41)	16(29)	19(34)	21(38)
	6+	18(62)	8(28)	3(10)*	7(24)	12(41)	10(34)	10(35)	13(45)	6(21)

* statistically significant at 0.05 level of significance

** statistically significant at 0.01 level of significance

DISCUSSION

Since the outbreak of the COVID-19 pandemic, lifestyles across the globe have been changed in many ways, including a change in working style, visiting public places, interaction with others, etc[24]. Literature has documented the impact on physical and mental health due to lifestyle medication from this pandemic[25,26]. However, literature is scarce regarding the information on post-pandemic perceived lifestyle. Hence, this study was designed to evaluate the perceived post-pandemic lifestyle among the people living in Pakistan.

In the pre-designed questionnaire for this study,

Table 2B: Participants' demographics' association with their perception of social activities

		I would feel normal/safe to attend my congrega-tional prayer in Masjid/Church/Temple			I would prefer to entertain myself by going to picnic spots/ shopping malls/din-ing out
		Disagree	Neutral	Agree	Disagree
Gender	Male	75(18)	68(17)	256(64)	399(44)
	Female	148(29)	111(22)	251(49)**	511(56)
Education	Postgraduate	65(29)	44(20)	115(51)	225(25)
	Graduate	65(22)	60(21)	165(57)	290(33)
	Undergraduate	85(24)	73(21)	191(55)	349(39)
	High school or less	5(22)	2(9)	16(70)	23(3)
Number of Adults	1-3	95(30)	67(21)	151(48)	313(36)
	4-6	93(23)	74(18)	239(59)	407(47)
	7-9	21(19)	24(21)	68(60)	113(13)
	9+	5(12)	6(14)	31(74)**	42(5)
Number of Chil-dren	1-2	96(27)	69(19)	191(54)	357(61)
	3-4	31(22)	31(22)	82(57)	144(25)
	5-6	9(16)	6(11)	41(73)	56(10)
	6+	2(7)	5(17)	22(76)*	29(5)

* statistically significant at 0.05 level of significance

** statistically significant at 0.01 level of significance

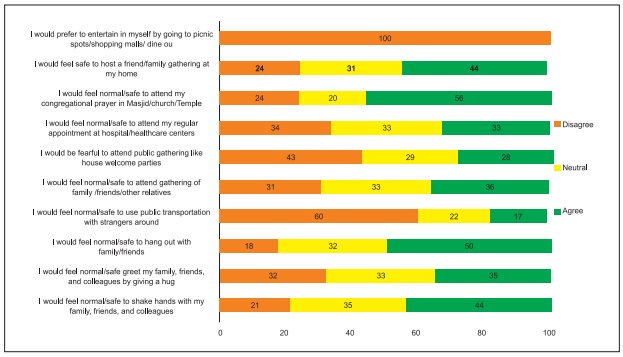

Fig 1: Overall Percentage of Participants' Behavior about the Post COVID-19 Life

recommended physical distancing measures were taken as questions and categorized into two components, (1) physical contact with others (handshake, hugging, etc.) and (2) using or visiting publicly shared places.

In general, many participants disagreed with visiting public places (shopping malls, picnic spots, or dining out) and using public transport. Conversely, most men agreed to attend congregational prayers at Masjid/ Church/temple and hang out with family/friends. Only 17% of the study population agreed to use public transport even after the pandemic. The results showed the same behaviour as hypothesized: people might avoid going outside, meeting with others, and using and visiting public places or transport, but due to the religious factor, they might not stop performing congregational prayers together. A similar study was conducted in Dammam, Saudi Arabia, in which over a thousand responses were collected from people with different educational levels and family sizes. The study's findings were similar to the current study in which participants were hesitant to visit public places and use public transport; however, when performing congregational prayers, males had higher agreement levels than females[18]. This cautious behaviour will have severe implications for the transportation industry, as a large proportion of Pakistan's working class depends on public transportation[27]. Studies suggested a framework for disaster management and agenda for post-pandemic management of the hotel industry and economic crisis management in general that can be followed in Pakistan as a precautionary method[28,29]. Another notable finding of the study highlights that one-third of the respondents were not sure about practicing physical distancing. Hence, it can be assumed that if they decide to continue or stop physical distancing behavior later in time, it will have a grave (positive/negative) impact on the tourism, entertainment, and transport industries. Khan et al. from Saudi Arabia found that about 30% of the participants disagreed with stopping physical distancing behavior[18]. Another noticeable finding of the present study was that 30 to 35% of the study participants responded with a neutral response to many questions (Figure 1). However, people cannot remain neutral after the ease of COVID restrictions.

Men were generally found less fearful than women when asked about physical distancing, as men mostly favored stopping physical distancing post-pandemic. In response to almost every question, the proportion of females was lesser than males who showed their agreement towards stopping practicing physical distancing. In some questions, it was significantly less. Contradictory to this, a study from Saudi Arabia reported that females were less

fearful, agreed more than males to stop physical distancing behavior, and found keener to start socialization[18]. Furthermore, study findings suggested that education had a significant association with physical distancing behavior. Participants at the lower level of education were keener to stop physical distancing behavior than participants with higher education. People who were more educated agreed less in favor of stopping practicing physical distancing. This observation showed that people with higher education levels might have more information and knowledge about the virus, and perhaps they are also aware that this virus cannot go to be subsided. Therefore, the fear of getting infected would remain longer among those who were more educated. Similar findings were reported by Khan et al. in a study published in Saudi Arabia[18].

As Pakistan is a Muslim-majority country and among Muslims, praying five times a day in Masjid is a religious obligation. Shaking hands when meeting others is also a religious and robust social aspect of society[30]. Hence, it was observed that a large group of participants showed agreement to attend to their religious obligations. As established since the start of the COVID-19 pandemic that vaccine will be required to boost immunity against the disease. Especially those with underline conditions or older adults so that the weak immune system, either because of other diseases or age, can respond more effectively in case of getting infected with a virus[31]. COVID-19 vaccine does not guarantee re-infection with the virus, but data has shown that it decreases the number of patients with severe COVID infections and the number of deaths[32]. Therefore, fear of getting an infection will exist even with getting vaccinated[33]. However, when this study was conducted, COVID-19 vaccination was not started at a detectable level in Pakistan; therefore, the impact of the vaccine could not be assessed with the post-pandemic physical distancing behaviour.

Although the study had a sufficiently large data size, there were also some limitations. Because data were collected by sending the survey link to personal contacts, all segments of society would not be covered. In addition, the participants' religion could be an essential factor causing variation in the responses. The present study only included only one geographical region. Inclusion and comparison between the regions perhaps contribute as a significant factor. Another study limitation was the occupation of the participants was collected as an open-ended question that caused problems in analysis. It is suggested for future studies to make a close-ended question for the participants' occupation to facilitate and serve the analysis purpose. The current study did not include a history of COVID infection; those who got infected with the virus could have a different perception than others. Finally, the data collection process was completed before the start of the vaccination campaign in Pakistan. After getting vaccinated, people may feel safer and respond differently.

CONCLUSIONS

Study participants disagreed with stopping practicing some of the physical distancing measures. Based on that, it is clear that people might carry the physical distancing behavior post-pandemically. Studies showed that females and the higher education population are willing to follow better adherence to SOPs of the COVID-19 pandemic. Hence, due to the high proportion of the participants, who disagreed with stopping physical distancing even after the ease of the restrictions, there would be severe effects on some industries like; transportation, tourism, traveling, hotel, etc. Therefore, this study portrayed the possible future public behavior which must be considered to retain the businesses by either making contingency plans or reducing the fear of the virus. Public awareness campaigns perhaps play a positive role in this regard. Future research should be conducted to assess the change in perception regarding post-pandemic physical distancing behavior after vaccination. Furthermore, if the perceived lifestyle persists for an extended period, it will have an impact on social life and a significant impact on culture and society.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan SQ:	Conception and overall supervision of research
Moheet IA:	Data collection
Farooqi FA:	Manuscript writing
Khan N:	Manuscript writing
Wahab S:	Data collection
Haider I:	Critical review/Statistical analysis
Al-Shayea N:	Bibliography, literature search
Ali S:	Data collection, manuscript writing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

FREQUENCY OF PANCYTOPENIA AMONG PATIENTS WITH VITAMIN B12 DEFICIENCY

Humaira Taj Niazi[1], Zahish Safiullah Jan[2], Nayab Safiullah Jan[3], Laila Bahadur[4], Khizar Abdullah Jan[5], Mohsin Ali[6]

[1]Department of Pathology, Rehman Medical Institute, Peshawar – Pakistan

[2]Consultant Hematologist, Shifa Health Centre, Peshawar - Pakistan

[3] Regional Blood Centre, Peshawar – Pakistan

[4]Pakistan Thalassemia Welfare Society, Rawalpindi - Pakistan

[5]Department of Pathology, Lady Reading Hospital, Peshawar - Pakistan

[6]Department of Pharmacology, Muhammad College of Medicine, Peshawar - Pakistan

ABSTRACT

Objective: To determine the frequency of pancytopenia among patients with vitamin B12 deficiency in a tertiary-care hospital, in Peshawar.

Materials and Methods: A descriptive cross-sectional study was carried out at the Department of Hematology, Hayatabad Medical Complex, Peshawar from 18/4/2021 to 18/10/2021. In this study, a total of 252 patients were observed. From all patients, a sample of venous blood was obtained and sent to the hospital laboratory for the peripheral smear examination. Pancytopenia was diagnosed based on a peripheral smear showing Hemoglobin below 10g/dL, Total leukocyte counts less than 4,000 cells per mL, platelets count less than150,000 cells per mL, and reticulocyte count <2%. All the peripheral smears were done by an expert hematologist. Strictly exclusion criteria were followed to avoid cofounders and make the study results clear of any bias.

Results: In this study mean age was 42 years with a standard deviation of ± 15.84. Thirty-eight percent of patients were males and 62% of patients were females. Moreover, 5% of patients had pancytopenia and 95% of patients didn't have pancytopenia.

Conclusion: The frequency of pancytopenia was 5% among the local patients with vitamin B12 deficiency.

Keywords: pancytopenia, B12 deficiency, Peshawar, Pakistan.

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INTRODUCTION

Pancytopenia is defined as a decrease in leukocytes, platelets, and erythrocytes in all three peripheral blood lineages. It is a group of findings rather than a disease that can be brought on by several different underlying disease processes. Pancytopenia can be caused by these conditions, which can either directly or indirectly affect bone marrow [1]. Pancytopenia may be acquired or inherited (genetic but not necessarily present at birth). Pancytopenia is caused by either a failure to produce hematopoietic progenitors or peripheral destruction of cellular elements caused by infection, immune-mediated damage, or hypersplenism [2]. To evaluate the overall cellularity and morphology of a bone marrow biopsy specimen and a marrow aspirate in pancytopenia, a microscopic examination is required. Bone marrow examination is one of the important diagnostic procedures for many hematological disorders. In most cases, it gives a specific diagnosis; however, in a few cases, additional tests are required. The presenting symptoms are often attributable to anemia, thrombocytopenia, or leucopenia. The etiological spectrum of pancytopenia varies according to geographical distribution and genetic disturbances [3].

Anemia caused by vitamin B12 (cobalamin) insufficiency is most typically caused by pernicious anemia and occurs far less frequently because of dietary inadequacy. However, as the adoption of veganism and vegetarian

Correspondence
Dr. Mohsin Ali
Department of Pharmacology, Muhammad College of Medicine, Peshawar - Pakistan
Cell: +92-321-5275212
Email: mohsin.ibms86@gmail.com
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diets rises, so does the prevalence of B12 deficiency [4]. The tissues that experience high cell turnover are most impacted by a vitamin B12 deficit since this vitamin, which is predominantly found in animal products, is a crucial component in the synthesis of DNA and RNA. It normally takes one to four years for a deficit to have clinical effects, with hematologic and neurologic signs being the most noticeable [5].

Implications of a B12 inadequacy may include hematologic or neurologic effects. A defining symptom of B12 deficiency is megaloblastic anemia, which is frequently accompanied by hyper-segmented neutrophils on a peripheral blood smear. The most common symptoms are low levels of white blood cells, red blood cells, platelets, or a combination of these, such as pancytopenia and hemolysis. Glossitis, exhaustion, palpitations, a pale complexion, weight loss, and infertility were some additional systemic symptoms. A B12 deficiency, on the other hand, is also associated with neurological changes such as sensory impairments, paresthesia, ataxia, weakness, and gait instability. Severe cases may also lead to spasticity and paraplegia [6]. The most concerning neurologic outcome of subacute combined degeneration is demyelination of the spinal cord's dorsal, lateral, and spinocerebellar tracts. Other symptoms of vitamin B12 deficiency include paresthesia, loss of fine touch, vibrational and pressure sensations, vision loss, mental changes, bilateral spastic paresis, or paralysis [7].Since vitamin B12 deficiency is an easily curable cause of demyelinating neurological disease and bone marrow failure, it is crucial to identify and treat it[8]. Vitamin B12 (cobalamin), which cannot be produced by humans, is made by the normal flora in the gut. Foods of animal origin also contain trace amounts of it[(7)]. Megaloblastic anemia is brought on by folate and vitamin B12 deficiency[9]. In peripheral blood granulocytes, macrocytosis, immature nuclei, and hyper-segmentation are caused by an imbalance between the cytoplasmic and nuclear maturation processes[10]. As a reversible cause of bone marrow failure, vitamin B12 deficiency must be promptly identified and treated. Finding the underlying cause of vitamin B12 deficiency after a diagnosis is crucial for individualized treatment[11]. In one study, out of 94 patients presenting with low vitamin B12 levels, macrocytosis was seen in 29.8%, and a dimorphic blood picture of microcytic hypochromic cells and macrocytes was seen in 17%. 27.7% of patients had a microcytic and hypochromic picture while 25.5% had a normochromic, normocytic picture. 5.4% had pancytopenia[12].

The purpose of the current study was to determine the prevalence of pancytopenia in patients with vitamin B12 deficiency. Vitamin B12 deficiency is common in our population, and because of its importance in bone marrow cell lines and the nervous system, it is critical to assess the complications associated with it. Reduction in cell lines due to bone marrow failure secondary to vitamin B12 deficiency is critical and therefore, we designed this study to determine the burden of pancytopenia among the local population with vitamin B12 deficiency.

MATERIAL AND METHODS

A descriptive cross-sectional study was designed and carried out at the Department of Hematology, Hayatabad Medical Complex, Peshawar, to achieve the goal of the study. The duration of the study was 06 months i.e., from 18/4/2021 to 18/10/2021. The sample size was calculated using an online World Health Organization (W.H.O) sample size calculator i.e., a total of 252 subjects were included in the study using a 4.27% proportion of pancytopenia among patients with vitamin B12 deficiency[10], 95% confidence level, and 2.5% margin of error. A simple non-probability consecutive sampling technique was employed. All patients with severe vitamin B12 deficiency were eligible for the study i.e., with serum level less than 118 pmol/L, with duration more than 2 years, patients in the age range 18-60 years of either gender while patients already on treatment for diseases like cancer chemotherapy, already diagnosed cases of iron deficiency anemia, aplastic anemia, leukemias, and infectious diseases were excluded from the study. Permission was taken from the head of the department before starting the study. Written informed consent was taken from all patients. The objectives of the study and the risks involved were informed and explained to patients. All the information including name, age, sex, duration of vitamin B12 deficiency, and serum B12 Levels was recorded on pre-designed Performa. The privacy implications of the collected information were clearly explained to the patients at the time of taking written consent. From all patients, a sample of venous blood was obtained and sent to the hospital laboratory for the peripheral smear examination. Pancytopenia was diagnosed based on a Peripheral smear showing Hemoglobin <10g/dL, total leukocyte count <4,000 per mL, Platelets <150,000 per mL, and reticulocyte count <2%. All the peripheral smears were done by an expert hematologist. Similarly, the presence of megaloblastic anemia was diagnosed based on mean corpuscular volume (MCV) great-

er than 115fL. Strictly exclusion criteria were followed to avoid cofounders and make the study results clear of any bias. All the collected information on proforma was entered and analyzed through SPSS 22. Mean and Standard Deviation were calculated for numerical variables i.e. age, duration of vitamin B12 deficiency, and serum B12 Levels. Frequency and percentages were calculated for gender, malabsorption, nutritional deficiency, and pancytopenia. Pancytopenia was stratified among the age, gender, duration of vitamin B12 deficiency, malabsorption, and nutritional deficiency to examine the effect modification using the chi-square test, with a p-value of 0.05 considered significant. Tables and graphs were used to present all the results.

RESULTS

Among 252 patients, 96(38%) patients were males while 156(62%) patients were females. The distribution of patients concerning age is shown in Table 1. The mean age was 42 ± 15.84 years. The status of pancytopenia among 252 patients was analyzed and 13(5%) patients had pancytopenia while 239(95%) patients didn't have pancytopenia. Table 2 shows the distribution of pancytopenia with clinical parameters. Stratification of pancytopenia with age and gender is shown in Table 3 while stratification of pancytopenia with vitamin B12 deficiency and megaloblastic anemia is shown in Table 4.

Table 1: Distribution of patient

Age (Yrs.)	Frequency	Percentage	Mean Age
18-30	30	12%	42± 15.84 Years
31-40	50	20%	
41-50	81	32%	
51-60	91	36%	

Table 2. Distribution of Patients W.R.T Clinical Parameter

Observation	Vitamin B12 Deficiency (n)	Megaloblastic Anemia (n) (%)
Present	252	165 (65.48)
Absent	0	87 (34.52)

Table 3: Stratification of pancytopenia w.r.t age and gender distribution

Stratification of Pancytopenia W.R.T Age Distribution						
Pancytopenia	18-30 Yrs.	31-40 Yrs.	41-50 Yrs.	51-60 Yrs.	Total	**p-value**
Present	2	3	4	4	13	0.9546
Absent	28	47	77	87	239	
Stratification of Pancytopenia W.R.T Gender Distribution						
Pancytopenia (n)	Male (n)	Female (n)	Total	p-value		
Present	5	8	13	0.9777		
Absent	91	148	239			

Table 4: Stratification of pancytopenia with Vit B12 Deficiency and Megaloblastic Anemia

Pancytopenia (n)	Vitamin B12 Deficiency (n)	Percentage (%)	**p-value**
Present	13	5.16	0.7590
Absent	239	94.84	
Stratification of Pancytopenia W.R.T Megaloblastic Anemia			
Pancytopenia (n)	Megaloblastic Anemia (n)	Percentage (%)	p-value
Present	165	65.48	0.7590
Absent	87	34.52	

DISCUSSION

Even though vitamin B12 (cobalamin) deficiency has been known for more than a century, it can still be challenging to diagnose and treat properly. Lack of vitamin B12 can cause a variety of symptoms, from neurologic to psychiatric. Many people who don't get enough vitamin B12 could suffer from megaloblastic anemia[13]. Numerous cases of vitamin B12 deficiency are ignored or even misdiagnosed in clinical settings[14]. A plasma concentration below 118 pmol/L (160 pg/mL) is deficient in vitamin B12. However, in general practice, plasma vitamin B12 levels greater than 140 pmol/L are commonly considered normal by physicians, but many symptomatic patients may have such levels, which may be because of taking oral vitamin supplementation. The range of signs and symptoms for a vitamin B12 deficiency is fairly established[15]. However, many of the symptoms are vague and could be brought on by other illnesses. As of right now, no studies have shown how well certain symptoms or symptom scores can predict whether a person has a vitamin B12 deficiency[16]. Previously, according to a study conducted by Marin JDM et al., vitamin B12 deficiency manifests as anemia, neuropathy, and myelopathy. More than 10% of people over the age of 65 suffer from anemia (defined by WHO as serum hemoglobin (Hb) levels below 12 g/dl in women and 13 g/dl in men). 17% of these cases are caused by vitamin B12 deficiency. Anemia (21%), leukopenia (11%), thrombocytopenia (9%), and pancytopenia (6.5%) are the most common hematologic manifestations in patients with vitamin B12 deficiency (200 pg/ml levels)[17].

Pancytopenia must be diagnosed using a thorough diagnostic process that is tailored to the clinical setting. Pancytopenia with anemias due to vitamin B12 deficiency is evaluated using a combination of known hypersensitivity, clinical, cytological, and biomarker factors. Pancytopenia has a variety of causes that vary in presentation and severity; its prevalence varies greatly across countries[18]. On the hand, megaloblastic anemia has been identified as the leading cause of pancytopenia worldwide. Megaloblastic anemia is diagnosed simply using a complete blood count, a peripheral blood smear, and bone marrow cytology, which is a low-cost procedure. Nutritional variables, recurrent infection, vitamin B12, and folate deficits appear to be closely linked to megaloblastic anemia[19]. In South Asia, megaloblastic anemia and aplastic anemia are major causes of pancytopenia. However, In Pakistan, aplastic anemia was found more common hematological disorder (20.2%) than megaloblastic anemia (14.6%) whereas iron deficiency anemia and idiopathic thrombocytopenic purpura were the other common causes with the frequency of 7.6% and 15.7% respectively[20]. Similarly, pancytopenia was found in 70% of individuals with megaloblastic anemia in a cross-sectional observational research in Pakistan[21]. In the current study, megaloblastic anemia was found in 65.48% of patients with serum vitamin B12 deficiency.

Although patients with low serum vitamin B12 levels may not exhibit any symptoms, they are highly likely to do so. When determining the etiology of pancytopenia in the beginning, the serum vitamin B12 level should be considered. The prevalence of vitamin B12 deficiency in pancytopenia patients ranges from 3% to 5% in the general population, and it ranges from 5% to 20% in those over 65 [22]. According to our findings, 5% of patients had pancytopenia and 95% did not experience a decrease in blood cells. Another study found comparable results conducted by Bhatia P et al., in which out of 94 patients presenting with low vitamin B12 levels, macrocytosis was seen in 29.8%, dimorphic blood picture of microcytic hypochromic cells and macrocytes was seen in 17%. 27.7% of patients had a microcytic and hypochromic picture while 25.5% had a normochromic, normocytic picture. 5.4% had pancytopenia [23]. In a study conducted by Mezalek ZT et al., 268 consecutive patients who were hospitalized for cobalamin deficiency from January 2000 to December 2015, their medical data identified and retrospectively examined which also showed that pancytopenia affected 104 (8.8%) of the total patient's [24].

CONCLUSION

Our study concluded that there was a low prevalence (5%) of severe pancytopenia in the local population with vitamin B12 deficiency based on a single institution with a significant number of consecutive patients with well-documented cobalamin deficiency. We haven't yet found a reason for those findings. These findings show that severe vitamin B12 deficiency can mimic a malignant hematologic disorder and that prompt diagnosis and supplementation result in the resolution of symptoms and blood abnormalities.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Niaz HT:	Conception of idea, Manuscript writing
Jan JS:	Data Collection, Laboratory Work
Jan NS:	Data Collection, Laboratory work
Bahadur L:	Statistical analysis, Bibliography
Jan KA:	Laboratory work, Data analysis
Ali M:	Results compilation, statistical analysis

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

AN EMERGING RELATIONSHIP BETWEEN CIRCULATING ESTRADIOL AND THYROID AUTOIMMUNITY IN POLYCYSTIC OVARIAN SYNDROME

Anam Rehman[1], Benash Altaf[1], Hira Zahid[1], Saba Tariq[2], Shireen Jawed[1], Sundus Tariq[3]

[1]Department of Physiology, Aziz Fatimah Medical and Dental College, Faisalabad - Pakistan

[2]Department of Pharmacology, University Medical and Dental College, Faisalabad - Pakistan

[3]Department of Physiology University Medical and Dental College, Faisalabad - Pakistan

ABSTRACT

Objectives: To find an association between circulating Estradiol and thyroid autoimmunity in females with polycystic ovarian syndrome (PCOS) and its impact on their health.

Materials and Methods: This study was conducted at Aziz Fatimah Medical and Dental College, after obtaining ethical approval from Institutional Ethical Committee (letter No. DME/568-19) from April to September 2017. Hundred PCOS females enrolled in the age range 17-35 years were taken who fulfilled inclusion and exclusion criteria. Blood samples were drawn and stored at Aziz Fatima Hospital, Faisalabad. All blood samples were analyzed for the levels of Estradiol, thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free tetra-iodothyronine (FT4), and thyroid peroxidase antibody (TPO-Ab). The data was analyzed using SPSS 23.

Results: Of the total population, TPO-Ab was positive in 26% of study participants. It was observed that 64% and 40% of TPO-Ab positive subjects were in the Estradiol quartiles E3 and E4 respectively and none of them were found to be in E1 and E2 quartiles. We have found a significant association of the E2 with TSH, FT4, and TPO-Ab, however, no significant correlation was found between TSH and TPO-Ab. Beta coefficient (β) of 1.006 shows that higher E2 was significantly related to higher TPO-Ab titer with p-value = 0.002. Similarly, a significant but weak positive association was found between E2 and TSH. E2 was significantly negatively associated with FT4.

Conclusion: OEstradiol is positively associated with TPO antibodies and TSH and negatively associated with FT4 in PCOS patients. Our findings suggest that thyroid autoimmunity is commonly found in PCOS females.

Keywords: OEstradiol, Polycystic ovarian syndrome, Thyroid peroxidase antibody

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INTRODUCTION

Autoimmune diseases are a major concern for health care providers globally in latest decades due to their associated comorbidities leading to high mortality rates.[1] The development of autoimmunity is a heterogeneous process. It is reported by previous research that the prevalence of autoimmune diseases is hiking in the current era including connective tissue diseases, autoimmune hepatitis, thyroid diseases, insulin-Dependent Diabetes Mellitus (IDDM) and skin diseases, etc. This auto-immune response is believed to be carried out due to the production of antibodies against own tissues and subsequently its destruction by the cytotoxic action of T cells.[2] In Pakistan, hypothyroidism is prevalent up to 4.1% and 5.4% in adults and children respectively. It is also reported that hypothyroidism and hyperthyroidism are more prevalent in females than in their male counterparts. Thyroid malfunctioning in subclinical hypothyroidism is interconnected with a raised risk of atherosclerosis and coronary artery diseases most probably also attributed to altered Estrogen levels.[3,4] Autoantibodies of the thyroid are not solely detectable in autoimmune thyroid disease (AITD) patients besides it they are also found in subjects who do not have evident altered thyroid function.[5]

Thyroid disorders are more rampant in females especially targeting the age of puberty and menopause. It is worrisome for the physicians that chances of thyroid carcinomas are more recurrent in women as compared to men. These findings are attributed to the altered levels of Estrogen in thyroid disorder pathogenesis.[6]Indirect role of Estrogen has been established on the thyroid affecting its

Correspondence
Dr. Anam Rehman
Assistant Professor
Department of Physiology, Aziz Fatimah Medical and Dental College, Faisalabad - Pakistan
Cell: +92-342-7398108
Email: doc.rehman158@gmail.com
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hormonal economy, thence, enhancing the thyroxin binding globulin, and subsequently making thyroid hormone more pivotal in hypothyroid females. Estrogen has a direct effect on thyroid cells stimulating them and forming the thyroid nodule, it also causes an increased production of thyroid-binding globulins by the liver thereby decreasing the availability of free thyroid for the proper functioning of the body. [7] Normally progesterone is responsible for declining IL-6 and the production of antibodies. On the other hand, Estrogen decreases the activity of suppressor T-cells but enhances the action of B cells as well as secretion of IL-6, all contributing to autoimmunity in Hashimoto thyroiditis. Hence it is concluded by the researchers that imbalances in Estrogen and progesterone (a low progesterone/Estradiol ratio), may promote the development of Hashimoto thyroiditis in PCOS subjects resulting from the immune-stimulating effects of unbalanced Estrogen.[8]

MATERIAL AND METHODS

This Cross-sectional study was done at Aziz Fatimah Medical and Dental College from April 2017 to September 2017 after obtaining ethical approval from the institute with letter no. DME/568-19. It comprised 100 female participants. Female Subjects were recruited having PCOS on ultrasound with an age range of 17-35. However, subjects with hypothyroidism, taking thyroxin and hyperthyroidism, and subjects with thyroidectomy and hysterectomy were excluded from the study. 5ml of fasting blood samples were drawn under aseptic conditions following the protocol. Serum was separated in a centrifuge machine and saved in an Eppendorf tube and transferred to a freezer at -80 c till analysis. Anti-TPO antibodies were measured with help of CLIA cut of the range was taken less than 14 IU/ml. Estrogen was measured using CLIA cut-off value was taken15-112pg/ml. Data analysis was performed using SPSS version 23. Continuous data are expressed as mean ± S.D and median (IQR). Categorical data are expressed in frequencies and percentages. Shapiro Wilk test was applied for the normality of data. Data for Estradiol, TSH, and TPO Antibodies were not normally distributed and skewed. So, a non-parametric test was used for analysis. Spearman correlation coefficients were used to assess pairwise correlation. Regression analysis was done to assess the association between Estradiol and TPO antibodies, TSH, and FT4. A p-value of ≤ 0.05 was considered statistically significant. Spearman correlation was used to find a correlation.

RESULTS

This study comprised 100 Female participants having PCOS. The mean and SD of biochemical parameters are presented in table 1. Twenty-six percent of the subjects were positive for TPO-Ab. To assess the interrelation between serum E2 and the detectability of TPO antibodies, Participants were categorized into Estradiol (E2) quartiles. It was observed that 64% and 40% of TPO-positive subjects were in the E3 and E4 respectively and none of them were found to be in the E1 and E2 quartiles of E_2. (Table 2)

Spearman's correlation indicates a significant association of the E2 with TSH, FT4, and TPO antibodies, however, no significant association was found between TSH and TPO antibodies (Table 3). To assess the strength of this relation simple linear regression model for E_2, as independent variables, and the TPO antibodies titter, TSH, and FT4 as the dependent variable was used. The beta coefficient (β) of 1.006 shows that higher E_2 was significantly related to higher TPO antibodies titer with p-value = 0.002. Similarly, significant but weak positive association was found between the E2 and TSH (β =0.004, p-value 0.000). E2 was significantly negatively associated with FT4 (β = - 0.375, p value 0 .012). (Table 4) Estrogen (E_2) is in the dependent variable P value of ≤0.05 was taken as significant.

Table 1: Descriptive of Study Population (n=100)

Biochemical Parameters	Mean ± SD	Range	Median (IQR)
Estradiol(E_2)	70.69 ± 271.14	0.73 - 2550.0	4.77 (14.96)
Free Thyroxine (FT4)	9.13 ± 5.84733	0.02 - 25.90	3.42 (582)
Thyroid-stimulating Hormone (TSH)	6.7302±16.60	0.06 - 100.00	2.65(1.56)
Thyroid peroxide titer (TPO)	6.29 ± 5.48	0.73 - 20.00	3.91 (8.73)
Free triiodothyronine FT3	4.29 ± 4.07	3.50 - 1590	10.75 (10.85)

Table 2: Detectability of Thyroid Peroxidase Antibodies in Various OEstradiol (E2 Quartiles)

E2 Quartile	Positive TPO N(%)	Negative TPO N(%)
E1 (n= 25)	00(00)	25(100%)
E2 (n= 25)	00(00)	25(100%)
E3 (n=25)	16(64)	9(36)
E4 (n=25)	10(40)	15(60)

Table 3: Spearman's correlation between serum OEstradiol (E2), TSH and TPO antibodies

E2 vs TSH	**0.194**	**0.053**
E2 vs TPO antibodies	0.742	0.000
TSH vs TPO antibodies	0.072-	0.479
E2 Vs FT4	-.0450	0.000

Table 4: Regression Analysis of OEstradiol (E2) with dependent variables

Dependent variables	Beta Coefficients (β)	Std. Error	P value
TPO	1.006	0.002	0.002
TSH	.044	.005	0.000
FT4	-.375	.147	0.12

DISCUSSION

Polycystic ovarian syndrome (PCOS) and thyroid disorders are frequent growing ailments globally. The association between autoimmune thyroid disease and PCOS is more and more being recognized by researchers, and the reason for this link is yet unstipulated. Most of the researchers have suggested their bidirectional relationship.[9] Enhanced ovarian volume, as well as cystic changes in ovaries, have been stated in primary hypothyroidism.

Apart from this, several previous studies have documented a higher incidence of thyroid diseases in PCOS patients as compared to normal females. The link between thyroid autoimmunity and PCO is gaining interest among researchers, as accurate interrelation is yet to be known. Whether this occurs as a consequence of some common predisposing factors or a pathophysiological linkage among both of these disorders has not been elucidated to date.[9]

But a previous study, indicating the pathogenesis of PCOS reported a high prevalence of PCOS phenotype in adolescent girls with euthyroid Hashimoto Thyroiditis (HT), indicating the feasible impact of other aspects like autoimmunity as compared to hypothyroidism.[10]

Arduc et al., has explained that the hypothyroidism has deteriorated PCOS by lessening the sex hormone binding globulin level, raising the conversion of androstenedione to testosterone and aromatization to Estradiol, and decreasing the metabolic clearance of estrone and androstenedione leading to PCO.

Additionally, raised TSH level promotes its spillover effect on FSH receptors. Enhanced deposition of collagen in ovaries because of hypothyroidism has also been reported by Singla et al., [9, 10]

On the other hand, Chailurkit et al. stated extra thyroidal causes of thyroid autoimmunity that might be due to elevated Estradiol levels. Some researchers have suggested that androgens as well as osteogeneses have a significant impact on autoimmunity because of their aptitude of modulating immune response via their receptors.[11, 12] Numerous other previous studies also suggested imbalance among Estrogen and progesterone or Estrogen testosterone levels might be the contributing factors. Previous research was performed to highlight the association between PCO and Thyroid autoimmunity by investigating the relationship between hormonal imbalances in patients with PCOS versus control patients.

The authors concluded that imbalances in Estrogen and progesterone (a decreased progesterone/ Estradiol ratio), may promote the development of autoimmunity in PCO patients. Immune-stimulating effects of unbalanced Estrogen are directly involved in elevations of anti-TPO.[10,13]

Arduc A et al., also suggested that E_2 and progesterone seem to impede differently with expression and mass production of proinflammatory cytokines through activated macrophages and control downregulation of immune as well as inflammatory reactions.[10] Current study was conducted to find the emerging relationship between Estradiol and thyroid autoimmunity.

In our study, we found the presence of TPO antibodies in 26% of PCO females. Our results are in agreement with a previous study by Garelli et al. that also reported the presence of TPO antibodies in 27% of their PCO patients when compared to 8% in controls.[14]

Janssen et al also documented higher thyroid antibody levels in females with PCOs as compared to a control group. Additionally, Janssen et al., also reported that females with PCOs have larger thyroid volumes and

more hypoechogenic thyroid glands when compared to controls.[15] These finding reflects that thyroid autoimmunity is commonly found in PCO patient.

In the current study, circulating E2 was found to be related to TPO Ab in PCO females. Our finding is suggestive of a connection between E2 level and TPO Ab proposes that E2 might have an impact on thyroid autoimmunity pathogenesis in PCO females. Our results are supported by the previous study ascertaining a positive correlation between anti-TPO and Estradiol.[10]

To assess the relationship between serum E2 and detectability of thyroid autoantibodies, we classified the subjects into E2 quartiles and we noticed that a higher number of anti-TPO positive subjects were fall in upper two E2 quartile (E3 and E4), whereas none of the TPO positive subjects was found in lower E2 (E1 and E2) quartile. This study's finding suggests that Estrogen may be an aspect of causing autoimmunity. On the contrary, Chailurkit et al.

Found TPO antibodies almost equally in all four E2 quartiles suggesting no relationship between E2 and TPO antibodies. Our results are justified by Chen et al., a study carried out in China, which reported increased Anti-TPO antibodies with increasing Estrogen levels.[11, 12]

Our results of regression analysis show a significant positive association between E_2 and TPO antibodies. The beta coefficient of 1.006 shows that a 1-unit increase in Estradiol will increase the 1.006-fold increase in thyroid peroxide antibody level. Our results are reflecting that the increase in E_2 and subsequent increase in TPO antibodies, will result in the occurrence of thyroid autoimmunity Wang C et al., results showed that a 1-unit increase in TPOAb/TGAb, will increase the risk for developing autoimmunity increased by 1.265-fold.[16]

The current study found a significant but weak positive relation between TSH and Estradiol levels contrary to our results, Chailurkit et al., reported a negative association between E2 and TSH, but only in those whose TSH levels fell below the reference range.

The association between E2 and TSH may suggest the influence of E2 on thyroid function through thyroid autoimmunity. The present result did not find a significant association between OEstradiol and FT4, this study's results are per Chailurkit et al., who did not find an association between E2 and FT4 evident.[11]

CONCLUSION

OEstradiol is positively associated with TPO antibodies and TSH and negatively associated with FT4 in PCOS patients. Our findings suggest that thyroid autoimmunity is commonly found in females with PCOS.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Rehman A: Study design acquisition of data and manuscript writing. Revised and approved the article.

Altaf B: Data collection and statistical analysis. Revised and approved the article.

Zahid H: Study design acquisition of data and manuscript writing. Literature review.

Tariq S: Writing of results and referencing. Revise all intellectual contents of the article and approved.

Jawed S: Data analysis and interpretation results.

Tariq S: Formulate all tables. Literature review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

HISTOPATHOLOGICAL ASSESSMENT OF ORAL LEUKOPLAKIA AMONG SNUFF USERS AND NON-USERS

Tehmina Naushin[1], Abbas Saleem Khan[1], Muhammad Ishfaq[2], Nasiha Bashir[1], Fatima Iqbal[1], Mahmood ul Hassan[3]

[1]Department of Oral Pathology, Peshawar Dental College, Peshawar - Pakistan

[2]Department of Oral & Maxillofacial Surgery, Peshawar Dental College, Peshawar - Pakistan

[3]Department of Orthopedic Surgery, Peshawar Dental College, Peshawar - Pakistan

ABSTRACT

Objectives: To assess histopathological characteristics of oral leukoplakia among snuff users and non-users.

Material and methods: The descriptive cross-sectional study was conducted at different hospitals in Khyber Pakhtunkhwa. The study consisted of 60 cases of oral leukoplakia of which 30 were snuff users and 30 were non-users and histopathological features were assessed in both groups. SPSS 20 was used for the evaluation and analysis of the data.

Results: The observed mean age of the cases was 50.3 years. In snuff users, the mean age was 56.97 (SD+14.71) while in non-users the mean age was 47.43 (SD+13.44). In snuff users, dysplasia 9/30 (30%) was the most common histopathological feature. The relationship between dysplasia in snuff users and non-users was found to be statistically significant with a p-value of 0.04.

Conclusion: It is concluded from the present study that oral leukoplakia showed a wide range of histopathological features and these variants exist even among snuff users however the cases of dysplasia are high in snuff users than non-users which shows a greater potential for conversion of oral leukoplakia into malignancy in snuff users.

Keywords: Oral leukoplakia, Dysplasia, Hyperplasia, Hyperkeratosis

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INTRODUCTION

According to WHO oral leukoplakia (OL) is defined as a" white plaque of questionable risk having excluded other known disorders which carries an increased risk for cancer".[1] Approximately 80% of oral malignancies result from oral precursor lesions.[2] OL is considered one such disorder. The histopathological features are epithelial hyperplasia and surface hyperkeratosis either hyperparakeratosis or hyperorthokeratosis. Epithelial dysplasia may or may not be present and if present it ranges from mild to severe. Epithelial dysplasia is considered a marker of the conversion of a lesion into malignancy.[3-8]

Tobacco use is among one the etiological factors of oral leukoplakia.[9, 10]. Tobacco is used in the Khyber Pakhtunkhwa province of Pakistan specifically in the form of oral snuff (naswar) which is a smokeless (SL) form. 40% of SL tobacco users develop OL in comparison to 1.5% of non-tobacco users.[1] Oral snuff is a mixture of crushed tobacco, powdered lime, ash, indigo, cardamom oil, and menthol.[11-13] The present study is designed to assess histopathological features of Oral leukoplakia to report the probable relation of smokeless tobacco with the development of the said pathological entity in Pakistan research literature. Moreover, one of the features, dysplasia is considered a marker conversion of oral leukoplakia into malignancy so timely treatment and follow-up of dysplastic lesions specifically in snuff users may help to prevent its malignant transformation.

Correspondence
Dr. Tehmina Naushin
Assistant Professor
Department of Oral Pathology, Peshawar Dental College, Peshawar / Riphah International University, Islamabad - Pakistan
Cell: +92-332-9395866
Email: tehminapdc@gmail.com
Date Received: 7-08-2022
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MATERIALS AND METHODS

This was an analytical cross-sectional study that was performed at Peshawar Medical College and Khyber College of Dentistry, after taking formal permission from the Review Board of the institution from August 2016 to March 2017 and a non-probability convenient sampling technique was adopted. The sample size was calculated by using the Open epi calculator and came out to be 60. These cases of oral leukoplakia were categorized into Group A, which comprised 30 cases of Oral leukoplakia in snuff users and Group B comprised 30 cases in non-users. All the relevant data including the habit of snuff use

or no use and duration of use in years was recorded on a structured proforma. Inclusion criteria for the snuff users and non-users included biopsied and histopathologically diagnosed cases of oral leukoplakia with a history of snuff use and non-use.

Incisional and excisional biopsies of oral leukoplakia were subjected to the standard histopathological procedure, which included grossing of the biopsy sample, and tissue processing followed by Hematoxylin and Eosin staining for slide review. Cases were confirmed by histopathologists. Histopathological features of dysplasia, hyperplasia hyperkeratosis, and a combination of features were found. The analysis of the data was carried out by using Statistical Package for Social Sciences SPSS version 20. The chi-square test was applied for statistical significance, and a p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The observed mean age of the cases was 50.3 years. In snuff users, the mean age was 56.97 (SD$\pm$14.71) while in non-users the mean age was 47.43 (SD$\pm$13.44). All 30 snuff users were males. Among non-users 13/30 (43.3%) were males and 17/30 (56.7%) were females.

Dysplasia was exhibited in 9 (30%) cases and non-users in 6 (20%) (Table 1). The relationship between dysplasia in snuff users and non-users was found to be statistically significant with a p-value of 0.04. The relationship between other features was not found to be statistically significant (Table 2). The results of the combination

Table 1: histopathological features among snuff users and non-users

Histopathological features	Snuff users	Non-snuff users
	N (%)	N (%)
Dysplasia	9(30)	6(20)
Hyperplasia	3(10)	11(36.7)
Hyperkeratosis	5(16.7)	7(23.3)
Dysplasia+ Hyperplasia	4(13.3)	2(6.7)
Hyperplasia + Hyperkeratosis	4(13.3)	4(13.3)
Dysplasia + Hyperkeratosis	4(13.3)	0(0)
Dysplasia + Hyperplasia + Hyperkeratosis	1(3.3)	0(0)
Total	30(100)	30(100)

Table 2: Comparison of histopathological features among snuff users and non-users

Histopathological features	Groups	Cases N (%)	p- value Chi square
Dysplasia	Snuff users	9(30)	0.04
	Non snuff Users	6(20)	
Hyperplasia	Snuff users	3(10)	0.015
	Non snuff users	11(36.7)	
Hyperkeratosis	Snuff users	5(16.7)	0.519
	Non snuff users	7(23.3)	

Table 3: Comparison of combination of histopathological features among snuff users and non-users

Histopathological features	Groups	cases	p- value
Dysplasia+ Hyperplasia	Snuff users	4(13.3%)	0.38
	Non snuff Users	2(6.7%)	
Hyperplasia+ hyperkeratosis	Snuff users	4(13.3%)	1
	Non snuff users	4(13.3%)	
Dysplasia+ hyperkeratosis	Snuff users	4(13.3%)	0.02
	Non snuff users	0(0%)	
Dysplasia+ Hyperplasia+ Hyperkeratosis	Snuff users	1(3.3%)	0.313
	Non Snuff users	0(0%)	

of histopathological features are summarized in Table 3.

DISCUSSION

Prolonged use of snuff changes the morphology of the placement site of the oral mucosa with initial wrinkled appearance and later thinner and more homogenous. This condition is known as oral leukoplakia.[14]

Architectural and cellular features of dysplasia may be the result of mutation of genome of the epithelial cells which ultimately leads to development of OL of the affected area.[7] Dysplastic feature has a high risk of conversion of a lesion of oral leukoplakia into malignancy.[15] In the present study 9 cases of dysplasia were diagnosed in snuff users. This is consistent with an Indian study conducted by Kumar et al., 2012 however in contrast to a study which showed no case of dysplasia in snuff induced oral leukoplakia.[16,17] The difference in the result of the studies conducted globally is probably due to the fact that the composition, manufacturing and application methods of snuff differ from region to region throughout the world.[16-18] Different forms of smokeless tobacco are used worldwide including Toombak in Sudan, Shammah in Saudi Arabia and Yemen, Gutka in India and South East Asia, and many other forms with different constituents however Snuff is mostly used only in Pakistan .[14]

In another study, dysplasia was observed in 60 cases indulged in tobacco smoking and chewing but not snuffs habit.[15] In the present study hyperkeratosis cases were more in non-users as compared to snuff users. Hyperplasia and hyperkeratosis in oral leukoplakia cases reveal a protective response of epithelial cells of the oral mucosa. Snuff and other etiological factors irritate epithelial cells of the mucosa and its permeability to carcinogens of tobacco is increased. Due to irritation, epithelial cells are stimulated and proliferation takes place which results in epithelial hyperplasia. Many studies were conducted globally to correlate hyperkeratosis and oral leukoplakia however no correlation could be found with snuff use.

In our study, there were 5/30 cases of combined histopathological features of dysplasia and hyperkeratosis in OL. This is in accordance with an international study conducted with 6/53 cases but it was not correlated with snuff use.[19]

The limitation of the present study is though smokeless tobacco is globally used however snuff is most commonly used in Pakistan therefore latest international literature regarding OL and snuff use cannot be extensively found in the literature search.

CONCLUSION

It is concluded from the present study that oral leukoplakia shows a wide range of histopathological features and these variants exist even in snuff users. An increased number of cases of dysplasia in snuff users as compared to non-users shows greater risk of malignant transformation in oral leukoplakia among the former group.

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Naushin T: Concept and Proofreading

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Bashir N: Data collection, Final approval

Iqbal F: Data collection and drafting the work

Hassan MU: Methodology

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REVIEW ARTICLE

A DESCRIPTIVE REVIEW OF RELATIONSHIP OF URINARY TRACT INFECTIONS WITH HEALTHCARE-ASSOCIATED AND COMMUNITY-ONSET BLOODSTREAM INFECTIONS

Amina Gul[1],Shevya Awasti[2], Momena Ali[3], Tamjeed Gul[4]

[1]Department of Pathology, Khyber Medical College Peshawar - Pakistan

[2]School of Public Health, University of California, Berkeley - United State of America

[3]Department of Pathology, Khyber Medical College Peshawar - Pakistan

[4]Department of Surgery Bacha Khan Medical College, Mardan - Pakistan

ABSTRACT

Background: Bloodstream Infections (BSIs) that arise secondary to urinary tract infections (UTIs) are frequently encountered in both community and hospital settings and are associated with significant morbidity, mortality, high healthcare costs and prolonged hospital stays

Objective: This descriptive review aims to evaluate available information on the relationship of urinary tract infections with healthcare-associated and community-onset bloodstream infections to get a deeper understanding of improved public health interventions and suggest possibilities for future research.

Material andMethods: A literature search was conducted using PubMed and Embase. Articles published during the last 10 years (2010 and 2020) were imported into covidence for the initial title and abstract screening. All study abstracts were reviewed by two independent reviewers and were eligible for full-text review if they mentioned urinary tract infection as a source of bloodstream infection. The data obtained were analyzed in Microsoft Excel.

Results: Out of 65 articles reviewed for full text, 10 studies were selected. In total 6763 BSI cases were reported. We observed 2075 (30.6%) community-acquired (CA) BSIs compared to 1102 (16.2%) healthcare-associated (HCA) BSIs, and 1484 (21.9%) hospital-acquired (HA) BSIs. UTI was a major source of BSIs in community settings followed by HCA BSIs in most studies. Escherichia. coli was the most common pathogen isolated in patients with CA-BSIs. Hospital Acquired and HCA bacterial infections have the most antimicrobial resistance, compared to CA-infections.

Conclusion: Urinary tract Infections are a major source of developing secondary BSIs. Escherichia. coli is a major pathogen in CA-BSIs. Multidrug-resistant organisms accounted for most of the BSIs, especially in hospital settings and among patients receiving health care.

Keywords: Bloodstream infection, UTI, Hospital Acquired, Community Acquired

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INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections around the world affecting over 150 million people annually.[1] The clinical phenotypes of UTIs are heterogenous and range from mild self-limiting illness to severe life-threatening complications.[2] Bloodstream Infections (BSIs) that arise secondary to urinary tract infections (UTIs) are frequently encountered in both community and hospital settings and are associated with significant morbidity, mortality, high healthcare costs, and prolonged hospital stays.[3-4] Traditionally community-acquired bloodstream infections (CA-BSIs) are BSIs identified in outpatients or in inpatients whose first blood culture tests positive within 48 hours of hospital admission, while hospital-acquired bacteremia (HA-BSIs) is defined as a BSI that occurs in an inpatient whose first blood culture tests positive after 48 hours of admission.[5]

In recent years, dramatic changes in the epidemiology of BSIs have been noted due to a shift in our approach to medical management. Some traditional inpatient procedures are now routinely performed on an outpatient basis. Examples include patients attending day-hospital centers for chemotherapy infusions, hemo-

Correspondence
Dr. Tamjeed Gul
Assistant professor of Surgery
Department of Surgery Bacha Khan Medical College, Mardan - Pakistan
Cell: +92-334-9022439
Email: tamjeedgul@hotmail.com
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dialysis clinics, patients undergoing ambulatory surgical procedures, and people living in nursing homes with on-site home medical care. These patients acquire infections under circumstances that cannot be classified as HA or CA infections and are referred to as community-onset healthcare-associated infections (HCA-BSIs).[5-6] Numerous studies have attempted to identify potential risk factors associated with the development of secondary- bloodstream infections and reported UTIs as one of the common sources of infection besides pneumonia, abdominal infections, and skin and soft tissue infections. Secondary-BSIs differ in their epidemiological and clinical characteristics and antibiotic resistance profiles and prognosis and are dependent in part on the population studied, study settings, the underlying infection focus, and other associated comorbid conditions. Available data to explain an adequate relationship between UTIs with either CA, HCA or HA-BSIs needs further evaluation. Here, we aimed to conduct a descriptive review of all the available literature published within the last 10 years that focused on risk factors for secondary BSI. In this descriptive review, we aimed to compare the characteristics of the three types of secondary BSIs in the context of UTIs to assess the potential impact of UTIs for each type of BSI and suggest future directions for improved public health and clinical intervention to prevent these serious complications of UTI.

MATERIAL & METHODS

A literature search was conducted using two databases--PubMed and Embase. Embase was searched for articles using the search terms ('bloodstream infection' OR 'bloodstream infection'/exp OR bloodstream infections OR 'bacteremia' OR bacteremia') AND ('urinary tract infection' OR 'urinary tract infection'/exp OR 'urinary tract infections' OR 'UTI' OR 'UTIs') AND ('healthcare associated infection'/exp OR 'healthcare associated infection' OR 'hospital acquired infection') AND 'community-acquired infection'/exp OR 'community-acquired infection*'). For PubMed we used the following search terms, ("Urinary Tract Infections"[Mesh] OR "Urinary Tract Infections" OR "Urinary Tract Infection" OR "UTIs") AND ("Bacteremia"[Mesh] OR "Bacteraemia" OR "Bloodstream infections" OR "Bloodstream infection") AND ("Cross Infection"[Mesh] OR "Hospital Acquired Infection" OR "Healthcare-associated Infection) AND ("Community-Acquired Infections"[Mesh] OR "Community-Acquired infection*".) Both of the searches were performed on 05-01-2020. Articles published in English during the last 10 years (2010 and 2020) were initially downloaded using Endnote software and then imported into COVIDENCE for the initial title and abstract screening. All study abstracts were reviewed by two independent reviewers and were eligible for full-text review if they mentioned UTIs as a source of BSIs. Since this review was descriptive, grey literature in the form of conference proceedings, newspapers, fact sheets, policy documents, and a thesis were not incorporated. Data was finally extracted and imported into an excel sheet for analysis. Characteristics of the studies including author names, year of study, study design (Table 1), and the total number of UTI cases and BSI cases were recorded (Figure 2).

RESULTS

The initial database search query outlined in the methods section yielded 1538 studies that matched our search criteria. About 264 studies were removed as duplicates and 1270 abstracts were reviewed. 1209 studies were found irrelevant and 65 articles were included for a final full-text review. In total 10 studies were selected for this systematic review after resolving any disagreements through consensus. This selection included all the studies where UTI was found in patients with Secondary BSIs, either as CA, HCA, or HA-BSIs. Out of 5 prospective, 3 retrospective, and 1 case-control and surveillance study that fulfilled our inclusion criteria, 8 were conducted in Europe and one each in Taiwan and Spain respectively

Every study that we analyzed, reported blood stream infections as either CA-BSI, HCA-BSI, or HA-BSI. The total number of BSIs and UTIs recorded from each of the 10 studies is shown in Figure 2. Due to variability in the definitions of BSIs, the bar graph shown below depicts some studies in which not all three types of BSIs were reported. Given the data that was presented to us however, we noted that community-acquired BSIs seemed to be the most prevalent infection in patients. 5 out of the 10 studies we analyzed had more community-acquired BSI reports than any of the other types of BSIs and we found the same trend after combining the data from every study. In total 6763 BSI cases were reported in total, and 2075 (30.6%) were community-acquired BSIs compared to 1102 (16.2%) healthcare-acquired BSIs, and 1484 (21.9%) hospital-acquired BSIs.

UTI was a major source of BSIs in community settings followed by HCA BSIs in most studies. Since 2018 we found only three studies (data collected between 2006-2013) taking into consideration the three major categories of BSIs and defining UTI as an important underlying source of infection (1-3, Figure 2). In two of the studies by Melzer and Freeman et al (9 and 10 in Figure 2), HCA-BSI was not recorded as a separate group and UTI was reported for CA and HA-BSI groups. For 5 of the above studies (4-8 in Table 1, Figure 2), the total proportion of UTI cases among the three BSI groups was collectively reported and therefore their study observations were limited by documenting UTIs irrespective of whether these infections were acquired in the community or were otherwise healthcare-associated or hospital-acquired.

Pathogen-specific Data and Antimicrobial Resistance. Escherichia. coli was the most common pathogen isolated especially in patients with CA-BSIs. K. pneumonia, P. aeruginosa, and Enterobacter were also reported as

potential pathogens implicated predominantly in HA, and HCA-BSIs. Staphylococcus aureus, streptococcal and enterococcal species were the commonly studied pathogens. Three studies (1, 3, 6) highlighted the importance of ESBL-producing GNB notably E coli and K. Pneumonia in patients with either HA or HCA-BSIs, while no study reported any information on specific Sequence Types of pathogens held responsible for S-BSIs. Many of the papers reported whether their pathogen of interest was resistant to certain antibiotics, without clarifying what kind of infection the pathogen was from. However, between the data of these three studies listed in Table 2, HA and HCA bacterial infections seem to have the most antimicrobial resistance, compared to CA-infections.

Klebsiella pneumoniae is an important human pathogen in the community and in the hospital setting. K. pneumoniae is the second most common cause of Gram-negative bloodstream infections after Escherichia coli. Horcajada et al in 2021 focused specifically on BSI secondary to Urinary focus and observed a high level of resistance for HCA-BSIs when compared to HA and CA-BSIs While comparing enterococcal bacteremia between the two enterococcal species, BSI caused by E. faecium were more resistant than those associated with E. faecalis. The precise role of antibiotic-resistant pathogens in HA-BSIs and HCA-BSIs points towards increased selection pressure in hospital environments and inadequate empirical treatment in these settings.

DISCUSSION

Every study we analyzed reported BSIs as either CA-BSI, HCA-BSI, or HA-blood stream infections. Due to variability in the definitions of BSIs, the bar graph above (Fig 2) depicts some studies in which not all three types of BSIs were reported. Given the available data that was presented to us, however, we noted that community-acquired BSIs seemed to be the most prevalent bloodstream infection in patients. We found 5 out of 10 studies that we analyzed had more community-acquired BSI reports than any of the other types of BSIs. Combining all of the data from every study, 6763 BSI cases were reported in total, we incorporated 2075 community-acquired BSIs, 1102 and healthcare-associated BSIs compared to 1484 hospital-acquired BSIs.

Earlier studies reported differences between HCA-BSIs and HA-BSIs in terms of the underlying diseases, infection focus, causative pathogens, their antibiotic susceptibility patterns, and prognosis, while others found that HCA-BSIs differed from both CA and HA-BSIs in terms of causative pathogens and prognosis.[6-9] Therefore, the

Table 1: Characteristics of the 10 studies included for review.

S No	Author/Year of Publication	Country	Study Design	Study Duration	Title of Study
1	Cubero et al., / 2018	Spain	Retrospective	2009-2007	Molecular Epidemiology of Klebsiella pneumoniae Strains Causing Bloodstream Infections in Adults
2	Hsu et al., /2018	UK	Prospective	2013-2012	Strategy to reduce E. coli bacteraemia based on cohort data from a London teaching hospital
3	Pinholt et al., /2014	Denmark	Prospective	2009-2006	Incidence, clinical characteristics and -30day mortality of enterococcal bacteraemia in Denmark: a population-based cohort study
4	Arco et al., /2017	Spain	Prospective	2010-2008	Results of an early intervention programme for patients with bacteraemia: analysis of prognostic factors and mortality
5	Frakking et al., /2013	Netherlands	Retrospective	2010-2008	Appropriateness of Empirical Treatment and Outcome in Bacteremia Caused by Extended-Spectrum--Lactamase-Producing Bacteria
6	Horcajada et al., /2012	Spain	Prospective	2011-2010	Healthcare-associated, community-acquired and hospital-acquired bacteraemic urinary tract infections in hospitalized patients
7	Kang et al., /2011	Korea	Surveillance	2009-2008	Clinical significance of nosocomial acquisition in urinary tract–related bacteremia caused by gram-negative bacilli
8	Kao et al., /2011	Taiwan	Retrospective	2005-2004	Isolated pathogens and clinical outcomes of adult bacteremia in the emergency department: A retrospective study in a tertiary Referral Center
9	Melzer et al., /2013	UK	Prospective	2011-2007	Thirty-day mortality in UK patients with community-onset and hospital-acquired MSSA bacteraemia
10	Freeman et al., /2012	New Zealand	Case control	2007-2003	Bloodstream infection with extended-spectrum beta-lactamase-producing Enterobacteriaceae at a tertiary care hospital in New Zealand: risk factors and outcomes

Table 2: Comparison of Antibiotic susceptibility patterns of pathogens isolated among patients with urinary tract related BSIs in three studies

Study	Pathogen	Type of Infection	AMR Pattern identified in patients with BSIs		
Cubero et al., 2018	K. pneumonia	S-BSI	Amc	Cip	Gent
		HA	223/56	223/72	223/13
		HCA	58/8	58/14	58/1
		CA	67/7	67/12	67/0
Pinholt et al.,2014	E. faecalis	S-BSI	Amp	Van	Gent
		HA	209/5	209/4	209/9
		HCA	104/1	104/2	104/54
		CA	144/0	144/1	144/28
	E. faecium	HA	207/191	207/3	207/145
		HCA	18/15	18/0	18/7
		CA	18/7	18/0	18/2
Horcajada et al.,2012	Enterobacteriaceae	S-BSI	Amc	FQ	Pip/Taz
		HA	142/45	142/51	142/27
		HCA	246/73	246/124	246/37
		CA	279/52	279/69	279/19

Amp: ampicillin; Amc: amoxicillin clavulanate; Cip: ciprofloxacin; Gent: gentamicin; Van: vancomycin; FQ: Fluroquinolone; Pip/Taz: piperacillin-tazobactam

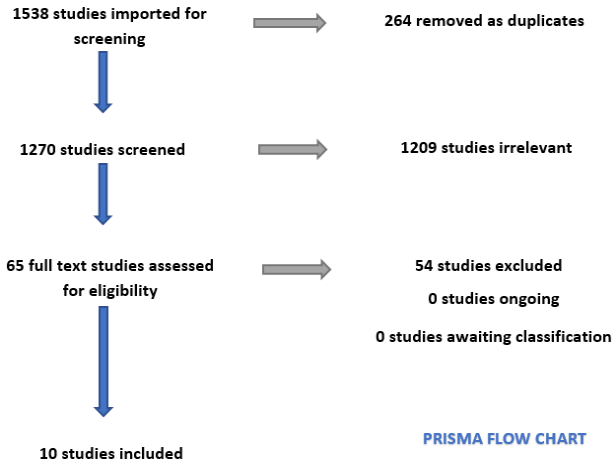

Fig 1: PRISMA Flow Chart showing the stepwise approach towards the inclusion of 10 studies for this descriptive review. The flow diagram depicts the flow of information through the different phases of a systematic review.

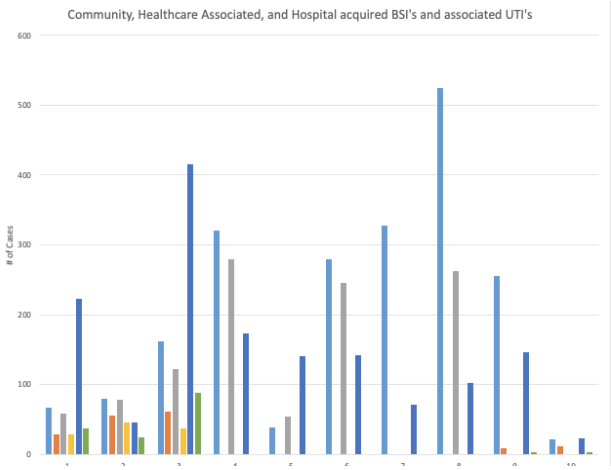

Fig 2: Total number of BSIs (CO, Community Onset; HCA, Healthcare Associated; HA, Hospital Acquired) and UTIs in 10 studies. Numbers from 1 to 10 correspond to studies represented in Table 1.

characteristics of BSI are different depending on the context of infection. A detailed analysis of all the studies included in the present review revealed that UTI was a major source of BSIs in community settings followed by HCA BSIs. Since 2018 we found only three studies (data collected between 2006-2013) taking into consideration the three major categories of BSIs and defining UTI as an important underlying source of infection.[10-12] In two studies by Freeman and Melzer et al, conducted in 2012 and 2013 respectively, found a high proportion of patients that had concurrent UTIs in CA-BSIs as compared to HA BSIs.[13-14] However, they were unable to report HCA-BSIs as separate groups assuming HCA-BSIs as part of CA-BSIs. The remaining 5 studies lack information with respect to UTI cases for each category of BSI and data reported was a total proportion of UTI among the three BSI groups collectively therefore their study observations were limited by documenting UTIs irrespective of whether these infections were acquired in the community or were otherwise healthcare-associated or hospital-acquired.[14-18] Further, it was observed that the standard definitions to meet the criteria for assigning a urinary focus as a definite source of BSI were not clearly stated especially for studies where the primary outcomes were not focused entirely on UTIs.

Most of the studies collected data from either hospital or laboratory records that in some instances was found incomplete in terms of important investigations like urine culture reports and matching organisms. Lack of data as to how many UTI cases were distributed between CA and HA-BSIs requires future studies to differentiate between infections that are truly community-acquired from those that occur as a result of healthcare acquired in the community i-e HCA BSIs. The basic classification of 'pre-day 2 of hospital admission' cases as 'community' may not truly represent infections acquired because of outpatient care that is being offered in the community, or those occurring immediately after discharge from the hospital to continue convalescing at home.[19] That would suggest that a high proportion of 'community' cases observed in some studies may, in part, be the result of this lack of precision as described earlier.[13]

Amongst various pathogens implicated in causing UTI-related BSIs, Escherichia coli was the most common pathogen isolated especially in patients with CA-BSIs.[11] klebsiella pneumonia, pseudomonas aeruginosa, and Enterobacter species were also reported as potential pathogens implicated predominantly in HA, and HCA-BSIs. Among the gram-positive bacteria Staphylococcus aureus including methicillin-susceptible Staphylococcus aureus and Methicillin-resistant Staphylococcus aureus, Streptococcus species, and Enterococcus faecalis and faecium were the commonly studied pathogens. Three studies highlighted the importance of ESBL-producing Gram-negative bacteria notably E. coli and K. pneumonia in patients with either HA or HCA-BSIs, while no study reported any information on specific sequence types of pathogens responsible for Urinary tract-related BSIs. Many of the papers reported whether their pathogen of interest was resistant to certain antibiotics, without clarifying what kind of infection the pathogen was from. However, between the data of these three studies, HA and HCA bacterial infections seem to have the most antimicrobial resistance, compared to CA-infections (Table 1). According to the Cubero et. al 2010 study, 141/223 (63.2%) of HA and 23/58 (39.6%) of HCA-K. pneumoniae infections had some form of antimicrobial resistance, compared to 19/67 (28.3%) CA-infections.[10] Similarly, the study by Horcajada et al, reported that 123/143 (86.6%) HA Enterobacteriaceae and 234/246 (95.1%) HCA Enterobacteriaceae had some form of antimicrobial resistance, compared to 140/279 (50.17%) CA infections. [16] Lastly, the study by Pinholt et al, 2014, reported 209 E. faecalis and 207 E. faecium HA infections. Of 209 HA-E. faecalis infections 103 (49%) isolates had some sort of antimicrobial resistance.[12] About 55/104 (52.8%) HCA E. faecalis infections and 22/18 (some infections had resistance to more than one antibiotic) HCA E. faecium-related BSIs were reported. In comparison, only 29/144 (20.1%) of the CA-E. faecalis and 9/18 (50.0%) of the CA E. faecium had some form of antimicrobial resistance. E. faecium did seem to have a higher antimicrobial resistance rate, as it matches the HA and HCA rates previously stated, however, it should be noted that only 18 CA-infections of E. faecium were recorded. Consequently, just 9 antimicrobial-resistant infections bring the rate up to 50%. Due to the stark difference in the number of infections of HA and HCA E. faecium infections versus CA-infections, the resistance rates should be compared with caution. The precise role of antibiotic-resistant pathogens in HA-BSIs and HCA-BSIs noted reflects the increased selection pressure in hospital environments in conjunction with inadequate empirical treatment in these settings. As the estimated burden of antibiotic-resistant HCA-BSIs is proportionately high, a separate classification of CA and HCA-BSIs is important as the problem of drug resistance in CA infections will be overestimated using the traditional classification.[18] The finding of this review is limited by a small data set and lack of data on other potential sources of HA-BSIs.

CONCLUSIONS

Urinary tract Infections are a major source for developing secondary BSIs. Escherichia. coli is a major pathogen in CA-BSIs. Hospital Acquired and HCA bacterial infections have the most antimicrobial resistance, compared to CA-infections. As UTIs are a potential risk factor for developing life-threatening BSIs further investigation into the true relationship of UTIs with S-BSIs is required to improve the clinical management and outcomes of patients. CDC/NHSN recommendations for establishing a definite association between BSI and UTI must be met to assess the actual burden of urinary tract-related BSI. Assuming that HCA-BSIs and HA-BSIs share characteristics based on their mode of acquisition, underlying infection focus, microbiological profile, antibiotic resistance patterns, and prognosis, collecting surveillance data on HCA and HA-BSIs secondary to UTI would have obvious implications for professionals involved in the care of sick patients in community settings.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Gul A:	Study conception, Literature search, Data Entry, Writing, Critical review
Awasti S:	Study conception, Literature search, Data analysis, Critical review
Ali M:	Literature search, data entry
Gul T:	Literature search, Writing, critical review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CLEAR CELL CARCINOMA OF ENDOMETRIUM IN A POSTMENOPAUSAL PAKISTANI WOMAN - A CASE REPORT

Samdana Wahab, Farzana Burki, Rabia Kareem

[1]Department of Obstetrics and Gynaecology, Mercy Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objective: This case reports a 54-year-old female patient, para 4, who presented with repeated episodes of postmenopausal vaginal bleeding, mild vaginal discharge, and dull lower abdominopelvic pain for a six-month duration. It was associated with a loss of appetite. The abdominal examination was non-significant, and on vaginal examination, a 4x2cm friable mass was seen protruding from the cervix. The uterus was 8-10 weeks in size, sand oft, with regular margins. Transvaginal ultrasound showed a 2.4 cm thick endometrium, 2 intramural fibroids 2x2 cm in size, and normal ovaries. There was no free fluid in the pouch of Douglas and no enlarged lymph nodes.

She was advised an endometrial biopsy, but refused and opted for a total abdominal hysterectomy. She underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO). Specimen biopsy showed poorly differentiated endometrial clear cell carcinoma, stage 2-B, and was referred for radiotherapy (vaginal brachytherapy) with regular follow-ups.

Keywords: Endometrial carcinoma, Clear cell carcinoma, post-menopausal bleeding.

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INTRODUCTION

Endometrial carcinoma (EC), a very rare but highly aggressive, is the sixth most prevalent malignancy and has a mortality rate of 2%. It is the 14th leading cause of malignancy-related deaths among women worldwide. [1] It constitutes up to 1-6% of all uterine malignancies and has a poor prognosis[2] The exact etiology is unknown, but usually develops in postmenopausal women with atrophic endometrium The presenting complaints of a patient are usually abnormal vaginal bleeding, vaginal discharge, and lower abdominal pain.

Microscopically, CCC is characterized by glandular atypia, clear, eosinophilic, hobnail cells, that appear clear because of the presence of glycogen content. These cells have different shapes and patterns including solid, papillary, and tubulocystic.[4]

CCC is very rare and the lack of retrospective data regarding standardized plans, thus makes the proper treatment plans more difficult.

Correspondence
Dr. Samdana Wahab
Department of Obstetrics and Gynaecology, Mercy Teaching Hospital, Peshawar - Pakistan
Email: samdana32@gmail.com
Cell: +92-345-9049933
Date Received: 04-11-2022
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CASE REPORT

A 54-year-old patient, Para 4 presented to the hospital, and outpatient department complaining of repeated episodes of postmenopausal vaginal bleeding, clear, non-offensive vaginal discharge, and dull non-radiating lower abdominal-pelvic pain for six months. She was also complaining of loss of appetite, weakness, and fatigue but no weight loss, or bowel or bladder symptoms. On examination, she was well-oriented and vitally stable. On physical examination, abdominal findings were non-significant. On the vaginal examination, the uterus was significantly enlarged, 8-10 weeks in size, soft, with regular margins, and globular in shape. There was a 4x2 cm soft, and not bleed-to-touch friable mass protruding from the cervix. There was no fullness or mass felt in the fornices. Transvaginal ultrasound showed a 2.4 cm thick endometrial layer, 2 intramural fibroids 2x2 cm in size, and normal-looking ovaries, no free fluid in the pouch of Douglas, and abdominal pelvic lymph nodes were not enlarged.

The patient was advised of an endometrial biopsy, but she refused and opted for a total abdominal hysterectomy. She underwent TAH+BSO. Histopathology report showed poorly differentiated endometrial clear cell carcinoma.

The longitudinal horizontal extent/length of stromal invasion was 16 mm while the circumferential horizontal extent/width of stromal invasion was 25 mm. Other tissue/organ Involvement was not seen. The ectocervical margin involved and paracervical margins were free of tumor.

The uterus measures 80 x 50 x 40 mm. On sectioning, the maximum thickness of the endometrium was 1 mm, myometrium 12 mm. Sectioning of the myometrium revealed two subserosal and intramural fibroids. The largest fibroid measured 50 x 10 mm. The attached right fallopian tube measured 40 x 10 mm. The right fallopian tube stump measured 15 x 10 x 10 mm. The left fallopian tube measured 43 x 4 mm. Sectioning of the both fallopian tube and ovary were unremarkable.

According to the Revised FIGO classification of endometrial carcinoma, she had stage 2-B poorly differentiated endometrial clear cell carcinoma. She recovered well from surgery, and now receiving radiotherapy (vaginal brachytherapy) with regular follow-ups. The follow-up plan included 3 3-monthntervals for the first year, 4 months for the second year, 6 months for the next five years, and then annually for life long.

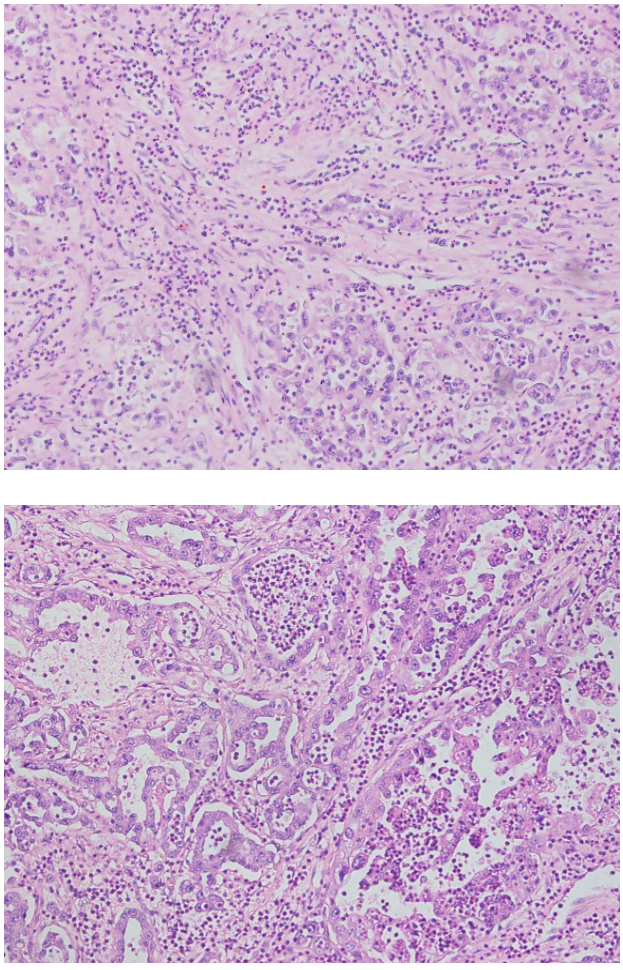

Fig 1: Histologic grade showed Stromal Invasion.

DISCUSSION

In affluent nations, (EC) is the most prevalent gynecological malignancy that typically manifests in post-menopausal women[5]. About 80% of (EC) are Type I tumors (endometrioid adenocarcinomas). They are estrogen-responsive with a better prognosis. Type-2 tumors make up 10–20 percent of EC and are high-grade endometrioid and non-endometrioid tumors. The non-endometrioid tumors include clear-cell, serous, mucinous, squamous, transitional cell, mesonephric, carcinosarcoma, and undifferentiated types. All these are non-estrogenic, very rare, and with a worse prognosis.[6]

The CCC of the uterus is a very rare, aggressive histo-type, constitutes up to 1-6% of all uterine malignancies, with worse outcomes. Because of the tumor's rarity, diagnosis is challenging as most patients present in the late stage of the disease.

Patients with CCC typically present with postmenopausal bleeding. Transvaginal ultrasonography and preoperative diagnostic endometrial biopsy help reach the diagnosis.[7] Computer tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are particularly useful for detecting the amount of tumor invasion, the presence of adnexal, distant metastases, and lymph-vascular involvement. Histopathology reports determine the final diagnosis.

CONCLUSION

In this case, it is very important to focus on taking informed consent, and proper counseling regarding the importance of diagnostic dilatation and curettage. The Oncologist gynaecologist's involvement is very beneficial while planning the staging laparotomy.

ACKNOWLEDGMENT

The authors thanked Dr. Hanzla Maryam and the Pathology Department of Shaukat Khanum Hospital Lahore for sharing histopathology pictures.

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INSTRUCTIONS FOR AUTHORS

Manuscript Submission

The Journal of Medical Sciences follows the uniform requirements for manuscripts submitted to Biomedical Journals as approved by the International Committee of Medical journal Editors as updated in Oct. 2004 and available at www:icmje.org. Manuscripts are accepted for consideration if neither the article nor any of its contents has been or will be published or submitted elsewhere before appearing in Journal of Medical Sciences.

Manuscript Formatting Guideline

While submitting the document on JMS website, the authors are advised to follow the following guidelines:

1) Always use MS Word format. Don't send any tables in JPG format.

2) Always use Calibri fonts.

3) use 12 size fonts.

4) Double space the manuscript.

5) Justify the margins

6) Keep the main headings bold and in size 14.

7) No extra spaces between paragraphs.

8) Black text on white background only.

Title and Authors Name

The first page of the manuscript must give the title of the article that should be concise and descriptive. Also include on this page the name(s) of the author(s), highest academic degrees, the name of the department and institution in which the work was done, the institutional affiliation of each author, and the name and address of the author to whom reprint requests should be addressed.

Any grant/support that requires acknowledgement should be mentioned on this page. Abstract's word count and article (excluding references) word count should appear at the bottom of this page.

Abstracts

Abstract must not exceed 250 words and the **article must not exceed 3000 words** (excluding references). Articles exceeding the word count or not conforming to "Instructions for authors" will be returned without processing. It is further emphasized that results must not be duplicated in text/tables/figures/graphs.

Key words

Three to 10 key words or short phrases should be added to the bottom of the abstract page. Terms from the Medical subject headings (MeSH) list of Index Medicus should be used.

Introduction, Material and Methods, Results, Discussion, Conclusion, Acknowledgments and references should all start on a separate page from page 03 onwards.

References

The total number of references in an original article must not exceed 40 while in the review articles maximum limit is 100. References must be written double-spaced and numbered as they are cited in the text.

The references must be written in Vancouver style. The style for all the types of references is given in the "Uniform requirements for manuscripts submitted to biomedical journals" at the website of International Committee of medical journal editors. **www.icmje.org**

List all authors when there are six or fewer. If there are more than six, list the first six followed by "et al".

Tables and Illustrations

Each of the tables and illustrations should be on a separate page, must have a title and be on a double space.

Figures should be professionally designed. Symbols, lettering and numbering should be clear and large enough to remain legible after the figure has been reduced to fit the width of a single column. The back of each figure should include the sequence number, the name of the author and the proper orientation (e.g. "top"). If photographs of patients are used, either the subjects should be unidentifiable or their pictures must be accompanied by written permission to use the figure. Duplication of results given in tables and into figures must be avoided.

Ethics

When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983. Do not use patients names, initials, or hospital numbers especially in illustrative material. When reporting experiments on

animals, indicate whether the institution's or a national research council is guide for, or any national law on the case and use of laboratory animals was followed. No article will be entertained without prior ethical approval from ethics committee/ board.

Units of Measurements

Authors should express all measurements in conventional units, with System International (SI) units given in parentheses throughout the text.

Abbreviations

Except for units of measurements abbreviations are discouraged. The first time an abbreviation appears it should be preceded by the words for which it stands. However title and abstract must not contain any abbreviation.

Statistics

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible quantify findings and present them with appropriate indicators of measurements error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as the use of ρ values, which fails to convey important quantitative information. Discuss the eligibility of experimental subjects. Describe the methods for and success of any binding of observations. Report complications of treatment. Give numbers of observations. Report losses to observation (such as dropouts from a clinical trial). Specify any computer programs used.

Put a general description of methods in the Methods Section. When data is summarised in the Results Section, specify the statistical methods used to analyse it. Restrict tables and figures to those needed to explain the argument of the paper and to assess its support avoid non technical uses of technical terms in statistics, such as "random" (which implies a randomizing device) "normal" significant, "correlation", and sample.

Define statistical terms, abbreviations, and most symbols.

Drug Names

Only generic names should be used.

Permissions

Materials taken from other sources must be accompanied by a written statement from both author an publisher giving permission to the journal for reproduction.

Case Report

Short report of cases, clinical experience, drug trials or adverse effects may be submitted. They must not exceed 500 words, 5 bibliographic references and one table or illustration. The report must contain genuinely new information. The format is title, abstract, introduction, case report, discussion, references.

Review and Action

All articles on receipt for publication are immediately acknowledged but that does not imply acceptance for publication.

Submitted manuscripts are reviewed for originality, relevance, statistical methods, significance, adequacy of documentation, reader interest and composition. Manuscripts not submitted according to the instructions will be returned to the author for correction prior to beginning the peer review process. All manuscripts considered suitable for review are evaluated by a minimum of two members of editorial board. The manuscripts is then sent to two or more than two reviewers who may take a couple of months time to review the manuscript. The ultimate authority to accept or reject the manuscript rests with the Editor.

Revised manuscripts are judged on the adequacy of responses to suggestions and criticisms made during the initial review. All accepted manuscripts are subject to editing for scientific accuracy and clarity by the office of the Editor. When the manuscripts is deemed fit for publication, letter of acceptance is issued to the author. No article is rejected unless similar comments are received from at least two reviewers.

FOR DETAILS, SEE OUR EDITORIAL POLICY IN THE NEXT SECTIONS

AUTHOR'S AGREEMENT

Journal of Medical Sciences (KMC Peshawar pISSN 1997-3438)

Journal_____

ArticleTitle_____

I certify that

A) None of the material in the manuscript has been published previously/currently under consideration for publication elsewhere.

B) The article has not been accepted for publication elsewhere

C) I have not signed any right or interest in the article to any third party

D) I am able/willing to produce the data on which this article is based, should the Editorial Board of the Journal of Medical Sciences request such data.

E) Animal Care Committee/Institutional Review Board approval was granted for this study.

I (including spouse and children), disclose financial interest at the level

a) Nothing to disclose b) Financial interest to the amount of _____

F) I/We confirm to comply fully with the suggestions/critical views of the reviewers/editor, failing which my/our article may be rejected at the sole discretion of the editor. I/we further confirm that if our article is rejected (whihc is the sole discretion of the editor) I/we will have no right to complain against the journal/editor/representative of the journal/printer in any forum including the court of law.

G) I/we suggest the following two overseas reviewers to review our article.

1) _____	_____	_____
2) _____	_____	_____
Name of reviewer	Postal address	Email address & Telephone No.

_____	_____	_____
Author name	Author signature	Author e-mail address

Note: Author agreement form must be signed by each author (one page for each) and submitted with the article.

Author's Checklist:

i) Eliminate nonstandard abbreviation in the titles
ii) Supply full author names (including institutional affiliation and contact informations)
iii) Contribution of individual authors
iv) Nomination of first 3 co-authors by the principal author
v) Abstract: 200 words, Article: 2000 words (excluding references).
vi) Supply references in Vancouver style, accurately cited in the text in numerical order
vii) Cite tables in the text in numerical order
viii) Send 03 Hard copies and on a R/W CD (in MS Word), in a protective envelop, do not use clips
ix) Cite figures in the text in numerical order
x) Author agreement is signed by all authors.
xi) Departmental Permission Letter for the study.
xii) Letter of ethical review of concerned hospital/study place.
xiii) Bank draft for Rs. 5000/- (Rs. Five Thousand) in the name of Journal of Medical Sciences, Peshawar, Pakistan/or deposit in cash with Managing Editor Account No. 4048685170 (3548-9) Can be transferred ONLINE to the Account No. 4048685170 (3548-9) Branch Code 0388 at National Bank of Pakistan, University Campus Branch, Peshawar.

EDITORIAL POLICY

THE EDITORIAL POLICY OF THE JOURNAL OF MEDICAL SCIENCES (JMS), KHYBER MEDICAL COLLEGE, PESHAWAR

Overview

This document highlights the mission, objectives, and editorial policy of JMS regarding the publication process by adhering to the guidelines of COPE (Committee in Publication Ethics) and ICMJE (International Committee of Medical Journals Editors). Each component of the editorial policy is explained in the next sections.

A MISSION OF JMS

To publish relevant, scientific, and accessible material to help medical students and health professionals in their practice, teaching and learning, and career development

B OBJECTIVES OF JMS

a. To publish clinical, epidemiological, public health, educational, translational, and allied sciences research to enable scientists, clinicians, and researchers to learn about developments and innovations in these disciplines

b. To publish high-quality descriptive and experimental research, review articles, editorials, and case reports enhancing the understanding of the scientific community regarding clinical practice and education

c. To provide a platform for the scientific community in promoting their career development through publishing quality research

C EDITORIAL POLICY

1 Open access

JMS is an Open access scholarly literature source that is free of charge and often carries less restrictive copyright and licensing barriers than traditionally published works, for both the users and the authors. However, it complies with well-established peer review processes and tries to maintain high publishing standards.

2 Peer review process

The review process of JMS is following a "triage approach". Upon submission of a manuscript, either online or physical, the document undergoes a preliminary open (un-blinded) review in the chief editor's office. The document is either accepted for further review, sent for revision back to the authors, or rejected at that time. Further review of JMS follows a blinded approach, where the article is sent to 2 reviewers, local and international reviewers. During this process, all the relevant information about the authors and reviewers is kept confidential. However, we encourage sharing reviewers' comments with co-reviewers of the same paper in a blinded manner, so reviewers can learn from each other in the review process. We also encourage the readers to send us the post-publication reviews about research work in the form of letters to the editors, which are then published and shared with the authors of relevant articles. The editorial board has the authority to retract an article if a serious violation of credibility or quality of research is found after the article is published.

The journal is under no obligation to send submitted manuscripts for review, and under no obligation to follow reviewer recommendations, favorable or negative at all times. The editor of a journal is ultimately responsible for the selection of all its content, and editorial decisions may be taken on issues unrelated to the quality of a manuscript, such as suitability for the journal. An editor can reject any article at any time before publication, including after acceptance if concerns arise about the integrity of the work.

3 Authorship

According to the ICMJE criteria, authorship is based on 4 criteria; (1) conceptualization and designing, (2) AND, data collection, (3) AND, writing and critical review,

(4) AND, taking responsibility for the authenticity and integrity of all the research process. All those designated as authors should meet all these 4 criteria. The co-authors should declare their roles and contributions to the research process explicitly. Those who do not meet all 4 criteria should be ACKNOWLEDGED only. If agreement cannot be reached about who qualifies for authorship, the institution(s) where the work was performed, not the journal editor, should be asked to investigate. If authors request removal, addition, or change in the sequence of an author after manuscript submission or publication, journal editors should seek an explanation and signed statement of agreement for the requested change from all listed authors and the author to be removed or added. The corresponding author is the one individual who takes primary responsibility for communication with the journal during the manuscript submission, peer review, and publication process. The corresponding author typically ensures that all the journal's administrative requirements, such as providing details of authorship, ethics committee approval, clinical trial registration documentation, and disclosures of relationships and activities, are properly completed and reported. The maximum number of authors for any manuscript must not exceed 6. If the number of authors exceeds this number, an explicit rationale for their role must be provided, which will be decided by the committee comprising the chief editor, executive editor, and managing editor.

4 Submission of manuscript

The manuscript should be submitted through the journal website which is using the Online Journal System (OJS) along with the Institution research and ethics board (IREB) certificate. The article should have the following format:

4.1: The abstract should be structured with a word count of not more than 250 words.

4.2: The fonts should be Calibri, with size 12, and spacing of 1.5, with justified margins in MS office format.

4.3: The whole document should not be more than 3000 words (excluding references and appendices).

4.4: The number of figures and tables should not exceed 5 in the whole document.

4.5: The pictures and tables should be black and white in color.

4.6: Copied pictures and tables from other sources will not be entertained unless written approval from the original researcher and publisher is provided

4.7: Only that article will be considered for publication where the data is collected during the last 5 years.

4.8: Fifty percent of the references must be from the last 5 years. The introduction section must not have more than 30% of the total references.

4.9: any article having a similarity index of more than 50% will be declined altogether. For those having a similarity index of more than 19% but less than 50%, the authors will be given one chance to correct the manuscript.

5 Institutional Research and Ethics Board (IREB) certificate

Under no circumstances, an article will be accepted if approval from the relevant ethical board/committee is not taken before the start of the research. The board/committee should assess the proposal of research in both ethical and technical aspects before giving a certificate of approval.

6 Conflict of interest

To ensure transparency in the research conduction, writing, and publication, the authors, peer reviewers, and editors have to declare conflicts of interest regarding financial aspects, academic competitions, and relationships during the writing, reviewing, and publishing of the manuscripts. Details of sponsors along with their roles and access to data should be clearly stated.

7 Confidentiality

The editorial board in no way should publicize the work of a researcher in any form unless it is published. They should not publicize the comments and critiques given by reviewers. Similarly, the reviewers are bound to keep the confidentiality of the work of researchers during and after the review. The work of researchers and the critique should never be discussed or exemplified in forums. The confidentiality of the researchers should be maintained in every possible way when the documents are sent for review. However, our review process is open (non-blinded) in the first phase, as per the policy of the journal. In this case, the policy is displayed on the journal`s website for the researchers. Reviewers must not retain the manuscript for their personal use and should destroy paper copies of manuscripts and delete electronic copies after submitting their reviews. If a manuscript is rejected, it should be deleted from the editorial system. If an article is published, the manuscript along with its reviews and other relevant documents should be retained for a period of 3 years and then deleted. The only situation where confidentiality needs to be breached is when a situation of fraud or misconduct is found during the review process or after publication. Still, the authors and sometimes the reviewers, have to be notified.

8 Correction and retraction of articles

The guidelines for the correction and retraction of articles are as follows:

8.1: A specific page is allocated in the journal (both electronic and printed) that will be used for news related to corrections in articles published in previous journals.

8.2: The editor should also post a new article version in the journal with details of the changes from the original version and the date(s) on which the changes were made.

8.3: Previous electronic versions will prominently note that there are more recent versions of the article (that will be placed at the end of the abstract). Similarly, the authors or others should cite the more recent version.

8.4: If the error is judged to be unintentional, the underlying science appears valid, and the changed version of the paper survives further review and editorial scrutiny, then retraction with the republication of the changed paper, with an explanation, allows full correction of that research paper.

8.5: If a serious violation of credibility or quality of a research paper is found after the publication, the article has to be retracted after approval of at least 3 members of the editorial board in consultation with the chief editor. The whole process will follow the guidelines presented by Committee on publication ethics (COPE).

8.6: The retracted article should be notified on the website and the word “retracted” should be mentioned along with the title of the article.

9- Correspondence

Correspondence for submitting an article in JMS will be through a corresponding author. The duties of a corresponding author have already been presented in a previous section. Correspondence regarding debating an article is given high value and a separate page for letters to the editors has been allocated. Derogatory and demeaning letters are screened and letters that promote debates and critique are encouraged to be published. However, correspondence about the articles published in the last 1 year will be included only.

10- The fee submission process

A processing and publication fee of Rs. 10,000/-(Pakistani) for local authors and $ 250 (US) for international authors have been approved by the competent authority. The fee should be submitted as bank draft/ online payment through the account (IBAN) no: PK56NBPA0388004048685170 (Branch code: 0388 / National Bank of Pakistan, University campus branch,

Peshawar, Pakistan) as follows:

01. Article processing fee of 3000/- PKR at the time of submission of the article. This amount will be non-refundable.

02. Article publication fee of 7000/- PKR at the time of acceptance of article after external review. This amount will be refundable if the article is rejected for any reason.

03. For international authors, the amount of 250 US dollars will be accepted after both internal and external review. Researchers belonging to countries other than Pakistan are advised to submit the fee after the whole process of review is completed and the article is accepted for publication.

04. There will be no fee exemption in any circumstances, including members of the editorial board.

11 Roles of the editorial board, editors, and members

The editorial board of JMS is following the Higher Education Commission (HEC) policy for research journals. The roles of the editorial board for JMS are mentioned below:

11.1: The roles of the Editorial Board are:

11.1.1: To offer expertise in their specialist area

11.1.2: To review submitted manuscripts

11.1.3: To advise on journal policy and scope

11.1.4: To work with the Editor to ensure the ongoing development of the journal

11.1.5: To identify topics for special issues of the journal or recommend a Conference that would promote the journal, which they might also help to organize and/or guest edit

11.1.6: To attract new and established authors and articles

11.1.7: To submit some of their work for consideration, ensuring that they adhere to Conflict of Interest rules and stating their relationship to the journal. This is very important as the journal cannot be seen to publish only papers from members of the Editorial Board.

11.1.8: Editorial Boards must have a regular communication forum with other boards of similar nature, either face-to-face in person (depending on their country of origin, funding availability, etc.) or as more journals are doing today, communicating by teleconference, Skype, or other web platforms.

11.2: The Patron:

The Patron is usually the Dean of the institute and is overall in charge of the journal, who needs to be kept informed of the decisions taken by the editorial board. The patron is the final authority to approve the decisions and policies of the editorial board.

11.3: The Chief Editor:

11.3.1: The criteria for selection of Chief Editor are:

i. Expertise and experience in the specialist field related to the journal

ii. Publication record of several articles and /or books (usually in / related to the specialist field)

iii. Being a reviewer for an international peer-reviewed journal

iv. Senior research position with equivalent experience in research and scholarship

v. Enthusiasm to undertake the Editor role

vi. Preferably a diploma, master or doctoral degree in Education and Research

It is not necessary to fulfill all the criteria to become a chief editor.

11.3.2: The roles of the Chief Editor are:

i. The key role of a journal`s chief editor is to promote scholarship in the specialist field associated

with the journal, whilst also promoting the journal as the best journal to publish in. For any journal, the editor will need to encourage new and established authors to submit articles and set up a reliable panel of expert reviewers. Editors are also responsible for offering feedback to reviewers when required and ensuring that any feedback to authors is constructive.

ii. Editors should also familiarize themselves with the Committee on Publication Ethics (COPE) 'Code of Conduct and Best Practice Guidelines for Journal Editors'.

iii. Depending on how the journal is managed and how it is structured, an Editor may have to make all the decisions regarding which articles to accept or reject for publication.

11.3.3: Managing editor:

i. The roles of managing editor are:

ii. To help the chief editor to achieve the above-mentioned goals

iii. To communicate with the authors, reviewers, publishers, and other agencies for the smooth running of the journal

iv. To regularly evaluate the research work

v. Communicate with funding and regulating agencies (HEC and others) for grants and accreditations.

11.3.4: Executive editor:

The roles of the executive editor are:

i. To evaluate the research articles presented for publication

ii. To help the editorial board in policymaking

iii. They help the editorial board in smooth publishing

iv. To communicate with reviewers and collaborate with external agencies for relevant purposes

11.3.5: Section editors:

Section editors are allotted different responsibilities. Some of these are mentioned below:

i. Bibliography

ii. Proof-reading

iii. Academic writing reviewing, grammar, and spell checking

iv. Dissemination of articles for review

v. Contact with publishers under the supervision of the senior editorial team

vi. Training of future reviewers, young members, other faculty members

vii. others

11.3.5: Editorial advisory board:

Editorial advisory board members consist of national and international senior academicians, researchers, clinicians, and others to help the current editorial board in designing, implementing, and evaluating policies regarding upgrading the quality of research work. These people also share best practices to help the editorial team to refine their research work.

12 Policy regarding recruitment and continuation of the editorial board

The policy for recruitment and continuation of the editorial board is based on the guidelines discussed in the previous section. The chief editor, managing editor, and executive editors are recruited by the patron in-Chief. Members are then selected by them from amongst the faculty who have an aptitude for research, and their names are endorsed by the patron. The tenure of the editorial board is decided by the Patron after a period of 3 years whether to continue or recruit a new team or member. The editorial advisory board members are recruited for an indefinite period by the editorial team of JMS.

13 Plagiarism policy

The journal is following the plagiarism policy of the Higher Education Commission of Pakistan, and for this purpose, a plagiarism standing and review committee has been established under the chairmanship of the Chief Editor of JMS along with 4 members amongst se-

nior faculty. The committee has been given the authority to review research papers and plagiarism complaints related to published work in the journal.

14 Allegations of research Misconduct

The policies of the COPE, WAME, and ICMJE serve as the foundation for the policy of research misconduct in our journal.

Before submitting, authors must carefully read the journal's author guidelines and research ethical principles and adhere to them.

While authors have the right to recommend potential reviewers for the peer-review process, all potential reviewers will have their credentials and potential conflicts of interest carefully examined before they are invited to review.

A manuscript that is undergoing peer review or a published article may be the subject of a report of research misconduct. The application and management process for claims of author misconduct should go as follows:

14.1: An article submitted or to be published in the JMS if allegedly suspected of scientific misconduct, an official complaint for the same must be received by the office of the managing editor via email, contact@jmdsci.com. For instance, in case of plagiarism, the copied section should be underlined and the original and suspected sections should be explicitly pointed out. The complaint must specify the particular matter and details of the misconduct.

14.2: an investigation will be carried out by the editorial board and the corresponding author of the suspected article will be kept in contact. An explanation will be asked from the corresponding author in this respect. If the misconduct is accepted, the managing editor will take the following steps:

In the case of published articles, retraction might be considered.

In the case of unpublished articles, the review process may stop or continue depending on the changes suggested to the corresponding author.

If the corresponding author does not respond in the stipulated time or the response is unsatisfactory, the article may be declined or retracted.

14.3: Before reaching any conclusion in case of retraction of an already published article, the editorial team will be in consultation with the experts within or outside the institution.

14.4: If during the review process, suspicion of gifted authorship is identified, the editor in charge of the article may ask the corresponding/principal author about the role of the authors, and if the response is found to be unsatisfactory, the review process may stop or the article may be declined altogether.

15 Appeal and complaint process

The JMS follows the recommendations of COPE regarding the appeal and complaint process (https://publicationethics.org/appeals) as follows:

15.1: The authors may ask the managing editor for inquiring about the status of the article through the official email of the JMS (contact@jmedsci.com) citing their official article ID.

15.2: The author may contact the managing editor for inquiring about the reason for the rejection of articles during the review process by the above email link.

15.3: Sometimes, the authors may re-upload an article as a new submission if they have modified the article as suggested by the editors

15.4: For withdrawal of an article during the review process, the corresponding author will write

a request through the OJS to the relevant editor for retraction.

15.5: Reconsideration of the decision will be conducted only at the discretion of the managing and chief editors.

16 Contact information

The office of the managing editor or chief editor should be contacted anytime during working hours or can be contacted through their emails for correspondence.

17 Archiving and Data Repository

- In accordance with our open-access policy, we permit the self-archiving of published papers after their publication in JMS. Without requesting permission from the journal or publisher, authors are free to archive their academic works in PDF format at any time and retain ownership of the intellectual property. However, a yearly subscription is required to access the print edition of the entire magazine issue, which can be stored in libraries in the country and overseas for 500 US dollars or 5000 Pakistani rupees respectively.
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