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Oasis of knowledge

The hand drawn illustration on the cover of JSTMU encapsulates philosophy of the University and its Journal. It depicts a traveler in the desert stopping by an oasis to take a note to themselves, symbolizing the point after which their journey requires steadfastness and dedication. The note is an excerpt from the Qur'an where God beseeches human beings to reflect. This is the essence of scientific research which prescribes itself in the University logo and is represented through red and blue color in the form of the water and the red sand, and taking further inspiration in the form of the notebook and the quill.

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The *Journal of Shifa Tameer-e-Millat University (JSTMU)* is an open access bi-annually peer reviewed medical journal of the Shifa Tameer-e-Millat University (STMU), Islamabad, Pakistan. The journal encompasses papers from biomedical research, clinical specialties and interdisciplinary medical fields; thereby entertaining the scientific, research and clinical work of a wide variety of health care professionals such as medical practitioners, surgeons, nurses, pharmacists, medical technicians, paramedics, laboratory scientists, physiotherapists, dietitians and bioengineers. The journal is premised on creating influence on the academic as well as corporate thinkers. It is dedicated to presenting advances in medical sciences supporting the recognition and publication of medical scientific research and its effects on human health and well-being. A key question we apply to submission is, "Is this paper going to help readers better understand and conceptualize the research topic while adding something new and innovative to the current pool of knowledge?"

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EDITORIAL

Sociocultural dimensions of research on public health roles for community pharmacists in tuberculosis disease control in a developing country

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Keywords: *Pharmaceutical Public Health, Health Policy, Implementation Research, Public Private Partnership, Health Systems and Planning.*

Community pharmacies are an important addition to public health initiatives in controlling infectious diseases in developing countries.[1] Pharmacists/ pharmacy staff counseling the presenting patients about their disease symptoms and untoward effects of self-medication has a vital role to play in infectious disease control such as Tuberculosis (TB).[2] Pakistan, which is a lower-middle-income, high-tuberculosis (TB) burden country, has a much higher consumer participation rate in private versus public health care.[3] Data collected in 2014 by the Pakistan Bureau of Statistics indicate that pharmacies in Pakistan, for example, are accessed more than the government (public sector) hospitals for healthcare services among households.[4]

Pharmacy case detection service implementation project

Given that the TB incidence reported annually in Pakistan is much lower than the World Health Organization's country prediction, it is clear that some TB cases go undetected.[3] To address this problem by using innovative Public-Private Mix (PPM) Health Partnerships, we proposed engaging community pharmacies (as a new private TB referral stakeholder) in Pakistan for conducting TB case detection according to the TB management guidelines developed by the National Tuberculosis Control Program (NTP) Pakistan (i.e., public sector).[5] The 'innovation' aspect involved utilizing existing PPM partnerships [(Public TB Coordinator and Private Primary Care Physician Model -or PPM-1 -or Private sector physician reporting new TB cases diagnosed in his clinic to district/public TB office][6] contained within Pakistan's NTP Framework in three districts in Pakistan through a new PPM partner i.e., private pharmacies. The alignment of existing PPM-1 with private pharmacies was named as PPM-1 Boosted project. Using an implementation science approach, we sequentially progressed this project through the following steps: resource allocation, mapping, recruitment criteria, sampling frame development, training, implementation, and auditing.

Using this systematic program planning approach, we were able to recruit 500 pharmacies into the project (PPM-1 Boosted) from a potential framework of 750 pharmacies in the three project districts. The trained and project 'ready' pharmacies then identified 547 new TB patients in the operational districts within one year. Implementation process data were collected, along with data on patient screening and referral volume per pharmacy.[5]

Research approaches in designing and modeling pharmacy public health interventions, services, and programs in developing countries

Based on 'implementation barriers/facilitators' identified in this large-scale work on scoping pharmacists' public health roles,[5] we propose a stepwise guideline (i.e., Fidelity-Advocacy-Consent-Technology-Training -or FACTT) for designing similar interventions, particularly for low- and lower-middle-income countries (such as Pakistan) still battling a high burden of infectious diseases and where private health care such as pharmacy is a high accessed health care venue (Figure 1).

Step 1: Advocating for pharmacy inclusion in national TB (or other infectious disease programs): The first step in undertaking such projects should be to engage community pharmacists in the national task force team in policymaking (e.g., National TB programs) and make public health processes within the national program mandatory for community pharmacies. This might prove beneficial in addressing the issue relevant to the resource allocation of pharmacies in such implementation programs. Sociologically, many cultures (and professional practice cultures) respect hierarchy (rather than feel constrained) and are willing to enact roles once they feel these roles are legitimized by a higher authority.[7]

The way forward: In the absence of pharmacy inclusion in national public health initiatives, one way forward may be to use national programs on which potential pharmacy contributions can be piggybacked – this is what we did with the PPM-1 Boosted project cited above.[5] This also allows enhanced willingness of pharmacist participants to participate in such research projects as well as, in turn, patients who then see the pharmacist's approach as a valid rather than an intrusive one. This is particularly important in nations where populations still view community pharmacies only as a venue for sourcing medicine supplies and the pharmacist as a business owner or drug seller rather than a healthcare professional.[8]

Step 2: Using technology to enhance viable and effective methods of initial recruitment of pharmacies: The advocacy of community pharmacists as national task force members should follow the careful recruitment of existing pharmacies utilizing effective technological scientific tools. In our case, (in the PPM-1 boosted model for pharmacist-boosted TB case detection), we first identified the available range of pharmacies in the operational districts by utilizing Geographic Information Science (GIS) principles. GIS-Based Site Selection Analysis involved visiting the localities all around (the NTP pre-established network) and identifying the population hotspots (slum areas), nearby landmarks, and health facilities (hospitals, general practitioners, and laboratories), not on the panel of the NTP network. GIS data led to the development of a mapping tool for identifying pharmacies that should be invited to participate. In the next step, this mapping tool was updated by hired staff during their pharmacy visits in the locality (three times a week) to observe patient flow at pharmacies, non-prescription use of medicines, and availability of anti-TB medications.

The way forward: GIS-Based Site Selection Analysis should be performed by an expert team with a background in urban planning, and mapping tools/algorithms should be updated by a team with a pharmacy background to ensure sensible development of sampling frameworks. This approach would also be useful for engaging pharmacies to assist with managing epidemics or pandemics;[9] in other words, these planning-mapping algorithms may be useful in locating disease hotspots, identifying pharmacies in the hotspots, and upgrading them to provide relevant services. A symbiotic relationship between upskilled hospital pharmacies and their application of technological tools (such as natural language processing (NLP) and machine learning) to analyze electronic health records (EHR's) for improving patient care exists in the literature.[10]

Therefore, it might be highly encouraging for community pharmacies to be supported and upskilled (by respective NTP's) to adopt artificial intelligence algorithms and big data analytics in exploiting existing TB patient databases either maintained at pharmacy software or referred through pharmacies to the NTP registries in the future. Moreover, organizing three weekly pharmacy visits of hired staff (1-visit each at the start of the week, during the mid-week, and at weekends) would assist in the extensive observation of patient flow at pharmacies, as the flow varies during different times of the week.

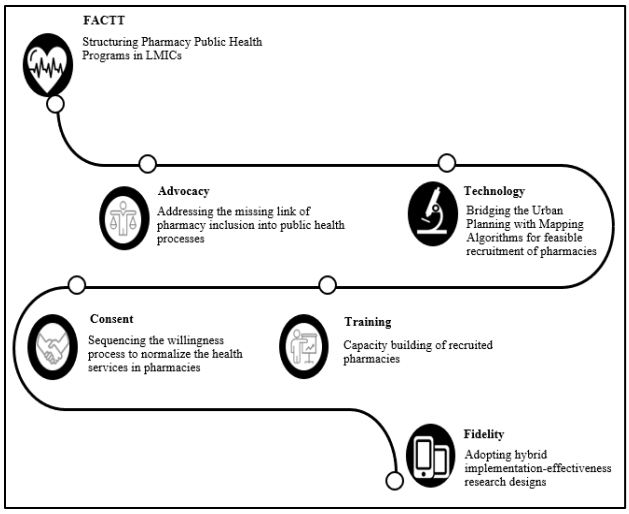

Figure 1: Schematic diagram for FACCT guidelines

Step 3: Managing the consent process using a sequential consenting process: In most developed countries, signed written consent is obtained from willing participants (i.e., pharmacies) before project implementation,[11] and verbal-only consent is strongly discouraged.[12] However, we used both verbal and written consent from willing pharmacies.[5] In our project, we used a verbal consent process at the initial stage – verbal consent was followed by providing the pharmacy with research materials. This allowed pharmacies to 'test' the potential for implementation, and in many cases given that health services such as TB screening are not 'normalized/socialized' processes in pharmacy, it allowed pharmacy owners to overcome any initial hesitation, progressing them to readily provide written consent after having tested the water. Written consent was then obtained at regional meetings held to debrief participants about how the project was rolling out and to provide more detailed clinical training and process support. Group debriefing also allowed 'socialization' of the TB case detection process in community pharmacies.

The way forward: Researchers aiming to engage pharmacies in public health initiatives as part of research projects need to have a culturally appropriate process for obtaining consent[13] –initial consent, immersion, second approach, and full written consent might be better ways of managing the informed consent process. Once engaged, the consented pharmacies, with time, can be utilized as a valuable and relevant source to debrief non-consenting but potential pharmacies (who are either reluctant or stigmatized to participate for any reason) about the ethical principles involved (beneficence) in referring the TB patients.

Step 4: Strategically constructed training for project participants (capacity building of recruited pharmacies for project implementation): Once consented, a strategic process needs to be developed to strengthen the skills, instincts, and abilities of willing pharmacy participants according to available resources. In our case, two layers of training were adopted; Training-1 (on-spot meeting, before the project implementation) and Training-2 (a didactic presentation during the ongoing project). Training-I focused on TB symptoms, national (i.e., Pakistani) TB treatment guidelines, the process of maintaining the referral register for presumptive patients, and a directory (resource) of GP clinics and private laboratories located near recruited pharmacies. The scope of conducting Training-2 during the project was to have a reminder call for referrals, troubleshooting, and a sign of project sustainability to the pharmacy staff. After comprehensive training, there appeared to be an increasing trend in the proportion of total referrals from 14% to 71% in the three districts.[5] The training layers also coincided with the two-layer consent process.

The way forward: A pedagogically 'heavy' training at project commencement could be replaced for such research projects (pharmacist roles in public health) by two layers of training where protocol and minimal clinical training are initially provided, and once the implementers are 'immersed' and have experiential learning, the process occurs, leading them to comprehensive clinical training, building a laddered scaffold for knowledge application that bodes well for retention of recruited pharmacists in such research projects. This two-layered training material can be forwarded to the Guidelines and Training Module section of the NTP, which is typically developed and regulated by the Monitoring and Evaluation (M&E) unit. NTP M&E units are already established through PPM intervention at district, province, and national levels in Pakistan to train TB healthcare staff in TB control activities.[14] So, assigning additional responsibilities (with relevance to two-layered training) to existing M&E officers

operating at the aforementioned three levels of the healthcare system or hiring an additional M&E officer (preferably with a background in community pharmacy services) can be employed to monitor the presumptive TB patients' record maintenance, referral, and anti-TB drug sales (with or without prescription) at pharmacies either solely run by pharmacy owners, qualified pharmacists, pharmacy technicians, or in combination with all of them.

Step 5: Using hybrid implementation-effectiveness research designs (implementation and outcome data collected in tandem): Finally, to ensure improved protocol fidelity and sustained engagement of participating pharmacies in the project (in the PPM-1 boosted model), we used a hybrid implementation and impact measurement design. During our study, an implementation science model i.e., COM-B -or ' Behavior system' involving three essential conditions such as Capability, Opportunity, and Motivation,[15] was adopted and used, and we conducted 'behavioral diagnostics' in real-time implementation. The barriers identified were then quickly addressed to maintain engagement with practice change (changing to provide a case detection role and work with primary care physician practices).[5]

The way forward: Utilization of implementation science principles (such as the COM-B model) and likely behavioral barriers (Capability, Motivation, and Opportunity) of pharmacy staff during implementation should be addressed as much as possible, and the use of hybrid research designs is a smart way forward. In general, such a hybrid research design process will not only assist in developing a specific method to improve the intervention design, and facilitate its scientific replication but also develop an understanding of the nature of behavior to be changed with relevance to professionals delivering healthcare and evidence-based public health.[15,16] Specifically, apart from TB, pharmacists if familiar with implementation science principles[17] and provided with a public health 'Opportunity' towards remaining infectious diseases control based on their 'Capability' along with continuous 'Motivation' by national programs can likely change the Behavior wheel of pharmacists and their contribution in developing countries.

Conclusion

The FACCT stepwise guideline will have implications for pharmacy-based TB case detection (active/passive case finding) in Pakistan, where 81% of initial health seeking is to private providers, and where community pharmacies remain the 2nd highly accessed health care facility across the country. The FACCT steps possibly can also be tested to trace highly stigmatized TB-related comorbidities such as Human Immunodeficiency Virus (HIV)-infected cases presenting at community pharmacies in Pakistan.

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ORIGINAL ARTICLE

Influence of smoking and other factors in development of cataracts in urban and rural areas. A cross-sectional study from Pakistan

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A B S T R A C T

Introduction: A cataract is characterized by the clouding of the crystalline lens fibers in the eyes. Smoking has been identified as a risk factor for several common and serious eye diseases, including age-related macular degeneration, glaucoma, and cataracts, all of which can lead to irreversible blindness. This study aimed to examine the relationship between tobacco smoking and non-smoking with the prevalence of cataracts in both urban and rural populations in Pakistan.

Methodology: This epidemiological study was conducted in Okara, involving approximately 2000 patients. Some participants did not provide information, resulting in a total of 1992 confirmed cases from both genders. Data was collected using a questionnaire-based form after obtaining informed consent from patients.

Results: Of the 1992 subjects, 46.13% were male and 53.87% were female. The age distribution of both groups showed a significant difference. A total of 24.60% of patients were from urban areas, while 75.40% were from rural areas, showing no significant difference. The marital status of age groups 20 to 60 and 61 to 100 showed no significant differences. For cigarette smokers aged 20 to 60, the OR / 95% CI was 10.41 / 2.34, while for the age group 61 to 100, it was 6.63 / 1.89, indicating a significant difference. Huqa smokers aged 20 to 60 also showed a significant difference, as did the age group 61 to 100.

Conclusion: Smoking, whether cigarettes or huqa, is strongly associated with the development of cataracts. Other factors, such as the use of pan, niswar, and marital status, also play a role.

Keywords: *Smoking, Huqa, Cataract, World, Urban, Rural*

Introduction

Cataracts are a leading cause of preventable blindness and vision loss worldwide. The challenge lies in preventing the development of cataracts and treating those that do occur.[1] Although current treatments can restore normal vision for many who suffer from vision loss, the problem of cataracts continues to grow annually. This is due to the high number of patients needing surgery and the increasing number of cataract cases driven by longer life expectancies. While surgery remains the only effective treatment for cataracts, identifying risk factors can aid in developing preventive measures at an early stage. The World Health Report, published in 1998, estimated that 19.34 million people were bilaterally blind due to age-related cataracts.[2]

Cigarette smoking is a well-known risk factor for nuclear cataracts, and growing epidemiological evidence indicates that smoking is also a risk factor for posterior subcapsular

cataracts. Smoking has been identified as a risk factor for several common and serious eye diseases, including age-related macular degeneration, glaucoma, and cataracts, all of which can lead to irreversible blindness.[3]

Furthermore, previous research indicates that cigarette smoking poses a higher risk for cataract development compared to non-smoking. Tobacco use is a major global public health issue and the leading preventable cause of disease, disability, and premature death. It has been reported to account for a significant proportion of mortality and morbidity among middle-aged individuals. In India, it is estimated that about one-third of women and two-thirds of men use tobacco in various forms, including cigarettes, bidis, cheroots, and smokeless tobacco such as snuff or chewing tobacco. Tobacco is also used in powdered form, inhaled through the nose.[5]

Low socioeconomic status (SES) has been associated with many age-related diseases, including senile cataracts. Previous studies indicate that lifestyle factors such as smoking and alcohol use, along with indicators of SES like education, household income, and housing conditions, are linked to a higher prevalence and progression of cataracts. However, most of this data has been derived from studies conducted on white populations in the United States, Europe, and Australia.[6-8]

While data has been collected from India[9] and China,[10] some studies have been conducted in urban areas that are representative of a large portion of the population in Asia.[11] Moreover, no research has been conducted on the Malay people, the third largest ethnic group in Asia, comprising about 5% of the world's population.[12]. No survey-based study has been conducted to examine the effects of smokeless tobacco on eye health. This study aimed to investigate the association between tobacco smoking and non-smoking with the development of cataracts in urban and rural populations in Pakistan.

Methodology

This population-based study aimed to assess the frequency of cataracts in urban and rural areas of Pakistan. Conducted at the Pakistan Ali Trust Eye Hospital in Okara, it was a cross-sectional retrospective epidemiological study involving 1992 individuals aged 20 to 100 years living in Pakistan. The study was carried out from June 2021 to December 2021. Patients at the Pakistan Ali Trust Eye Hospital in Okara provided informed consent forms. The study adhered to the principles of the Declaration of Helsinki, and ethical approval was obtained from the ethics committee, represented by Dr. Muhammad Ejaz Anjum, affiliated with the Ali Trust Eye Hospital in Okara, Pakistan, under the reference ATFEH-HR-1199.

The study involved 1992 subjects who were unidentified individuals attending the hospital. Only patients diagnosed with cataracts by ophthalmologists were included, while those without cataracts were excluded from further analysis. Individuals aged between 20 and 100 years were considered for inclusion. This was a small-scale study aimed at assessing the association between cataracts and socioeconomic status. The potential for systematic errors or inaccuracies in the study is estimated to be up to 5%.

Comprehensive information was gathered from all participants enrolled in the study. Given that many patients lacked formal education, the questionnaire was administered by the study personnel through verbal interviews. Detailed data on the use of tobacco, including whether they smoked cigarettes or used huqa, pan, or niswar, was collected, regardless of whether they were current users.[13] Additionally, questions regarding age, gender, education level, marital status, and place of residence were included in the study questionnaire.

Analyses were conducted for all variables, with age, sex, and age-adjusted odds ratios (ORs) along with their corresponding 95% confidence intervals (CIs) calculated. Chi-square tests were utilized where necessary to obtain p-values, with $p<0.05$ considered significant and $p>0.05$ considered non-significant. All analyses were performed using Microsoft Excel 2010.[14]

Results

Among the 1992 patients included in the study, 46.13% were male and 53.87% were female, ranging in age from 20 to 100 years.

Age distribution: Two age groups were examined in the study: one comprising individuals aged 20 to 60 years and the other aged 61 to 100 years. Within the 20 to 60 age

group, 15.91% were male and 24.70% were female, while within the 61 to 100 age group, 30.22% were male and 29.17% were female. The distribution of age groups showed a significant difference (p<0.05), with an odds ratio of 0.62 and a 95% confidence interval of -0.48.

In this study, it was noted that 24.60% of the total population under investigation resided in urban areas, while 75.40% were from rural areas. This difference was found to be non-significant, with a p-value greater than 0.05 (i.e., p>0.05). The calculated odds ratio was 0.93, with a 95% confidence interval of -0.08 (Table 1).

Table 1: Residence of cataract patient

Residence of cataract patients						
Residence	Gender	No. of people	Percentage	Total	P-value	OR/ 95% CI
Urban	Male	219	10.99	24.60	0.46	0.93/-0.08
	Female	271	13.60			
Rural	Male	700	35.14	75.40		
	Female	802	40.26			
Total		1992	100.00			

In this study involving 1992 patients, the marital status of individuals in different age groups was compared. Among patients aged 20 to 60 years, 40.16% were married (both males and females), while only 0.60% were unmarried (both males and females). The calculated p-value, which was greater than 0.05 (i.e., p>0.05), indicates that the difference was non-significant, with an odds ratio (OR) of 1.29 and a 95% confidence interval (CI) of 0.26. Similarly, among patients aged 61 to 100 years, 59.94% were married (both males and females), and only 0.30% were unmarried (both males and females). Once again, the p-value was greater than 0.05, indicating a non-significant difference, with an OR of 0.52 and a 95% CI of -0.66. These findings are summarized in Table 2.

In different age groups, both smokers and non-smokers were observed, as detailed in Table 3. For individuals aged 20 to 60 years, 5.87% were cigarette smokers (both male and female), while 34.74% were non-smokers, with a p-value greater than 0.05 (i.e., p>0.05), indicating a non-significant difference. The odds ratio (OR) and 95% confidence interval (CI) were 10.41 and 2.34, respectively. However, among individuals aged 61 to 100 years, 13.70% were cigarette smokers (both male and female), while 45.68% were non-smokers, with a p-value less than 0.05 (i.e., p<0.05), indicating a significant difference, with an OR of 6.63 and a 95% CI of 1.89.

Similarly, for huqa smokers aged 20 to 60 years, 1.86% were smokers (both male and female), while 38.76% were non-smokers, with a p-value less than 0.05 (i.e., p<0.05), indicating a significant difference, with an OR of 2.11 and a 95% CI of 0.75. Among individuals aged 61 to 100 years, 5.82% were huqa smokers (both male and female), while 53.56% were non-smokers, with a p-value less than 0.05 (p<0.05), indicating a significant difference, with an OR of 1.80 and a 95% CI of 0.59. In the study involving 1992 patients, an analysis of pan and niswar usage among different age groups revealed interesting patterns.

Among individuals aged 20 to 60 years, only 0.15% were identified as male and female pan users, with a significant majority, 40.46%, abstaining from pan use. Interestingly, the statistical analysis yielded a non-significant difference, as indicated by a p-value exceeding 0.05, with an odds ratio of 0.00 and a 95% confidence interval of none. Conversely, among the older age group of 61 to 100 years, a higher proportion, 5.82%, were identified as pan users, while 53.56% remained non-users. Despite this disparity, the statistical analysis again failed to show significance, with a p-value greater than 0.05. The odds ratio calculated was 1.61, with a 95% confidence interval ranging from 0.48 to none. Similarly, for niswar usage, among individuals aged 20 to 60 years, 5.82% were identified as users, but statistical analysis showed no significant difference. Likewise, in the older age group of 61 to 100 years, 53.56% were users, with the statistical analysis again failing to demonstrate significance.

Table 2: Marital status of patients

Marital status of cataract patients							
Married	Gender	Age	No. of people	%	Total	P-value	OR/ 95% CI
Yes	Male	20-60	314	15.76	40.16	0.68	1.29/ 0.26
	Female		486	24.40			
No	Male		4	0.20	0.60		
	Female		8	0.40			
Yes	Male	61-100	597	29.97	58.94	0.44	0.52/ -0.66
	Female		577	28.97			
No	Male		4	0.20	0.30		
	Female		2	0.10			
Total			1992	100.00			

Table 3: Cigarette and Huqa smoking status of patients

Cigarette Smokers							
	Gender	Age group	No. of people	%	Total %	P-value	OR/ 95% CI
Smokers	Male	20-60	97	4.87	5.87	0.98	10.41/ 2.34
	Female		20	1.00			
Non-smokers	Male		220	11.04	34.74		
	Female		472	23.69			
Smokers	Male	61-100	225	11.30	13.70	0.00	6.63/ 1.89
	Female		48	2.41			
Non-smokers	Male		377	18.93	45.68		
	Female		533	26.76			
Total			1992	100.00			
Huqa Smokers							
Smokers	Male	20-60	21	1.05	1.86	0.02	2.11/ 0.75
	Female		16	0.80			
Non-smokers	Male		296	14.86	38.76		
	Female		476	23.90			
Smokers	Male	61-100	74	3.71	5.82	0.00	1.80/ 0.59
	Female		42	2.11			
Non-smokers	Male		528	26.51	53.56		
	Female		539	27.06			
Total			1992	100.00			

Discussion

The study was carried out at the Ali Trust Eye Hospital in Okara, aiming to investigate the correlation between smoking and various factors associated with the development of cataracts. A total of 1992 patients participated in the study, each providing informed consent before inclusion. Their observations align with previous findings indicating that smoking increases the risk of nuclear cataracts.[15-17] Recent research has also highlighted a connection between cigarette smoking and cortical cataracts. The study's results corroborated earlier research, revealing that individuals who smoke cigarettes or cigars face a higher risk of developing both nuclear and cortical cataracts. Furthermore, they emphasized the significant role of cumulative cigarette smoking in the development of these types of cataracts.[18].

Numerous cross-sectional studies have consistently observed a high prevalence of nuclear and cortical opacities among females.[19-21] Additionally, research on cataracts has consistently highlighted the relationship between education level and senile cataracts. These studies have consistently suggested that individuals with lower socioeconomic status (SES) face a higher risk of cataracts, a finding supported by other investigators. Moreover, smoking has been identified as a risk factor for nuclear cataracts, and recent research has also linked cigarette smoking to cortical cataracts. These findings are in line with earlier studies indicating that both cigarette and cigar smoking pose significant risks for nuclear and cortical cataracts. However, their study results, particularly regarding the association between cigar smoking and nuclear cataracts, contradict some previous findings but align with others.

Notably, they observed a significantly higher frequency of cortical cataracts among individuals with a history of cigarette smoking, a finding consistent with some studies but not all. Furthermore, their study identified significant differences among patients in various age groups, except for cigarette smokers aged 20 to 60, where the difference was non-significant. However, they found non-significant differences among individuals who use pan and niswar. It's worth mentioning that other studies have also observed a relationship between cataracts and alcohol usage, particularly in individuals aged 65 to 74 years. [15]

Smoking unequivocally stands as a primary contributor to disease and premature death. Over time, the prevalence of smoking has increased significantly in numerous Asian countries, emerging as a major cause of mortality.[22] Although efforts towards comprehensive anti-tobacco initiatives have resulted in a decline in smoking rates to less than 30% in developed nations such as England and Australia, the scenario remains starkly different in many Asian countries,[23] In these regions, approximately 50-70% of adults are reported to be current smokers,[24] posing substantial risks of cancer, heart diseases, and respiratory infections.[35] Furthermore, the impact of smoking on eye diseases such as cataracts, diabetic retinopathy, and age-related macular degeneration has been extensively documented in Asian countries where smoking rates remain high.

Previous studies have revealed a smoking rate of 40% among Singaporean Malay individuals, which was associated with a significantly increased risk of senile macular degeneration,[26] retinal arteriolar emboli,[27,] and thyroid-related ophthalmopathy.[28] Previous research has consistently demonstrated a relationship between cataracts and cigarette smoking, with smoking playing a significant role in the development of cataracts across various populations. This association has been observed not only in people from the United States but also in European and Australian populations.[29-32] India and China also show that cigarette smoking has been a threat for NC,[33] CC,[13,] and any type of cataract.[18] The relationship of other types of tobacco like cigars,[34] pipes, smokeless tobacco,[13] or cooking smoke with cataracts was also observed.

In their research, they observed that cataracts predominantly manifest in older individuals, indicating a strong correlation with age. This explains why the incidence of cataracts was higher among nonsmokers or former smokers, who were on average older (59 years), compared to current tobacco users, who were slightly younger (55.3 years).

However, upon adjusting for age, it became evident that smoking was indeed a significant factor in the development

of senile cataracts.[28] In their observations, individuals who smoked Beedis presented a somewhat unclear picture due to the higher prevalence of beedi smokers compared to cigarette smokers (23.9% vs. 13.3%). Surprisingly, the risk for cataract development appeared to be lower among beedi smokers, with the odds ratio indicating a more significant effect of reduced risk (OR 0.81). Similarly, in the current study involving 1992 patients, the prevalence of pan and niswar users was lower compared to cigarette and huqa smokers. Specifically, among male and female pan users aged 20 to 60 years, the prevalence was only 0.15%, with non-users comprising 40.46%.

However, statistical analysis revealed a non-significant difference ($p>0.05$) with an odds ratio (OR) of 0.00 and none for the 95% confidence interval (CI). Conversely, among individuals aged 61 to 100 years, the prevalence of pan users was higher at 5.82%, with non-users accounting for 53.56%. Once again, the difference was non-significant ($p>0.05$), with an OR of 1.61 and a 95% CI ranging from 0.48 to none. Similarly, for niswar users among males and females aged 20 to 60 years, the prevalence was 5.82%, with a non-significant difference observed ($p>0.05$) and an OR of 0.77, but with a wide 95% CI ranging from -0.26 to none. Among individuals aged 61 to 100 years, niswar users accounted for 53.56%, with a non-significant difference observed ($p>0.05$) and an OR of 1.61, with a 95% CI ranging from 0.15 to none.

Low socioeconomic status has emerged as a documented risk factor for various chronic eye conditions, including age-related macular degeneration, glaucoma, diabetic retinopathy, and cataracts. A plethora of studies consistently highlight the association between lower economic status and an increased likelihood of developing cataracts. In their research, consistent with earlier findings, a significant relationship was identified between nuclear cataracts and indicators such as lower education levels and reduced income, as well as between posterior subcapsular cataracts and poor living conditions.

It can be inferred that individuals with lower socioeconomic status may have limited access to cataract surgery, leading to a higher prevalence of cataracts among this demographic. In earlier investigations among Malay individuals, there was no observed correlation between socioeconomic status and cataract operation,[31] However, numerous survey-based studies consistently indicate a higher incidence of cataracts among females.[28] In this study, I also noted a higher prevalence of cataracts in females compared to males. They observed that in rural populations, a majority were uneducated and engaged in farming, while also using cigarettes and bidis.[13]

In this study, I examined populations from both rural and urban areas, with 24% residing in urban settings and 76% in rural areas. Additionally, they reported the regular use of cigarettes, pan, and niswar among the participants. Interestingly, the difference between urban and rural areas was found to be non-significant. Furthermore, marital status was described among the patients, revealing a non-significant difference across different age groups.

Conclusion

The study concludes that smoking, whether cigarettes or hookah, is strongly associated with the development of cataracts. Additionally, factors such as the use of pan, niswar, and marital status also play a minor role in cataract development. It emphasizes the importance of raising awareness, particularly in rural areas, to reduce smoking habits and thereby mitigate the risk of cataract disease

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ORIGINAL ARTICLE

Comparison of intermittent compression-decompression with glides and conventional physical therapy protocol for knee osteoarthritis

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A B S T R A C T

Introduction: Osteoarthritis (OA) is among the most prevalent types of arthritis and a fundamental cause of disability in people around the globe. Elderly population particularly females over the age of 65 years, patients with uncontrolled obesity have the highest risk of developing OA. To compare the effects of intermittent compression-decompression with glides and conventional physical therapy on pain, range of motion, and functional status in knee osteoarthritis.

Methodology: A randomized controlled trial was conducted with 60 participants having knee Osteoarthritis. The subjects were randomly allocated to Group A (intermittent compression-decompression with glides), Group B (conventional physical therapy), and Group C (intermittent compression-decompression with glides and conventional physical therapy) using a lottery method. The treatment was provided for 3 days per week alternatively and continued for 4 weeks. The assessment was done at the baseline and post-12th treatment day using NPRS, range of motion, WOMAC scale, and KOOS scale as outcome measures.

Results: Based on the results attained through the Kruskal Wallis test, there was a statistically significant effect ($p<0.05$) on scores of NPRS, Flexion, WOMAC, and KOOS, while extension showed no superlative effects after the application of the novel technique. More significant results were obtained in Group C ($p<0.05$) as compared to Groups A and B respectively.

Conclusion The application of compression and decompression with glides supplemented with conventional treatment protocol resulted in a massive reduction in pain and related symptoms, and improvement in range of motion with enhanced functional proficiency of patients affected with knee osteoarthritis.

Keywords: *Flexibility, Knee Osteoarthritis, Knee joint, Quadriceps muscle, Range of motion.*

Introduction

Osteoarthritis (OA) is among the most prevalent types of arthritis and one of the fundamental causes of disability in people around the globe. The term arthritis usually refers to more than over 100 joint-related diseases affecting joint surfaces, surrounding soft tissues, and connective tissue as well. According to the World Health Organization's recently available data, osteoarthritis has a higher worldwide incidence which is drastically affecting the economy and is now considered the fourth biggest cause of death and disability by 2020.[1] It is considered a degenerative joint disorder, is gradually progressive which impacts almost around 250 million humans throughout the

world.[2] The elderly population particularly females over the age of 65 years, patients affected with uncontrolled obesity highest risk of developing OA. This is about the inefficiency and disability associated with this condition and its deleterious impression on the social and economic aspects of society. People usually experience reduced movement at the knee joint, recurrent and progressive pain along with deterioration in strength and balance with compromising and facing restrictions in daily routine activities of life.[3]

OA was often thought to be solely a degenerative illness, but novel data shows that it is a complex disease involving various causal elements such as traumatic events, imbalanced mechanical forces, joint and soft tissue inflammation, biochemical, and inflammatory reactions, and various metabolic abnormalities. It is similarly worth noting that cartilaginous tissue isn't the only one affected. The cartilage, due to its lack of vascular supply and corresponding innervation, is unable to cause inflammation or discomfort on its own, particularly in the early onset of the disease.

Changes to the non-cartilaginous elements, such as the joint capsule, surrounding joint lining, underlying bone, adjoining ligaments, and connecting muscles, are the principal source of pain. These tissues are impacted as the condition worsens, and alterations such as bone remodeling, osteophyte growth, atrophy of surrounding muscles, ligament flexibility, and synovial effusion can be seen.[4] Mobilization with Movement is premised on the theory that slight positional faults in the joint emerge as a result of some trauma or stress. These faults produce mobility limitation, discomfort, and pain that is aggravated by active muscular contractions inside the faulty joint segments.

This includes the application of glides at right angles to the joint plane by the practitioner for correcting the fault within the joint, as well as the defaulting movement which is repeatedly performed by the patient and maintained for several repetitions. It produces hypoalgesia that improves ROM, improves muscular activation, and function, and addresses particular disorders. It shows beneficial results in treating tennis elbow, sprains at the ankle joint, impingement at the level of the shoulder joint, and hip along with knee OA are all treated effectively. In individuals with knee OA, other mobilizations such as anterior and posterior tibial glides at the knee joint generate both regional and global benefits.[5]

Mobilizations performed at the knee joint comprise the mobilization of the tibio-femoral joint specifically. This consists of anterior and posterior glides applied along with compression and decompression at the knee joint. Mobilization is a technique that is implemented to improve the intensity of unremitting discomfort and related pain, escalation in joint range of motion, and upturns functional outcome or independence of the patient because optimum provocation or signal for the regeneration of the damaged cartilage is the application of intermittent compression and decompression along with gliding.[1]

Intermittent compression-decompression with glides aids in the activation of osteoplastic action within the joint and helps to improve osteoarthritis complaints, hence prolonging the degradation process. Owing to its poor metabolic rate and insufficient blood flow, cartilage seems to have a lower healing ability, allowing for a slower reaction to injury. This damaging cartilage injury can be extremely progressive at times. As a result of this massive damage, early management aims to reduce this gradual damage to articular cartilage, which could be important in reducing the impairments and persistent discomfort causing disability. Compressive pressure performed on the knee joint helps in washing the fluid and minerals out of the surface of the cartilage, which is then reabsorbed back into the cartilage during performing decompression.

This occurrence aids cartilage repair by giving essential nutrients and minerals along with the supply of oxygen as well.[6] The main purpose of the study was to investigate the effects of accessory knee joint mobilization or compression and decompression with glide on outcomes of pain intensity and functional independence in individuals with knee osteoarthritis. The application of this innovative technique could help in better, improved, and innovative non-invasive management of knee osteoarthritis. The recent technique is highly cost-effective as compared to surgical interventions and intra-articular injections. This study also helped to set the foundation for further studies designing magnificent protocols of treatment for the affected population.

Methodology

The randomized clinical trial was conducted at the Physiotherapy Department of Yahya Welfare Complex Hospital, Chaudhary Medical Center, DHQ Haripur, and Akhter Jahan Medical Centre, Wah Cantt. The RCT was registered with the International Standard Randomized Controlled Trial Number NCT05262049. The approval was acquired from the ethics review committee of Riphah College of Rehabilitation Sciences, Riphah International University, Islamabad, Pakistan with the reference number mentioned as RIPHAH/RCRS/REC/Letter-00862.

The sample size determined using the OpenEpi sample size calculator was 60 with confidence level (95%) and each group was allocated with 20 participants. The outcome used for the sample size calculation was Range of motion.[2] Non-probability purposive sampling technique was used. The subjects diagnosed with bilateral knee OA (stage 3), ranging from 40 to 70 years of age and able to comprehend certain commands were included in the study. Moreover, the subjects who had undergone any surgery of the lower limb had inflammatory joint disease or neurological disorder of the lower limb, or had received intra-articular injections of corticosteroids in the past 6 months were excluded from the study.

Patients who met the specific criteria were placed into three groups (i.e. Group A, Group B, and Group C) randomly using the lottery method. Data from baseline and after the intervention was then compared after 4 weeks. The information was gathered using questionnaires and forms. Information about osteoarthritis, such as knee ROM, pain, and functional activity score, was requested from the patient.

Group A: Intermittent compression-decompression with glides: Knee decompression (traction) was applied for 10 seconds with 30 repetitions of anterior-posterior oscillatory glide followed by compression for 10 seconds for 5 minutes. This treatment plan was continued for 4 weeks (3 days a week, alternate days).

Group B: Conventional physical therapy: Hot pack for 10 minutes, Low-frequency TENS for 10 minutes, Stretching of Hamstring (10reps*3set) and calf (10reps*3set), Strengthening of peri-articular muscles especially the quadriceps through straight leg raising, pillow squeeze and knee isometrics (10reps*3set). In this group, conventional therapy was given for 4 weeks (3 days a week, alternate days).

Group C: Conventional physical therapy and intermittent compression and decompression with glides: Patients in this group received the combination of conventional physical therapy and intermittent compression and decompression with glides for 4 weeks (3 days a week, alternate days).

Data Collection Tools

Numeric Pain Rating Scale (NPRS): This outcome was used to evaluate the intensity of pain. The score 0 represents “Having no pain at all” whereas a score of 10 means “The most terrible pain ever felt”. The participants were instructed to select one number from the scale that reflects their actual state of knee pain.[7] The interclass correlation was 0.95 represented by a study in patients with knee OA respectively.[8]

Knee Injury and Osteoarthritis Outcome Score (KOOS): It is a detailed questionnaire that is used to evaluate brief and long-term outcomes related to a patient's condition after a knee injury. This evaluates five objectives: pain during certain difficult activities like walking and using stairs, related symptoms, everyday activities of life like rising from a chair and using a car, sports participation, knee-related life quality, as well as recreational performance. This takes about 10 minutes to complete. The internal reliability of this questionnaire was above 0.70 respectively.[9]

Western Ontario and McMaster Osteoarthritis Index (WOMAC): It is widely utilized to evaluate pain, its related stiffness, and the functional status of the lower extremities. It comprises 24 questions: from which 17 questions are based on physical status, 5 questions are based on status of pain, and 2 questions are related to stiffness. Each question has five options starting from 0 which means no symptom or difficulty at all to 4 which represents extreme difficulty in performing activities with severe symptoms. Subscale scores are present for pain, stiffness, and functional status. Total scores were defined as the sum of all mentioned 24 items ranging from 0 to 96 scores respectively. The intraclass correlation coefficient values were 0.86 in patients with knee OA.10.

The data was entered and evaluated by using SPSS-21 software and expressed in a structure of tables and figures. All the individuals were analyzed at baseline and then after the completion of 4 weeks. Kolmogorov Smirnov test was used to evaluate the normality of data. The score of the normality test revealed that the data was non-normally distributed ($p<0.05$). Kruskal-Wallis test and Friedman tests were applied for the statistical analysis.

Results

The mean age of individuals in Group A was 58.60±8.34, the individuals in Group B were depicted mean age of 59.30±7.46 and Group C showed a mean age of 59.60±7.42 respectively. The frequency of females was 32 (53%) and that of males was 28 (47%). Kolmogorov Smirnov test was used to evaluate the normality of data. The score of the normality test revealed that the data was non-normally distributed ($p<0.05$). Furthermore, for the analysis of significance between groups, the Kruskal Wallis test was applied for all the outcomes as the data was non-parametric. All variables depicted significant differences ($p<0.05$) among all groups except Extension ($p=0.1$). (Error! Reference source not found.).

Table 1: Results of the Kruskal Wallis Test

Variables	Intervention	Median (IQR)	Sig.
NPRS	Pre	8.00(2.00)	0.22
	Post	3.00(3.00)	0.00
Flexion (Degrees)	Pre	110(13.00)	0.28
	Post	127(10.00)	0.00
Extension (Degrees)	Pre	5.00(10.00)	0.95
	Post	0.00(5.00)	0.10
WOMAC Scale	Pre	50.00(15.75)	0.07
	Post	22.00(21.00)	0.00
KOOS Scale	Pre	44.90(19.00)	0.10
	Post	71.70(25.00)	0.00

Similarly, the Friedman Test was applied for within-group analysis. For NPRS, flexion ROM, extension ROM, WOMAC, and KOOS, Group C depicted superlative improvement in range of motion and activities of daily living as compared to Group A and Group B (Error! Reference source not found.).

Table 1: Results of the Friedman Test

Variables	Groups	Time	Median	Outcome
NPRS	Group A	Pre	3.55	8.0 (2.00)
	Group B		3.65	8.0 (1.75)
	Group C		3.93	7.0 (1.00)
	Group A	Post	2.35	5.0 (3.00)
	Group B		2.23	3.5 (1.75)
	Group C		2.23	1.0 (1.00)
Flexion (Degrees)	Group A	Pre	9.10	110 (15.00)
	Group B		9.00	110 (19.00)
	Group C		9.03	112.5 (10.0)
	Group A	Post	9.90	125 (14.00)
	Group B		9.95	125 (15.00)
	Group C		9.98	130 (5.00)
Extension (Degrees)	Group A	Pre	2.75	5.0 (10.00)
	Group B		2.68	5.0 (10.00)
	Group C		2.88	5.0 (10.00)
	Group A	Post	1.45	0.0 (5.00)
	Group B		1.50	0.0 (5.00)
	Group C		1.40	0.0 (0.00)
WOMAC Scale	Group A	Pre	6.80	49.5 (14.25)
	Group B		6.85	52.0 (15.00)
	Group C		6.45	41.0 (20.50)
	Group A	Post	5.10	32.0 (17.25)
	Group B		5.10	30.0 (13.00)
	Group C		4.63	11.0 (7.75)
KOOS Scale	Group A	Pre	6.10	44.9 (11.75)
	Group B		6.15	40.8 (17.82)
	Group C		6.50	50.30 (21.2)
	Group A	Post	7.90	60.85 (18.8)
	Group B		7.90	66.70 (16.8)
	Group C		8.00	84.20 (6.23)

The statistics of the Friedman test showed statistically significant differences in Group A ($X2=170.91$, $p=0.00$), Group B ($X2=171.71$, $p=00$), and Group C ($X2=171.72$, $p=0.00$). Moreover, Group C showed more exceptional progress as compared to Group A and Group B (Error! Reference source not found.).

Table 2: Statistics of Friedman Test

Groups	Chi-Square (X2)	Significance
A	170.91	0.00
B	171.71	0.00
C	171.72	0.00

Discussion

The study was performed to compare the effects of intermittent compression-decompression with glides and conventional physical therapy on pain, ROM, and functional status. The interventions were applied for 4 weeks with 3 sessions per week alternatively to investigate which one was proved to be more efficacious. The outcomes of the study showed that Maitland Mobilization along with conventional therapy was more effective in knee osteoarthritis as the combination showed improvement in NPRS, increased range of motion, WOMAC, and KOOS scale representing functional independence respectively. Demographic data of the subjects was thoroughly collected in terms of age, gender, occupation, and education respectively.

A great number of processes are explained about the hypoalgesic effects of mobilization. The mobilizations or glides when applied at the joint trigger pain-inhibitory signals from the spinal cord through the brainstem. Moreover, it is also postulated that mechanical stimulation at joints helps in the modification of the surrounding chemical atmosphere and changes the amount and activity of inflammatory mediators, this again leads to decreasing the stimulus or experience of pain and discomfort.[11] In the recent study, the pain was significantly reduced after the application of glides on the knee joint, and the motion of the joint was also enhanced and the patient felt much independent in performing daily life tasks.

The reduction of pain and improvement in functional status following the application of Maitland's mobilization with conservative treatment was observed in a study. In addition to this, the 6-meter walk test depicted significance of <0.001 between the groups. It was concluded that the combination of both produces greater hypoalgesic effects, thus Maitland's mobilizations along with the conservative treatment caused an effective reduction in pain and improvement of functional status than conservative therapy alone.[12] This observation is similar to the findings of the present study. The intensity of pain showed a significance of $p<0.05$, the range of flexion of the knee joint was drastically improved and the functional status of patients represented by WOMAC and KOOS scale was also enhanced respectively.

The evidence suggested that physical therapy assists in the reduction of pain, discomfort, and swelling. In addition to this, it also elevates the level of physical functioning in patients by decreasing the joint locking or stiffness within the joint. Moreover, daily routine exercises are beneficial as well as cause enhancement in the condition of the patient. Also, the combined treatment of Mobilization with other exercises and modalities has proved to give better results as well.[13] The present study also included a couple of exercises and the application of modalities with the most superlative results. The patient's physical function was highly enhanced. The patient faced less difficulty in using stairs, sitting and standing, using the toilet, walking over even and uneven grounds, and domestic chores, assessed through the WOMAC scale which depicted exemplary significance. There were fewer complaints of stiffness or catching, locking, grinding, and swelling assessed through the KOOS scale respectively.

Implementation of Compression-decompression can assist in avoiding surgical intervention, as this appears to be very expensive and chances of healing and regaining mobility are not that much satisfactory. The recent technique is cost-effective and highly significant in the reduction of symptoms of OA as compared to surgical interventions and intra-articular injections. The movements are performed to assist in increasing the thickening and resilience of the cartilage. The mainstream geriatric population of Pakistan is suffering from knee OA, particularly females above 40 years because of the post-menopausal effect. The decline in the amount of estrogen hormone leads to the weakness and fragility of bones and prompt degeneration of the cartilage. The emergence of osteoarthritis has the worst impact and causes the emergence of physical, psychological, and social unfavorable implications.[14]

The present study depicted that mobilization (compression and decompression with glide) in individuals with knee OA, causes in establishment of noteworthy improvement in the discomfort and related symptoms. There was a massive reduction in the pain of patients and enhanced functional proficiency of affected patients. This demonstrates the reliability and validity of the present research study. Results delivered innovative evidence that mobilization of an osteoarthritic knee joint may result in producing an effective way of reducing unremitting pain in various tasks of daily living and thus produce enlightening of functional competence. Mobilization applied in osteoarthritic knee helps in the production of general hypoalgesic effects which therefore can cause pain relief and increase the movement of the knee joint. Based on the respective findings of various research studies, it can be easily concluded that the manual therapy and exercise protocols together benefit patients with knee osteoarthritis and may postpone or avert the requirement for surgical involvement.

Conclusion

The study concluded that after the application of Maitland's mobilization comprising of compression and decompression with glides supplemented with conventional treatment protocol, there was a massive reduction in pain and related symptoms. The results of this study also exhibited an enhancement in range of motion with enhanced functional proficiency of patients affected with knee osteoarthritis. The patient faced less difficulty in using stairs, sitting and standing, using the toilet, walking over even and uneven grounds, and domestic chores. Moreover, there were fewer complaints of stiffness or catching, locking, grinding, and swelling observed after the application of the technique.

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ORIGINAL ARTICLE

Clinical pharmacist's role in identification and management of medication errors in different wards of a hospital in Karachi

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A B S T R A C T

Introduction: Medication errors are a frequent issue within healthcare facilities. The ratio of patients who suffer harm due to these errors, in contrast to those who do not, is a concerning 100:1. The research aimed to ascertain the prevalence and categories of medication errors, as well as the function of pharmacists in identifying and addressing these errors across different wards of a private tertiary care facility located in Karachi, Pakistan.

Methodology: A cross-sectional case study, conducted in a private hospital in Karachi and including 200 patients, was assumed to explore drug therapy errors and evaluate the pharmacist's contribution to their detection.

Results: Through the meticulous efforts of clinical pharmacists, an extensive assessment encompassing 200 patients was conducted with a gender distribution of 110 females (55%) and 90 males (45%). Within this cohort, a cumulative total of 250 errors (averaging 1.25 per patient) were detected and appropriately addressed. The observed frequencies of error categories were as follows: above therapeutic dose (2.8%), sub-therapeutic dose (3.2%), dose adjustment (30%), drug-drug/drug-food interaction (3.6%), duplication of drug class (4.0%), dose Rounded off (3.6%), intravenous to per oral switch (3.2%), incomplete drug order (4.8%), transcribing error (4.8%), wrong medication (22%), wrong frequency (8%), wrong route (3.6%), wrong dilution/incompatibility (3.6%), wrong infusion rate (1.6%), and miscellaneous (1.2%).

Conclusion This research highlighted the pervasive problem of medication errors and highlighted the critical role clinical pharmacists played in identifying and correcting errors to improve patient safety and streamline healthcare procedures.

Keywords: *Medication error, Category of medication error, Clinical pharmacists, Intervention.*

Introduction

Globally, medication errors pose a widespread challenge. A recent study estimated a staggering 237 million incidents of Medication Errors (MEs) in the past year within the primary and secondary care settings of the UK, incurring a cost of £98 million to the National Health Service.[1] Research indicates a threefold higher incidence of MEs in the pediatric population (1.1%) compared to adults (0.35%), emphasizing the need for heightened.[2] Pediatric medication prescriptions, often based on precise dosage calculations related to body weight or surface area, are susceptible to confusion and errors, especially when dealing with multiple dosage forms and strengths. Additionally, the incomplete development of metabolic and elimination functions in premature infants up to the age of six months increases the risk of errors or toxicity in this vulnerable patient group.[3] Clinical pharmacists are the most reliable source of medication-related information in hospital settings.[4] Pharmacists now play a variety of roles,

ranging from clinical practice to patient outcomes, patient counseling, national healthcare education, and community involvement. All prescriptions should be examined before distribution by pharmacists, according to a recommendation by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO).

The recommendation emphasizes the need for recording the consequences of the pharmacy's direct patient care. Any unnecessary event may trigger or lead to improper pharmaceutical use or patient injury when the drug is within the control of healthcare professionals, patients, or users.[5–7] Professional practice, healthcare goods, methods, and systems, such as prescription, order interaction, product labeling, packaging, nomenclature, compounding, dispensing, delivery, administration, education, supervising, and use, may all be influenced by such circumstances.[8, 9] The pharmacist should intervene to identify these issues so that remedial measures may be taken, or medicine therapy may be tailored to the patient's needs. The forms of this intervention have evolved over the course of time, and range from the most basic handwritten form to digital libraries.[10]

Moreover, by educating medical professionals about these issues, many of them can be avoided. Medical practitioners anticipate that pharmacists and pharmacies will have a variety of duties, including managing repeat prescription services, assessing medications for chronic users, dispensation as per standards, providing management advice for common illnesses, and taking part in regional and national health promotion or disease prevention initiatives.[11]

For a pharmacist to be able to defend their services to patients, hospital administration, practitioners, and client caregivers, as well as to advance their profession and community as a whole, they must document their actions. These therapeutic actions are taken by pharmacists not only to affect patient outcomes but also to reduce costs. In the past few years, electronic systems and software programs have replaced physical methods as the most effective means of documenting clinical pharmacy treatments. However, the majority of outpatient pharmacies lack a centralized registry for documenting treatments at different sites.[12] In the past, several studies have been conducted on medical faults in the healthcare setting. Past studies have shown a high rate of medication errors in low and middle-income countries.[13] Assessing the incidence of medical mistakes is challenging due to the numerous characterizations and classification procedures. The proportion of incidence differs from region to region.

Different proportions of medical faults have been reported. The rate of medication errors depends on many factors including patient treatment.[14] Various regions of the globe reflected distinct rates of incidence of medication errors.[15] UK research was conducted on prescription faults that revealed that 30% of prescription errors of those patients who took five drugs for one year. Improper monitoring of prescriptions led to 12% of adverse events in patients and 38% in those patients whose age was above seventy years. Prescription mistakes were found in 5% of all prescriptions.[16] Another study was conducted in Swedish that studies estimated medication errors of about forty-two percent. These medication errors encompassed 1% of inappropriate doses and two-thirds of unsuccessful goals of treatment.[17]

In Saudi Arabian survey revealed, that slightly below one-fifth of primary care prescriptions had been mistaken, nevertheless, only a tiny percentage were reported.[18] In Mexico survey was conducted that found that fifty-eight percent of prescription medication errors are related to dose schedules.[19] All works of literature have shown that medication error is a universal problem. A survey on medication error events revealed that in 72% of cases, the 3% error ratio at step dispensing was due to improper prescription monitoring, with 40-60% of errors attributed to differences between hospitalized and discharged medicines.[20]

Clinical pharmacy facilities have become firmly entrenched in several nations, which has decreased the frequency of medication errors, prescription mistakes, duration of hospital visits, overall therapeutic costs, morbidity, and death. The main goals of clinical pharmacy services are to encourage judicious prescribing and encourage the use of high-quality pharmaceutical goods. Clinical pharmacy incorporation with the health service is still in its adolescence throughout many emerging economies like Pakistan. According to a World Health Organization assessment, more than half of the medications for use by individuals are now either

recommended or given out improperly.[21] In a hospital, a clinical pharmacist's job is to ensure reasonable prescriptions, avoid drug mistakes, and enhance therapeutic effects. A tremendous improvement in the pharmacy profession has been seen in Pakistan during the past several years.

The increase has also been seen in the recognition of pharmacy as a separate profession, in addition to retail services. Contrary to industrialized nations, clinical pharmacists are still an underutilized part of the healthcare team in underdeveloped nations.[22] The research aimed to ascertain the prevalence and categories of medication errors, as well as the function of pharmacists in identifying and addressing these errors across different wards of a private tertiary care facility located in Karachi, Pakistan.

Methodology

The cross-sectional study was carried out in many wards at a private tertiary medical Centre in Karachi. This study was conducted for two months from 1st November 2023 to 31 December 2023. The study involved the examination of all eligible adult and pediatric patients admitted to medical wards over a two-month data collection period, utilizing a convenient sampling method.

Every patient that was admitted to the hospital wards was included in the trial for the whole time it was conducted and excluded all OPD (outpatient department) patients. The ethical authorization to conduct this study was granted by Jinnah University for Women's IERB committee with the reference number JUW/IERB/PHARM-ARA-009/2023.

Data collection for this investigation was conducted through a systematic approach aimed at capturing comprehensive insights into medication errors and interventions within the observed wards. Firstly, observations were made on the manual ordering and delivery process of medications, documenting the transcription of doctors' orders by nurses onto distinct papers and medical charts. Additionally, daily medical rounds conducted by consultants and doctors, along with instructional visits by department heads, were observed, with attendance records of medical officers, nurse staff, and clinical pharmacists carefully documented. Clinical pharmacists actively participated in training sessions during these rounds, contributing to discussions and interventions related to medication errors.

Furthermore, clinical pharmacists meticulously reviewed patient records and test results during morning and evening shifts in the wards, systematically recording any identified medication errors. These errors encompassed a range of issues, including the selection of incorrect medicines, doses, dosage forms, frequencies, or modes of administration. Upon identification of errors, clinical pharmacists engaged in discussions with the responsible medical officers to effect necessary modifications to prescriptions.

The types and frequencies of medication errors identified were tabulated and analyzed according to predefined criteria (Table 1). Subsequently, quantitative analysis was performed to ascertain the frequency and percentage distribution of each type of medication error, with results summarized in Table 2. Statistical analyses were performed with SPSS version 16.0.

Results

Clinical pharmacists assessed 200 patients for medication errors during the trial, of whom 110 (55%) were females and 90 were male patients (45%). In 200 individuals, 250 faults (1.25 per each) were found and effectively handled. The following frequency of faults was found: Above Therapeutic Dose 7 (2.8%), Sub Therapeutic Dose 8 (3.2%), Dose Adjustment 75 (30%), Drug-Drug/Drug-Food Interaction 9 (3.6%), Duplication of Drug Class 10 (4.0%), Dose Rounded Off 9 (3.6%), Intravenous to Per Oral Switch 8 (3.2%) Incomplete Drug Order 12 (4.8%), Transcribing Error 12 (4.8%), Wrong Medication 55 (22%) Wrong Frequency 20 (8%) Wrong Route 9 (3.6%) Wrong Dilution/Incompatibility 9 (3.6%) Wrong Infusion Rate 4 (1.6%) Miscellaneous 3 (1.2%) (Table 1).

55 (22%) cases of wrong medication prescriptions were found that involved all classes of medicines. 75 (30%). Patients admitted to ICU needed dose adjustment for antibiotics, antihypertensive, and anti-diabetic drugs which was done by the pharmacist. The classes of medication errors with the lowest probability were infusion rate 4 (1.6%) and miscellaneous 3 (1.2%). The two error categories with the same prevalence included wrong route and wrong dilution which were more common in IV

antibiotics and painkillers 9 (3.6%). Other most frequent errors in post-operating drugs were Transcribing Errors 12 (4.8%), incomplete Drug Orders 12 (4.8%), and IV to PO switch 8 (3.2%). The most frequent errors with agents affecting the central nervous system were incorrect selection, sub-therapeutic dose 8 (3.2%), and above therapeutic dose 7 (2.8%).

Table 1: Categories of medication errors and their definitions

Categories of medication error: Definitions
Above Therapeutic Dose: The dose is given higher than therapeutic doses.
Sub Therapeutic Dose: The dose is given less than therapeutic doses.
Dose Adjustment: A statement that describes or provides a dose modification.
Drug-Drug/Drug-Food Interaction: The modification of a drug's effects brought about by the presence of another one, which may have an impact on the drug's distribution, metabolic processes, elimination, or absorption. / Alterations in the way that drugs behave as a result of interactions with specific meals, which may have an impact on the effectiveness of treatment or have negative side effects by altering metabolism, elimination, or absorption.
Duplication Of Drug Class: The act of recommending several drugs for the same condition or goal.
Dose Rounded Off: Medication dosage adjustments are made to the closest useful or convenient numerical value.
Intravenous To Per Oral Switch: Changing treatment route from intravenous (IV) to oral (PO).
Incomplete Drug Order: An unclear or inadequate medical prescription.
Transcribing Error: An error that occurs frequently in data input done by human operators and involves inaccurate information copied or transcribed.
Wrong Medication: refers to the unintentional use or administration of a medication that is not intended for a particular patient or medical condition, carrying the risk of ineffectiveness or negative side effects.
Wrong Frequency: Variation from the specified dosage schedule, including going above or under the recommended frequency of medicine administration.
Wrong Route: Incorrect administration route or transmit medicine to the wrong location.
Wrong Dilution/Incompatibility: The incorrect combination of a medicine with a fluid, vessel, or other compounds, resulting in an unsuitable and sometimes dangerous mix.
Wrong Infusion Rate: Describes a mismatch that may lead to the incorrect and dangerous delivery of medicine or fluids to a patient between the dose that is programmed on an intravenous (IV) device and the recommended or prescribed dose for that patient.
Miscellaneous: A varied assortment or combination of different drugs, chemicals, or products that might not have a similar theme or effect.

The interaction between ciprofloxacin and calcium accounted for drug-drug interaction while the second most significant interaction was between omeprazole and clopidogrel 9 (3.6%). The duplication of drug class was found to be more prevalent in proton pump inhibitors and anti-hyperlipidemic 10 (4.0%). Round-off dose errors were recorded in pediatric doses 9 (3.6%) (Table 2, Figure 1).

Table 2: Categories of medication errors

Categories of medication error	No of incidences frequency	Percentage of frequency
Above Therapeutic Dose	7	2.8%
Sub Therapeutic Dose	8	3.2%
Dose Adjustment	75	30%
Drug-Drug/Drug-Food Interaction	9	3.6%
Duplication Of Drug Class	10	4.0%
Dose Rounded Off	9	3.6%
Intravenous To Per Oral Switch	8	3.2%
Incomplete Drug Order	12	4.8%
Transcribing Error	12	4.8%
Wrong Medication	55	22%
Wrong Frequency	20	8%
Wrong Route	9	3.6%
Wrong Dilution/Incompatibility	9	3.6%
Wrong Infusion Rate	4	1.6%
Miscellaneous	3	1.2%

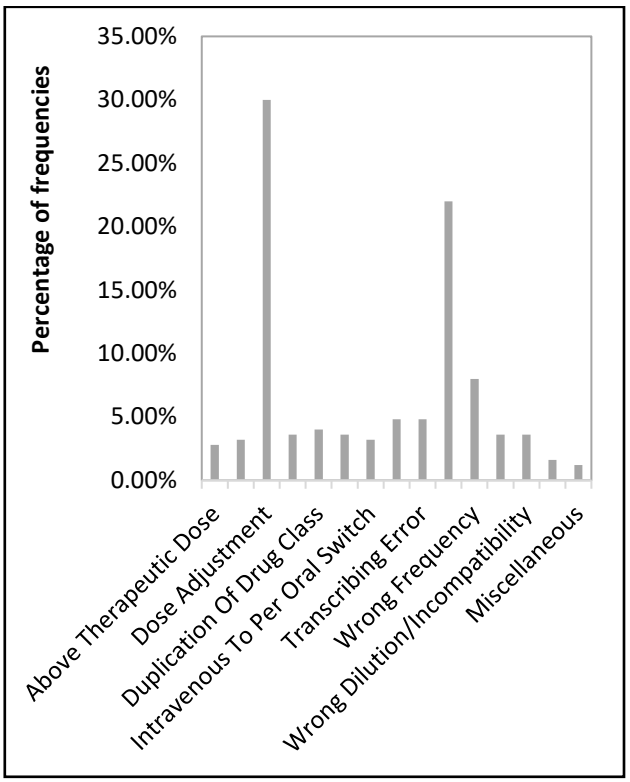

Figure 1: Categories of medication errors and percentage of frequencies

Discussion

The primary objective of medicine development is to enhance patient outcomes and alleviate ailments. Despite the swift progress in pharmaceutical production, the design of therapeutic regimens, and the implementation of electronic medical programs and applications in healthcare settings, Medication Errors (MEs) remain prevalent and pose significant concerns in both developed and developing countries. MEs contribute to an escalation in drug-related complications, including adverse events and side effects, leading to potential hospitalization and the extended use of additional healthcare resources.[23] The research focused on improving the patient's quality of life and achieving the greatest treatment results by lowering medication errors. The safety of patients is greatly impacted by errors in medicine. The ordering, prescribing, dispensing, and administering phases are all where these errors happen. Most of the medication errors occurred during prescribing and ordering in this study. these types of errors are reduced when the clinical pharmacist is with on clinical round of physicians.[24]

Medication errors often stem from illegible handwriting and the use of abbreviations, leading to misinterpretation by dispensers and subsequent dispensing of incorrect medications. Additionally, prescribing errors frequently occur due to inadequate knowledge of clinical characteristics and insufficient information about patients' medical histories. These issues, consistent with findings from prior studies, highlight the recurring nature of these errors in healthcare settings.[25] The World Health Organization (WHO) defines health as reducing the risk of sickness or disability but also includes a person's total physical, mental, and social well-being.

According to this notion, healthcare professionals are crucial in promoting population health. Research has found that among the objectives for obtaining the highest level of public health in terms of modern healthcare delivery is utilizing interdisciplinary expertise. Although the pharmacy profession is valued for its role as a supplier of healthcare in many industrialized nations, it is still undervalued in the majority of developing nations.[26] The way pharmacies are operated in developing nations differs greatly from one another. In Pakistan, the growth of the pharmacy profession in terms of pharmaceutical treatment is still in its infancy. Most public hospitals do not have a suitable number of pharmacists working there. Therefore, their roles were restricted to purchasing, supply chain management, as well as the distribution of drugs.[27]

By enhancing pharmacological treatment, the clinical pharmacist improves overall health outcomes. This study offered proof that clinical pharmacist-initiated interventions lead to patients using medications in a more beneficial manner that was both effective and safe. According to several studies, clinical pharmacist engagement in hospitals, especially inpatient settings led to better and more efficient medication usage through the detection, avoidance, and solution of drug treatment issues.[28,29] Drug treatments play a significant role in medical care and are a source of prescription mistakes and other issues. Keeping up with the expanding list of prescription drugs is a tedious task for doctors. According to numerous types of research, pharmacists can enhanc e patient safety and results by minimizing adverse events by providing advice on the best treatments and doses.[30, 31]

Physicians must acknowledge and make use of the specialist information held by pharmacists, and pharmacists must also make themselves more accessible to the physicians. Fortunately, pharmacy practice has altered dramatically because of the development of clinical pharmacy. The focus of the pharmacist has changed from the drug itself to the drug's interaction with the patient. True change has been difficult to achieve, and there are still many obstacles to be addressed. Many patients and doctors in Iran still do not completely grasp the role of pharmacists as an important element of the healthcare team. Unexpectedly, this is also true in wealthy nations.[31]

Conclusion

The study's findings reinforce the significance of clinical pharmacists' role in raising the standard of medical treatment, improving patient care and outcomes, and lowering drug expenditures for both patients and the community.

Limitation: This study was limited to one tertiary care facility.

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ORIGINAL ARTICLE

Assessment of risk factors associated with sociodemographic status of hepatitis. A cross-sectional study from Pakistani population

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A B S T R A C T

Introduction: One of the most urgent health concerns in Pakistan is the high prevalence of hepatitis C virus infection. Despite the availability of potent antiviral medications, the overall burden of the illness has not diminished, possibly due to the asymptomatic nature of the infection, leading to delayed diagnosis. This study was conducted to assess risk factors associated with the sociodemographic status of Hepatitis C disease in Pakistani patients.

Methodology: This study adopts a cross-sectional design, employing a questionnaire-based Performa to collect data from the Pakpattan district. This hospital-based, study was conducted in Pakpattan, the largest district in Punjab province, Pakistan, and collected data of 500 patients.

Results: The study reveals a higher frequency of male patients than females, with more individuals belonging to nuclear families than joint families. Unmarried individuals face greater risk than married multiple times, and more people reside in rural areas than urban areas. The average family size does not differ between cases and controls, and the prevalence of uneducated individuals is higher than educated individuals. Gender, family status, and residence exhibit non-significant results, age, marital status, family size, and education status show significant associations. The multivariate analysis indicates p-values below the significance threshold, reinforcing the reliability of the results.

Conclusion: Hepatitis C infections are more prevalent in males, and socioeconomic status significantly influences its distribution in both genders. Education emerges as a crucial factor in the spread of this disease. Establishing Hepatitis-related societies for awareness campaigns is essential to facilitate early detection and treatment.

Keywords: *Hepatitis C, Risk factors, Pakpattan, Cross-sectional studies, Pakistan.*

Introduction

Worldwide, around 71 million individuals suffer from chronic hepatitis C, with 3.5 million of them residing in the United States.[1, 2] The prevalence of hepatitis C in the United States has experienced a steady climb over the last two decades, primarily linked to the growing population of injection drug users.[3] Additionally, there has been a notable rise in hepatitis C cases among pregnant women in recent times.[4] Approximately 3% of the global population, equivalent to 180 million people, is affected by the hepatitis C virus, leading to about 36,600 deaths yearly, primarily from hypertension and primary liver cancer. Studies indicate that between 3 to 8 percent of

Pakistan's total population and 2% of pregnant women are affected by HCV.[5] HCV infections have been related to diseases like cirrhosis and nasopharyngeal cancer, persisting despite extensive research efforts globally. Hepatocellular cancer, the prevalent form of liver cancer, impacts about 71 million people with HCV infection worldwide, resulting in over three million new HCV cases each year and approximately 0.4 million annual deaths.[6]

In Pakistan, the high prevalence of HCV is attributed to factors like insufficient sterilization of medical equipment, needless clinical use of syringes, polluted instruments in barbershops, needle distribution to drug users, and inappropriate blood transfusions. Public lack of awareness regarding viral transmission variables also contributes to the spread of disease. Hepatitis refers to liver inflammation caused by viral infections, with strains A through G identified. Hepatitis A and E spread primarily through contaminated food and water, while types C and D are transmitted through blood-to-blood contact or unsafe intercourse.[7-9]

The chronic nature of HCV and the prevalence of hepatocellular carcinoma have led to increased mortality rates in affected individuals. Pakistan faces a growing burden of hepatitis, with an estimated 10 million Pakistanis affected, making it a significant cause of illness and death in the country. Limited studies on hepatitis C exist in Pakistan due to the lack of a national reporting system. The prevalence varies across demographics, with different prevalence rates observed in the pediatric population, blood donors, adults, pregnant females, healthcare staff, and high-risk sets such as household contacts of infected individuals.[10] Earlier investigations, primarily carried out in large urban centers, have consistently indicated that Pakistan is characterized by high prevalence rates [11-18] with 3 to 8% of the general population and 2% of pregnant females reported to be infected.[12]

Notable risk aspects found in Pakistan involve the reuse of non-sterile syringes[19] and other iatrogenic contacts, including unscreened blood transfusion.[10,11] Pakistan exhibits significant social and economic variations.[8] Pakpattan, specifically, has a higher risk of blood-borne virus transmission compared to other large cities in Pakistan due to factors like lower literacy rates, economic challenges, limited access to healthcare services, and the widespread availability of opium from Afghanistan.[20] This study was conducted to assess risk factors associated with the sociodemographic status of Hepatitis C disease in Pakistani patients.

Methodology

Pakpattan, a district in the southwest of the Punjab province, was chosen as the study site. The cross-sectional study took place from September 2021 to February 2022, focusing on sub-districts Pakpattan and Arifwala within the larger Pakpattan District. The research strictly adhered to the Declaration of Helsinki. Ethical clearance was obtained from the Ethical review board, Ref No. UO/ERC/2024/30 ensuring compliance throughout the study. Formal consent was acquired from the relevant department, specifically addressing the publication of research findings.

This study employed a cross-sectional design, with the choice of study design considered crucial for research success. The study was conducted in a District hospital to understand the causes of HCV infection. This method is more efficient and cost-effective than healthy individuals (controls) with (cases). The data was obtained from cases and controls from the same population.[17] Prior approval from hospital administration was secured before collecting data from patients. Physicians were briefed on the study goals and assisted in identifying cases and controls. Cross-sectional surveys were conducted at the hospital, utilizing consecutive sampling to select cases and controls. A standardized questionnaire covered demographics, socioeconomics, family history, and clinical variables.[5, 6] In this study, a mismatched case-control study, a sample size of 500 was calculated using Google Form, considering a type 1 error risk of 5% and statistical power of 80%.

Descriptive and statistical analyses were performed using IBM SPSS version 26. Variables with univariate $p<0.05$ were included in multivariate analysis to determine true significance, aligning with a similar method used in a Brazilian case-control research assessing risk factors for HCV infection.

Results

The primary objectives were to study the risk factors associated with HCV in the Punjab area of Pakistan. The study involved computing the frequencies, means, and standard deviations of different factors to identify and analyze the risk factors associated with hepatitis C.

Analysis of 500 patients revealed a higher frequency of male patients, accounting for 76%, compared to females at 24%. This disproportionate impact on men aligns with previous research findings. The study indicated that 63% were males, while 37% were females. Similarly, Pakpattan found a 76% higher incidence of HCV among men compared to women. The age was categorized into three subgroups: age under 18, age between 19 to 40, and age above 40. The distribution of cases across age groups showed that 14.2% were under 18, 79.4% fell within the 19-40 age range, and 6.4% were over 40.

Table 1: Socioeconomic status of patients

Categories	Number	Percentage
Family status		
Joint families	352	70.4
Nuclear families	148	29.6
Marital status		
Divorced	20	4.0
Married	195	39.0
Single	280	56.0
Widowed	5	1.0
Residential status		
Rural area (more populated)	134	26.8
Rural areas (fewer populated)	91	18.2
Urban area (more populated)	130	26.0
Urban area (fewer populated)	145	29.0
Education status		
Uneducated	286	57.2
1 – 5	84	16.8
6 – 10	73	14.6
11 – 16	57	11.4

Examining the correlation between HCV infection and marital status, the study analyzes four conditions: single, married, divorced, and widowed. The risk appears to increase with the duration of marriage, as indicated by the higher incidence rate among those who have never been married (56.0%). Specifically, 39% of respondents were divorced, 56% were single, 1% were widowed, and 4% were divorced or separated.

Table 1 reveals that 26.6% of the overall sample resides in urban highly populated areas, 18.2% in urban less populated areas, 26.0% in rural highly populated residences, and 29.0% in urban less populous areas. The majority of cases and controls come from urban settings, with 45% from rural and 55% from metropolitan areas. In examining the average family size of individuals and its association with HCV infection, the study considers family size as a continuous variable, with an average family size of seven members across all three samples (7.38±3.71, 7.53±3.84, and 7.4±93.76). There was no significant difference found. The education status is treated as a constant variable, with a breakdown into four subgroups based on educational attainment.

Uneducated individuals comprise 57.2%, while educated individuals make up 42.8%. The study emphasizes the generally high levels of education among patients, making the results applicable to the entire Pakpattan district. Table 2 provides a comprehensive overview of these findings, highlighting the potential influence of education on hepatitis C risk factors and overall well-being.

Table 2: Reveals the univariate study

Variable	Chi-square (p)	Univariate logistic regression	p-value
Sex	3.560	0.6450	0.056
Age	10.450	1.560	0.001
Marital status	39.640	1.980	0.001
Family status	2.570	1.670	0.052
Residence	3.890	4.260	0.005
Family size	0.650	2.010	0.027
Patients'education	188.350	9.450	<0.001

Different tests were employed to observe the significance of relations among variables and disease status. Although gender, family status, and residence show non-significance i.e., ($p>0.05$), age, marital status, family size, and education status show significance i.e., $p<0.05$ (Table 2). The multivariate LR analysis was conducted to thoroughly examine and assess relevant risk factors associated with hepatitis C. The table presents regression coefficients and their 95% confidence intervals, accompanied by explanations of their respective implications. The intercept value in this analysis is -0.496. All p-values for various factors are below the significance threshold of 0.05, affirming the reliability of the results.

A significant risk factor studied is a family history of the disease, with a related 95% Confidence Interval CI of (1.6830 to 2.5960). The results reveal that an individual's likelihood of contracting hepatitis C increases by 2.180 times if they have a first-degree relative with the virus. This crucial finding underscores the importance of familial history as a contributing factor to hepatitis C infection (Table 3).

Table 3: Multivariate logistic regression

Variable	B	SE	p-value	95% CI	
				Lower	Upper
Gender	0.496	0.219	0.000		
Age	0.948	0.124	0.000	0.140	0.259
Marital status	1.495	0.268	0.000	2.057	3.267
Family status	0.248	0.239	0.003	1.249	3.045
Residence	0.649	0.193	0.000	1.385	2.595
Family size	0.385	0.134	0.000	1.294	3.295
Patients' education	0.496	0.294	0.000	1.496	2.256
Family history of hepatitis C	0.519	0.238	0.000	1.683	2.596

This multivariate analysis not only provides insights into the various risk factors associated with hepatitis C but also validates the robustness and reliability of the results. The inclusion of a family history of the disease as a significant risk factor further contributes to our understanding of the complex dynamics influencing the prevalence of HCV in the studied population. Comparisons with similar research in domestic and international literature enhance the broader relevance and applicability of these findings.

Discussion

The research delves into the distinctions among nuclear families NF and joint families JF in Pakpattan. A Gallup poll conducted in the region indicates that nearly two-thirds of respondents prefer living in JF, while over a third opt for NF. As NF has been on the rise, the JF structure has expanded in central Punjab. Individuals in joint households may face a higher risk of contracting hepatitis C due to the frequent sharing of personal items such as kitchen utensils, nail clippers, toothbrushes, and more. Joint family members sharing personal items may inadvertently contribute to the transmission of hepatitis C within the household. In the study, 70.4% live with NF while 29.6% live with JF.

The random selection reveals an estimated frequency of HCV among adults at 6% (62%) and a 95% confidence interval of 5.5–9.6. The elderly were identified as having the highest risk, and the exclusion of young people raises the possibility that this frequency may decline with time. The gender distribution in this study indicates that approximately 76% of cases are males, while 24% are females. This finding aligns with other research, both within and outside Pakistan, where males have been reported to be disproportionately affected by HCV. However, conflicting reports exist, and some studies suggest that females might be more disposed to contracting the infection.[17] The study's significance lies in its use of multiple LR models across various data settings, such as overall data, gender-based data, and urban and rural areas. The inclusion of relevant risk factors is based on a thorough univariate analysis, and only predictors with a p-value less than 0.2 are considered for the final LR Model.

Diagnostic checks for multicollinearity and the identification of outliers are conducted before committing to the final model.[5, 6] Our data uncovered a reasonable positive trend (P = 0.130) linking family size to the risk of HBsAg positivity. The test for trend accounted for socioeconomic and ethnic status. This discovery aligns with findings from other studies.[7] Notably, this study found

no significant difference in average family size between cases and controls. Family size exhibited significant variations concerning the risk of hepatitis C. The prevalence of various risk factors for HCV infection varied across different geographical regions. In Western states and Australia, anti-HCV is related to tattooing, intravenous drug intake, sexual interaction, and history of blood exposure.[21-23] Our study observed a higher proportion of individuals residing in rural areas than in urban areas. However, residence did not exhibit significant differences.

The outcomes suggest that increased age and a history of transfusion, rather than socioeconomic status, are robust risk factors for anti-HCV. Other potential risk factors, including a history of surgery, alcohol use, and cigarette smoking, were also noted, but none demonstrated statistically significant associations with this viral infection. Our data indicated that familial clustering was not a risk factor for anti-HCV. Moreover, we identified only one household member with anti-HCV positivity in households where infection occurred.

This finding suggests that intrafamilial clustering of HCV infection within households is low compared to HBV infections.[24] This study explores risk factors related to HCV in the Pakistani population, encompassing gender, age, family status, residence, marital status, family size, and education status. The results highlight significant differences in age, marital status, family size, and education status, while gender, family status, and residence of patients did not show significant differences.

The investigation revealed that engaging a barber for shaving poses a risk factor for the transmission of hepatitis B and C, aligning with findings in other studies.[25] Barbers in rural settings often employ the same blade on multiple clients, and these rural areas exhibit a higher incidence, as evidenced in the current study. The global occurrence of HCV infection remains relatively low among children, with an anti-HCV incidence rate ranging from 0.2% to 0.4% in the Western world. [26] Local studies indicate that risk factors for HBV and HCV infections in this region differ from those in Western countries.

Noteworthy risk factors here include high poverty coupled with low educational attainment, unwarranted use of injections and syringe reuse, and a lack of awareness regarding the modes of hepatitis transmission. Typically, multiple risk factors are identified in most hepatitis patients. For instance, a study from upper Sindh highlighted HCV as a primary cause of Chronic Liver Disease, with contaminated syringe usage being a prominent risk factor.[26]

Prior reports from Hafizabad demonstrated a high prevalence of anti-HCV antibodies, with reused syringes and frequent therapeutic injections identified as significant risk factors for hepatitis B and C in Pakistan.[21] The common practice of reusing disposable syringes and needles after soaking in tepid water in a boiler or bowl is prevalent in Pakistan. Moreover, the proportion of injections per prescription in Pakistan is considerably higher compared to some other countries. [22] This study underscores the role of syringe use in contributing to Hepatitis C among patients.

Conclusion

To conclude, this is the first work to focus specifically on rural areas and its individuals in Pakpattan District, offering unique insights into the frequency and risk factors related to Hepatitis C. It is crucial to acknowledge that potential risk factors are intertwined with the patient's socioeconomic status, medical history, behavioral features, and family history. The study underscores that Hepatitis C is more prevalent in the male population, emphasizing the gender disparity in the distribution of the disease.

Additionally, various socioeconomic factors play a role in the spread of disease, with education emerging as a crucial factor. The research highlights that illiterate individuals may face challenges in early diagnosis, leading to more complicated cases, Education is identified as a key factor in the distribution of Hepatitis C, emphasizing the importance of awareness and early detection. The call for Hepatitis-related societies to spread awareness among the population is emphasized, aiming to facilitate early diagnosis and timely treatment. The findings underscore the need for a combination of strategies to reduce infection rates, considering the multifaceted nature of the risk factors associated with Hepatitis C.

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ORIGINAL ARTICLE

Estimation of body fat mass percentage as measure of obesity among undergraduate medical students and its correlation with clinical markers of obesity

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A B S T R A C T

Introduction: This study was conducted to assess the burden of overweight and obesity among UG medical students by measurement of body fat mass percentage (BF%) and to evaluate the validity of BF% as a clinical marker of obesity by its correlation with BMI.

Methodology: The research was conducted as a cross-sectional, observational study using the principle of Bioelectric Impedance Analysis for the measurement of body fat.

Results: There are a total of 420 students among them, there were 233 males (55.4%) and 187 females (44.5 %) among the study participants. The burden of overweight and obesity among the students was found to be 26% and 9.8 % respectively according to WHO global BMI criteria whereas it was 18.8 % and 35.7 % respectively, if the Asian criterion was used. This abnormality was pervasive across all four years of UG MBBS students. The startling finding is that students who were labeled as 'Normal' using the BMI criterion were found to be obese by BF% assessment (43%) and even 'Underweight' students were found to have more than normal levels of BF% (15.2%). Measurement of waist circumference (WC) showed that 146 (34.8%) of the students had WC higher than normal. Likewise, 145 (34.5%) of the students had Waist-Hip Ratio higher than normal. Abnormalities of all the above parameters put the students at risk of NCDs(Non-Communicable diseases).

Conclusion: The study shows a high burden of overweight and obesity in medical students. Using body fat percentage as a clinical marker of adiposity is more desirable than using BMI only to screen for clinical obesity

Keywords: *BMI, Body fat mass, Epidemiological Investigations, Hip circumference, Obesity, Overweight, Waist circumference, Waist hip ratio.*

Introduction

Being overweight and obese leads to serious health consequences and increases the risk of morbidities and mortalities due to NCD (Non-communicable diseases). An increase in body fat alters the body's response to insulin, potentially leading to insulin resistance, and also creates a pro-inflammatory state, leading to the risk of thrombosis.[1, 2] India is currently experiencing an epidemic of Type 2 Diabetes Mellitus and related disorders.[3, 4] Obesity also increases the risk for coronary artery disease, hypertension, stroke, etc. The measurement of obesity (prevalence) in populations has thus become an important index of risk assessment of predisposition to NCDs. It has thus become very important to screen all adults and adolescents for obesity to ensure positive health. Body Mass Index (BMI) is the most commonly used measure of obesity.[5] It is commonly used as an important clinical marker of adiposity even though it is a surrogate measure of body fat since the index directly does not measure body

fat. Young people who have great muscular mass and hence more weight for a given height may have a higher BMI even though there is no extra adiposity. In such cases, assessment of BMI to screen overweight or obesity may have its drawbacks.[5]

Moreover, the relationship between body fat and BMI differs in different populations.[6] It has been demonstrated that Indians have different body fat and BMI relationships compared to Caucasians and African Americans and Indians tend to have more adipose tissue for a given BMI.[7, 8] This even prompted WHO to revise the BMI cut-off for Asians to define overweight and obesity.[9-, 10] Thus the use of BMI in a person is limited by its inability to discriminate between fat and lean body mass i.e. fat-free mass (FFM).

Therefore, the estimation of body fat mass as a percentage of the total body weight is an alternative and direct measure of abnormal body adiposity. Various tools are available for the assessment of body fat mass like hydrostatic weighing, air displacement plethysmography, dual-energy x-ray absorptiometry [DEXA], Computerised Axial tomography [CAT] scan, Magnetic Resonance imaging [MRI], and bio-electric impedance analysis [BIA] and measurement of skin fat by calipers. Among these BIA is the least invasive and perhaps the most convenient to use tool for body fat percentage assessment. The objectives of the current study are the following:

1. Burden of overweight and obesity among the UG medical students by using body fat mass and its correlation with BMI.

2. To assess the burden of overweight and obesity among UG medical students of PRMMCH(Pandit Raghunath Murmu Medical College and Hospital, Baripada, India) by measurement of body fat mass percentage.

3. To evaluate the validity of body fat mass percentage as a clinical marker of obesity by its correlation with BMI.

Methodology

Study Population The study which was designed as a cross-sectional, descriptive study was completed within two months after obtaining due ethical clearance at PRMMCH (Pandit Raghunath Murmu Medical College and Hospital; ICMR STS Id no; 2022-02901), Baripada, India. Assuming a prevalence of 50 % obesity among the UG MBBS students a minimum of 384 MBBS students was calculated as the minimum desired sample size. The study was conducted in the clinical anthropometry lab of the Department of Community Medicine of PRMMCH (Pandit Raghunath Murmu Medical College and Hospital) using a Bioelectric Impedance Analysis (BIA) machine for measurement of body fat % and weight, measurement tape for waist and hip circumference and stadiometer for assessing the standing height of the study subjects. All healthy students who consented to participate in the study were included in the study provided they were not disqualified by any of the exclusion criteria.

The criteria for categorizing BMI are based on two widely accepted standards. The first one is the WHO global standards which classify BMI as Underweight (< 18.5), Normal (18.5 –24.9), Overweight (25.0 –29.9), and Obese (>=30). While there are no universally acceptable norms for body fat percentage like BMI, one set of criteria recommended by the ACSM (American College of Sports Medicine) in its ACSM Health Related Physical Fitness Assessment Manual 2008 is widely used and referred to.

Exclusion criteria:

1. All students who were suffering from any illness (acute or chronic) which does not permit anthropometric evaluation

2. All students with any locomotor disability that prevented accurate estimation of standing height measurement by stadiometer

3. All students who had implants or prosthetics (either electrical or non-electrical) on their person.

The assessment of the students was done in batches of 10 to 20 students each. After recording the socio-demographic details, the anthropometric measurements were recorded using the equipment listed above. For body fat percentage measurement by bioelectric impedance analysis (BIA) machine, the students were advised to come on empty stomachs (8-12 hours overnight fasting) with minimal clothing and remove all metallic objects from their person like coins, mobiles, hair clips, etc, which is known to interfere with the measurements. For the BIA

measurements (i,e body fat %), the OMRON Karada body composition monitor HBF-375 was used.

The BIA machine also gave the reading of body weight in kilograms. The anthropometric measurements of waist and hip circumference (in centimeters) were assessed using SECA 201 measuring tape. Height in centimeters was measured using a commercially available stadiometer (Prestige). The collected data was tabulated and analyzed as per the standards for BMI recommended by the World Health Organization (WHO) and their modified version recommended for Asians, particularly Indians. The statistical significance of the results was evaluated by appropriate comparisons and statistical tests (Chi-square).

Results

The medical college has an intake capacity of 100 students per year with an additional capacity for 25 students in the EWS (Economically Weaker Sections) category from 2019 onwards.

The college therefore has an enrollment capacity of 100 students in 4th year MBBS and 125 students each in the first, second, and third year respectively adding to 475 students in total. From the first year MBBS 108 students, 119 students from 2nd year MBBS, 116 students from 3rd year MBBS, and 77 students from the final year MBBS, adding up to a total of 420 students from all four years consented to participate in the study. Thus the research had the participation of 88.4% of the enrolled students.

There were 237 males (55.5%) and 187 females (44.5 %) among the study participants. From among them, 169 students (40.2%) were from a rural background and the rest 251 students (58.2%) were from an urban background. Analysis of the religious faith of the students revealed that 408 were Hindus (97.1%), 7 were Muslims (1.7%) and the remaining 5 study participants (1.2%) were Christians. The mean age of the students was 20.72±1.69, 21.26±1.20, 22.32±1.2 and 23.34±1.4 for the first-year, second-year, third year and final-year students respectively. The overall mean age of the students was 21.8 years across all four years of the students (21.8±1.6) with a minimum age of 18

Table 1: Anthropometric Measurements of the Study Subjects

Parameter	Height (cms)	Weight (kgs)	BMI (Kg/ m^2)	Body fat (%)	Waist Circum. (cms)	Hip Circum. (cms)	W/H ratio
Overall (n=420)	163.8 ± 9.51	64.2 ± 13.25	23.9 ± 4.25	26.5 ± 7.36	82.4 ± 10.22	95.7 ± 8.88	0.86 ± 0.05
Year Wise							
1st-year MBBS	164.6 ± 10.0	65.0 ± 13.68	23.9 ± 4.34	26.5 ± 6.90	82.3 ± 10.8	96.7 ± 9.26	0.85 ± 0.06
2nd-year MBBS	163.7 ± 8.6	65.0 ± 13.93	24.1 ± 4.27	26.2 ± 7.43	82.2 ± 10.1	95.1 ± 9.01	0.86 ± 0.05
3rd-year MBBS	163.8 ± 9.4	63.3 ± 13.54	23.7 ± 4.66	26.0 ± 7.79	82.6 ± 10.76	95.03 ± 9.39	0.86 ± 0.05
4th-year MBBS	162.9 ± 10.2	63.1 ± 11.01	23.7 ± 3.45	27.6 ± 7.25	82.5 ± 8.7	96.1 ± 7.17	0.85 ± 0.05
Gender Wise							
Female	153.6 ± 6.19	58.3 ± 11.7	23.9 ± 4.52	32.1 ± 4.73	80.8 ± 10.44	97.1 ± 9.06	0.83 ± 0.05
Male	169.9 ± 7.03	68.9 ± 12.4	23.9 ± 4.04	22.0 ± 5.84	83.7 ± 9.87	94.6 ± 8.58	0.88 ± 0.04
Residence							
Rural	164.5 ± 9.31	64.8 ± 13.5	23.8 ± 4.12	25.6 ± 7.20	82.7 ± 10.30	95.3 ± 8.67	0.86 ± 0.05
Urban	163.4 ± 9.6	63.8 ± 13.07	23.9 ± 4.35	27.1 ± 7.42	82.2 ± 10.18	95.9 ± 9.02	0.85 ± 0.05

years and a maximum age of 27 years. The anthropometric measurement of the study subjects (Table 1).

Table 2: Distribution of overweight and obesity among the various subgroups

BMI Category	Underweight	Normal	Overweight	Obese
Range	< 18.5	18.5—22.9	23—24.9	>=25
Overall (n=420)	33 (7.9%)	158 (37.6%)	79 (18.8 %)	150 (35.7%)
Year Wise				
1st-year MBBS	27 (6.5%)	43 (39.8%)	19 (17.6%)	39 (36.1%)
2nd-year MBBS	10 (8.4%)	40 (33.6%)	23 (19.3%)	46 (38.7%)
3rd-year MBBS	14 (12.1%)	43 (37.1%)	17 (14.7%)	42 (36.2%)
4th-year MBBS	2 (2.6%)	32 (41.6%)	20 (26.0%)	23 (29.9%)
Gender Wise				
Female	19 (10.2%)	67 (35.8%)	32 (17.1%)	69 (36.9%)
Male	14 (6.0%)	91 (39.1%)	47 (20.2%)	81 (34.8%)
Residence				
Rural	13 (7.7%)	61 (36.1%)	37 (21.9%)	58 (34.3%)
Urban	20 (8.0%)	97 (38.6%)	42 (16.7%)	92 (36.7%)

The breakup of the data on BMI computed from the anthropometric measurements on the study subjects reveals that 33 (7.9%) students were underweight, 109 (26%)students were overweight, and 41 (9.8%) students were obese while the remaining 237 (56.4%) students had normal BMI. So, one of the questions about the burden of overweight and obesity among the UG medical students was found to be 26% and 9.8 % respectively according to WHO global criteria of assessing obesity by using BMI.

Table 3: Distribution of body fat percentage (BF%) of BMI and their co-relation

BMI Category	Underweight	Normal	Overweight	Obese	Overall
Range	< 18.5	18.5—22.9	23—24.9	>=25	(n=420)
Body Fat Percent (BF%)					
Normal	28 (84.8%)	90 (57.0%)	26 (32.9%)	10 (6.7%)	154 (36.7%)
Obese (At risk)	5 (15.2%)	68 (43.0%)	53 (67.1%)	140 (93.3%)	266 (63.3%)
r^2	-0.24	0.24	0.14	0.42	0.57
P value	0.16	0.00	0.20	0.00	0.00

The second set of standards is by the WHO for classifying BMI in Asians and Indians.[9, 10] This standard classifies BMI as Underweight (< 18.5), Normal (18.5 - 22.9), Overweight (23.0 - 24.9) and Obese (>=25). When the dataset was reanalyzed with the Asian standards the underweight group remained unchanged (7.9%) but there was a remarkable reduction in the normal fraction as well as the overweight fraction i.e. normal (56.4 % to 37.6%) and overweight (26 % to 18.8 %) as compared to the WHO global standards. The obese fraction rose sharply from 41 to 150 students i.e 9.8 % to 35.7 %. Thus the burden of overweight and obesity among UG MBBS students of our college was found to be 18.8 % and 35.7 % respectively, if the Asian criterion for BMI was used.

It is already a well-established fact that all the risk factors for non-communicable diseases (NCDs) operate on a continuum of risk concepts i.e. even within the so-called 'normal' range of BMI the persons on the higher side of the range are at higher risk of NCDs than those lower than them. Furthermore, it is also a well-accepted scientific fact that Asians are at a higher risk of NCDs compared to their Western counterparts even at lower levels of obesity, thus necessitating the separate criteria for Asian Indians with lower limits.

Thus in the present study using the Asian criteria was considered prudent as it helped in identifying the higher

burden of risk among the students. The sub-group analysis of the BMI data (Table 2) shows that the distribution of overweight and obesity among the students from rural backgrounds (21.9% and 34.3%) is comparable to those from urban backgrounds (16.7% and 36.7%), which dispels the myth that obesity is an urban problem as students from both backgrounds are at equal risk. The burden of overweight and obesity seen from the sex perspective also mirrors a similar picture with 17.1% and 36.9% of the females while 20.2% and 34.8% of the males being overweight and obese respectively. The male students as well as female students are at similar risk.

Table 4: Distribution of Waist Circumference (WC) and Waist/ Hip Ratio (WHR) to BMI

BMI Category	Underweight	Normal	Overweight	Obese	Overall
Range	< 18.5	18.5—22.9	23—24.9	>=25	(n=420)
Waist Circumference					
Normal (<=90 cm in males and <= 80 cm in females)	31 (93.9%)	152 (96.2%)	53 (67.1%)	38 (25.3%)	274(65.2%)
At risk (High)	2 (6.1%)	6 (3.8%)	26 (32.9%)	112 (74.7%)	146 (34.8%)
Chi square =184.23					p=0.00
Waist/ Hip ratio					
Normal (<=0.9 in males and <=0.85 in females)	31 (93.9%)	129 (81.6%)	51 (64.6%)	64 (42.7%)	275(65.5%)
At risk (High)	2 (6.1%)	29 (8.4%)	28 (35.4%)	86 (57.3%)	145 (34.5%)
Chi square =184.23					p=0.00

Table 5: Distribution of Waist Circumference (WC) and Waist/ Hip Ratio (WHR) to Gender

Waist Circumference (WC)			
Sex	Female	Male	Total
Normal	93 (49.7%)	181 (77.7%)	274 (65.2%)
At risk (High)	94 (50.3%)	52 (22.3%)	146 (34.8%)
Chi square=35.73			p=0.00
Waist/ Hip ratio			
Normal	120 (64.2%)	155 (66.5%)	275 (65.5%)
At risk (High)	67 (35.8%)	78 (33.5%)	145 (34.5%)
Chi square = 0.254			p=0.614

The year-wise distribution of the students shows that the pattern of the burden of overweight and obese is seen in all four years of students with minor differences in the absolute proportions, which reflects the pervasive nature of the malady across the entire student population. The research study also attempted to explore the utility of other clinical markers of obesity like body fat percentage (BF%) in assessing obesity compared to the often-used parameter of BMI. The students were assessed for body composition using a BIA (Bioelectric Impedance Analysis) machine which gave out a cluster of measurements related to body composition for each study subject. Since our objective was to study the relationship and utility of body fat percentage, only that parameter was recorded and the rest of the output was conveniently ignored for this study.

While there are no universally acceptable norms for body fat percentage like BMI, one set of criteria recommended by the ACSM (American College of Sports Medicine) in its ACSM Health Related Physical Fitness Assessment Manual 2008 is widely used and referred to[11]. The standards are different for men and women and again vary for different age groups within each gender. The categories in each group have a scaling approach starting from the best end of the spectrum labeled as 'Essential fat' followed by 'Excellent', 'Good', 'Average', 'Below average', and the worst being ' Poor'.

For our analysis, the value of 22.4 was used as the upper limit for BF% in males and 27.7% for females as they correspond to the upper limit for the age group 20—29 years which includes most of our study subjects. For subjects below 20 years, no separate standards were available in the ACSM guidelines, hence the 20—29 year

was used as default. It is worthwhile to note that many research studies take an average of both 22.4% and 27.7% instead and use BF% >25% as a universal cutoff to define obesity for both males and females.

The analysis of the BF% (Table 3) of the students shows that 266 (63.3%) students have BF% higher than the cutoff value for their respective sex and age (i,e obese) whereas the remaining 154 (36.7%) have BF% within limits. Further analysis reveals that the agreement between BF% and BMI in identifying the 'high risk' is the highest in the 'obesity' category (93.3%) followed by the 'overweight' category (67.1%). The startling finding is that students who were labeled as 'Normal' using the BMI criterion were found to be obese by BF% assessment (43%) and even 'Underweight' students were found to have more than normal levels of BF% (15.2%). Thus the BF% was found to be a more sensitive indicator of obesity compared to BMI.

The study of the linear relationship between BF% and BMI reveals (Table 3) that there is a statistically significant ($p<0.00$) strong positive correlation (0.57) between BF% and BMI. However sub-group analysis shows a weak correlation in the underweight, normal, and overweight categories and a modestly positive correlation in the obese category. This also underscores the fact that the linear relationship of BF% is independent of BMI, especially in the lower BMI ranges of 'underweight' and 'normal' where the person is considered as having a low risk. Thus a person could well be at high risk because of higher than normal body fat percentage and yet remain in the false realm of normalcy if only BMI is used as the clinical criterion to define or screen obesity.

The measurement of the waist circumference (WC) is an important marker of cardiovascular risk since it overtly measures abdominal girth which is the principal site for extra fat deposition. The government of India's National Program for Prevention and Control of NCDs has a set limit for WC as a screening tool where more than 90 cm in males and more than 80 cm in females is considered a risk for NCDs. The analysis of the anthropometric data in (Table 4), shows that 146 (34.8%) of the students had WC higher than normal which puts them at risk of NCDs. The breakup of the data shows that 55.3% of the female students had a higher than normal WC compared to only 22.3% of the male students, which was statistically significant. Likewise, the distribution of the WHR across the different BMI categories is summarized in (Table 5) which was also statistically significant.

The waist circumference to hip circumference ratio (W/H ratio) is also an important predictor of cardiovascular risk vis-a-vis its ability to measure abdominal obesity. The WHO criterion upper limit for the W/H ratio is 0.9 for males and 0.85 for females.[12] Any value above these two is considered a high-risk category. The analysis of the anthropometric data in (Table 4), shows that 145 (34.5%) of the students had WHR higher than normal which puts them at risk of NCDs. The breakup of the data shows that 35.8% of the female students had a higher than normal WHR compared to 33.5 % of the male students. However, the distribution of the WHR across the different BMI categories (Table 5), was statistically significant.

Discussion

Medical undergraduate students are more prone to obesity due to their extended hours spent on the study table as well as very little time for physical activity within their packed course schedule. In several studies done across India, it has been reported that the burden of overweight and obese is high in medical students.[13-15] In one study done in Gwalior by Tiwari et al showed a prevalence of overweight at 9.93% and that of obesity at 1.53%. Deotale et al in Gran Medical College, Mumbai have reported a prevalence of 14.33% and 3.34% respectively for overweight and obesity. Likewise, Fernandez from Pune reported a combined proportion of 13.2% among medical students for overweight and obesity together.[15] Khan et al in a study in our neighboring country Pakistan reported that 30.5% of males and 16% of females had a BMI exceeding 25 kg/ m^2.[16] However most of the studies have used the WHO global BMI criterion which has 25 kg/m^2 as a cut-off. In one of the few studies that used the modified WHO criteria (for Asians and Indians) by KK Manojan et al done in a medical college in Kerala, the prevalence of obesity was 25.7% and overweight was 24.5%.[17] Our study which also uses the modified WHO criterion affirms the findings with the burden of overweight at 18.8% and obesity at 35.7% among the students of our college.

One of the research objectives of the present study was to explore the validity of the measurement of body fat percentage (BF%) as a marker of obesity compared to the often-used BMI. The relationship between BMI and BF% has been studied across various ethnic groups, particularly in Western countries.[18-21] The Body composition of Indians is different from other ethnic groups around the world. From the very few studies that have been published in India, it has been reported that for the same degree of obesity measured by BMI, the BF% among South Asians particularly Indians may be much more than other ethnic populations.[22-25] This was also established in our analysis where students who were labeled as 'Normal' using the BMI criterion were found to be obese by BF% assessment (43%) and even 'Underweight' students were found to have more than normal levels of BF% (15.2%). Thus the use of BMI alone as a screening tool in clinical practice to detect or rule out obesity can be fallacious and dangerous as people who are indeed at risk' may be given the false impression of 'normalcy'.

Earlier research has indicated a positive correlation between BMI and BF% in various populations.[18,19, 22] Although our study shows a strong positive correlation in the overall population (r^2=0.57) between BF% and BMI which was also statistically significant, the linear relationship was not uniform across all categories of BMI. It was minimal and negative in the underweight category (r^2= - 0.24) and gradually increased to a positive correlation as one moved up the BMI categories from 'Normal' to 'Obese' through 'overweight'. In the 'Normal' and 'Obese' categories the correlation was positive and statistically significant as well. Similar findings have also been reported from a study in British adults (correlation between BF% and BMI).[11, 17]

Conclusion

The present research work was designed as a simple observational descriptive study to give a picture of the burden of overweight and obesity among UG medical students of our college. The study findings of a high burden of overweight and obesity in medical students will hopefully convince research institutions like ICMR to establish a demographic health surveillance system for medical students. Indian medical students can be subjected to annual or semi-annual health assessment and their clinical and other parameters can be logged and they can be followed up (in a longitudinal format) to study the burden of risk factors and outcomes for various health conditions especially NCDs among them. [similar to the famous British Doctors study of Doll and Hill].

The country's medical regulator—the National Medical Commission (NMC) can be also motivated to include mandatory physical activity in the curriculum for all medical students and also endorse the prescription of annual health assessments for all medical students.

That BMI of 23 kg/m^2 is not an effective predictor of obesity particularly in Indians is strikingly borne out in this study. The analysis of the body fat percentage even in this sample of relatively young study subjects reveals the so-called "Indian paradox", that Indians are more prone to obesity (due to their smaller body frame) even at much lower BMI cut-offs compared to their western or Caucasian counterparts. Thus using BF% as a clinical marker of adiposity is more desirable than using BMI only to screen obesity.

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ORIGINAL ARTICLE

Incidence of hyperoxia and excess of oxygen use in critically ill pediatric patients

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[1,5,6] *Data collection, data interpretation, drafting, and literature review*

[2] *Data collection, drafting*

[3] *Study concept, methodology*

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A B S T R A C T

Introduction: Oxygen therapy is a crucial aspect of quality care in the pediatric Intensive Care unit. It is not only necessary for preventing hypoxia but also important for reducing the burden of labored breathing in a child maintaining saturation at the cost of a higher basal metabolic rate. To determine the incidence of hyperoxia in patients receiving supplemental oxygen therapy in a pediatric intensive care setting.

Methodology: A cross-sectional prospective study was conducted at the pediatric intensive care unit of Shifa International Hospital from November 2022 to October 2023. A total of 137 patients were included in the study. Consecutive non-probability sampling was used for patients who matched the inclusion and exclusion criteria. Data regarding demographic and clinical factors was collected and evaluated using SPSS 23. The incidence of hyperoxia and its relationship to mortality, organ dysfunction, mode of ventilation, and length of stay was determined.

Results: The mean age of the patients participating in the study was 4.97 ± 4.35 years and 101 (73.7%) were males. Mean fractional inspired oxygen, saturation, and partial pressure of oxygen were 0.37 ±0.19, 94.58 ±3.20, and 102.77 ±21.95 mmHg respectively. The overall incidence of hyperoxia was 9.5%. There was no statistically significant difference in mode of ventilation, organ dysfunction, and length of stay when compared between those who had hyperoxia and those who did not.

Conclusion: The study concludes that the overall incidence of hyperoxia remains low at 9.5% as only 13 out of 137 patients experienced it.

Keywords: *Hyperoxia, Oxygen, Mortality, Pediatric Intensive Care, Ventilation.*

Introduction

Oxygen therapy is a crucial aspect of quality care in the pediatric Intensive Care unit. It is not only necessary for preventing hypoxia but also important for reducing the burden of labored breathing in a child maintaining saturation at the cost of a higher basal metabolic rate. Small children tend to have fewer fat stores and energy reserves. Therefore, such children are at increased risk of type 2 respiratory failure from exhaustion. Oxygen therapy is also indicated in patients at increased risk of organ hypoperfusion. Hypoxia may be a result of poor gaseous exchange at the lungs or tissue level such as in pneumonia and sepsis, respectively. While there may be a difference in the optimum oxygen saturation targets recommended for patients in different clinical settings, there is agreement on the need for oxygen therapy to avoid hypoxia. World Health Organization generally recommends oxygen therapy for anyone with saturations below 90%.[1] Meanwhile, the American Heart Association advocates for target saturations between 94% and 99%.[2] However, studies also demonstrate that excessive oxygen saturation can lead to adverse outcomes in the pediatric population. Hyperoxia is found to be associated with higher mortality in critically ill children.[3] Supplementing spontaneous breathing with exogenous oxygen is a common medical treatment. However, it must also be considered a treatment modality in itself because no drug

is without its adverse effects. It is beneficial but not completely benign. Similarly, while oxygen therapy may be necessary for sustaining life, it should not be considered completely benign. While oxygen metabolism in the human body produces vital molecules like adenosine triphosphate, it also produces reactive oxygen species. When the levels of these reactive agents exceed the antioxidant activity of blood enzymes it results in a state called oxidative stress.[4]

However, this is largely based on theoretical knowledge. Carr et al published a clinical study in 2020 that was based on critically ill patients. It revealed that the difference in blood levels of molecules produced as a result of oxidative metabolism in patients receiving conservative oxygen therapy was statistically non-significant when compared to those receiving standard therapy.[5] Previously, most research concerning hyperoxia was focused on neonates with retinopathy of prematurity and bronchopulmonary dysplasia being the most common themes.[6] Researchers are now interested to find out if higher oxygen levels in the blood of pediatric and adult patients (that is, those beyond the neonatal age) have similar risks. Morbidity and mortality have been evaluated for their association with hyperoxia in critically ill pediatric patients.[7]

However, in the absence of robust clinical trials, most guidelines for pediatric patients regarding optimum saturation targets are based on expert opinions and international consensus amongst colleagues including the European Resuscitation Council guidelines on pediatric life support.[8] The objective of our study is to determine the incidence of hyperoxia in patients receiving supplemental oxygen in pediatric intensive care via invasive or non-invasive ventilation and its relationship with mortality, length of stay, multi-organ dysfunction, and mode of ventilation.

Methodology

A single-center cross-sectional prospective study was conducted at the pediatric intensive care unit of Shifa International Hospital, Islamabad from November 2022 to October 2023. Ethical review board approval was obtained before the study vide letter number IRB # 481-23 dated 10-Nov-2023. The sample size was calculated using the open sample size calculator. Taking the frequency of hyperoxemia at 15% with a confidence interval of 90% and absolute precision of 5%, the estimated sample size was calculated as 137 patients. Non-consecutive sampling was employed. All patients who reported to the department during the study period and met the criteria were included in the study. Written informed consent was taken from the parents or guardians of patients included in the study.

Inclusion criteria included all children between the ages of one year and 15 years who received supplemental oxygen therapy either non-invasively as High flow nasal cannula, continuous positive airway pressure, bi-level positive airway pressure, and nasal cannula or invasively through the endotracheal tube via mechanical ventilation in the first 24 hours of admission in the pediatric intensive care unit. Exclusion criteria included patients not willing to participate in the study. Also, children who died or were discharged within 24 hours of admission were not included in the study. Children with cyanotic heart diseases and methemoglobinemia, acquired or congenital were excluded. Any child who had a previously diagnosed hemoglobinopathy such as thalassemia or sickle cell disease that would affect the oxygen-binding capacity of blood was also excluded. Further to this principle, children with hemoglobin below 10mg/dL were not included to remove confounders from the study.

Demographic data was collected regarding their age, gender, any co-morbid conditions, and whether they received invasive or non-invasive supplemental oxygen therapy. Data was collected by a team of pediatricians working in the PICU and shared with the author who entered it into SPSS 23 for further analysis. Clinical data included fractional-inspired oxygen concentration received and the saturations detected on a pulse oximeter attached to a cardiopulmonary monitor at the time of blood gas analysis. The partial pressure of oxygen was also noted for each of these patients after 24 hours of receiving oxygen therapy.

Hyperoxemia is defined as saturations greater than or equal to 98% or partial pressure of oxygen greater than or equal to 100mmHg. Excess oxygen usage is defined as

Fractional oxygen greater than or equal to 0.50 in any patient experiencing hyperoxemia.

Descriptive statistics were used to describe the relevant data. Mean and standard deviation were used for the age of the patient, fractional inspired oxygen, saturations, partial pressures of oxygen, and length of stay in Paediatric intensive care. Gender, presence of co-morbid, mode of ventilation, mortality, and morbidity (in terms of MODS) were described in percentages. Pearson chi-square was used to compare mortality, MODS, and mode of ventilation between patients who experienced hyperoxia and those who did not. An Independent t-test was employed to compare the length of stay between the two groups. SPSS-23.0 was the software used to process all the data and perform the analysis. Differences between groups were considered significant if p-values were less than or equal to 0.05.

Results

A total of 137 patients admitted to the pediatric intensive care unit of our hospital receiving supplemental oxygen therapy were included in the study. The mean age of participants in the study was 4.97 ± 4.35 years. Table 1 describes the demographics and clinically relevant data of patients participating in the study. A total of 101 (73.7%) patients were male and 36 (26.3%) were females. 78 (56.9%) patients were ventilated invasively while 59 (43.1%) were on non-invasive modes of ventilation such as high-flow nasal cannula, continuous positive airway pressure, bi-level positive airway pressure, and low-flow nasal cannula. 77 (56.2%) patients had preexisting co-morbid conditions while 60 (43.8%) did not.

The mean fractional inspired oxygen provided to patients was 0.37 ± 0.19 while the mean saturations recorded over these patients were 94.58 ± 3.2%. The mean of partial pressures of oxygen as determined by arterial blood gases was 102.77 ± 21.95 mmHg. Overall, 13 (9.5%) patients experienced hyperoxia while 124 (90.5%) maintained saturations within the recommended range. Table 2 illustrates the comparison of various factors between those experiencing hyperoxia and those who did not. Pearson chi-square determined that there was a significant difference in mortality between the two groups. Mortality was only 29 (23.4%) in the group not having hyperoxia while it was 7 (53.8%) in the group experiencing hyperoxia. The P-value was 0.018 which was considered statistically significant. The average length of stay was 5.52 ± 3.85 days in the group without hyperoxia but 5.00 ± 1.15 days in those with hyperoxia.

Table 1: Characteristics of patients

Parameters		Frequency
Age		4.97 ± 4.35 years
Gender	Male	101 (73.7%)
	Female	36 (26.3%)
Mode of ventilation	Invasive	78 (56.9%)
	Non-Invasive	59 (43.1%)
Co-morbidities	Yes	77 (56.2%)
	No	60 (43.8%)
Oxygen levels	FiO2	0.37 ± 0.19
	SaO2	94.58 ± 3.20%
	PaO2	102.77 ± 21.95 mmHg
Hyperoxia	Yes	13 (9.5%)
	No	124 (90.5%)

Table 2: Relationship of various factors amongst children with hyperoxia.

Factors	No hyperoxia	Hyperoxia	P-value
Mortality			
No	95 (76.6%)	6 (46.2%)	0.018*
Yes	29(23.4%)	7 (53.8%)	
MODS			
No	72 (58.1%)	10 (76.9%)	0.271*
Yes	51 (41.9%)	3 (23.1%)	
Mode on ventilation			
Invasive	68 (54.8%)	10 (76.9%)	0.187*
Non-invasive	56 (45.2%)	3 (23.1%)	
Length of stay	5.52 ±3.85	5.00±1.15	0.126**

*Pearson Chi-square test; **Independent T-test

The difference was not significant with a p-value of 0.126 as per the independent t-test. P-values were 0.187 and 0.271 for a mode of ventilation and multi-organ dysfunction between the 2 groups respectively hence considered non-significant.

Discussion

Currently, Pakistan has only 1 PICU bed for every 500,000 children 14 years of age.[9] Being a developing country with limited resources, Pakistan needs to use its resources wisely. It is even more pertinent to be cautioned in cases where the resource if used excessively may be harmful to the patient. Fayazi et al conducted a retrospective study collecting data from patient records. Analyzing 64 patients revealed that in this particular pediatric intensive care unit patients were hypoxemic almost 61% of their time on supplemental oxygen.[10] Though, our study did not assess the duration of hyperoxia, the incidence was much less compared to this study. A systematic literature review of 13 studies was conducted in 2021 by Napolitano et al. It recommended that disease-specific saturation targets should be set for each child at the time of admission. This revealed a better result in terms of prognosis for the child.[11]

While our study set the hyperoxia cut-off at 98% or more, some studies advocate lower oxygen saturation targets. Cunningham et al investigated if oxygen saturation targets of 90% brought any difference in outcomes as compared to a target of 94%. It was found that a target of 90% led to an earlier discharge while bringing about no significant difference in adverse events.[12] Lillien et al conducted a systematic review of the literature of 16 studies that included more than 27 thousand patients. It concluded that while the definition of hyperoxia may vary amongst set-ups, it invariably led to increased mortality with an odds ratio of 1.5. This is similar to our study which found a statistically significant difference in mortality between the two groups.[13]

There have been no local studies in Pakistan to evaluate the effect of hyperoxia in human patients in Pakistan. However, Raza et al experimented with rats to assess the effect of hyperoxia on weight, fasting blood glucose levels, and its potential role in treating obesity. Results showed increased weight and fasting blood glucose in rats receiving hyperoxia hence proving it not a useful treatment for obesity.[14]

In 2020, Mackle and colleagues published a study in the New England Journal of Medicine. This randomized trial exhibited no significant difference in ventilator-free days between the two groups receiving liberal versus conservative oxygen therapy. This particular trial revealed that mortality in the group receiving conservative and liberal oxygen therapy was 35.7% and 34.5% respectively. With an odds ratio of 1.05, it can not entirely vouch for the safety of liberal oxygen usage or justify its usage in intensive care settings.[15] Though the figures from our study had more differences in percentages between the two groups, neither study revealed a statistically significant difference.

A clinical practice guideline published in the British Medical Journal in 2018 strongly urges maintaining oxygen saturations of no more than 96% in medical patients.[16] Certain research analyses advocate higher oxygen saturation targets in peri-operative patients such as a meta-analysis by Cohen and colleagues that included more than 14 thousand patients from 26 trials. It concluded that the relative risk for wound infection was 0.81 in the group receiving higher levels of oxygen as compared to the lower oxygen group.[17] A recent multi-center trial was conducted by Ferrando et al in Spain that demonstrated no significant difference in surgical site infection between patients receiving fractional-inspired oxygen of 0.30 and those receiving 0.8018.

Most previous studies evaluating the role of hyperoxia on patient outcomes have focused on mortality rather than organ dysfunction. While mortality in pediatric intensive care usually lies around 2-3%, it rises drastically for any child requiring respiratory support.[19] Organ dysfunction is of prime importance in childhood. Any dysfunction, mild or severe for any period may lead to impaired organ development during periods of active growth. The OXY-PICU trial included a lung function score to address this vital concern.[20] Similarly our study included multi-organ dysfunction syndrome as one of the outcomes compared. While mortality was found to be significantly different between the two groups, the difference in organ dysfunction was statistically significant. However, it is suggested that in the future scoring should be employed to assess organ function separately.

Limitations of the Study

It is also imperative to note that hyperoxia-related adverse effects are also affected by the timing, duration, and extent of hyperoxia.[21-23] However, our study limitation included taking readings at a certain point in time for each patient rather than repeatedly throughout admission. Hence, we cannot comment on the duration of hyperoxia exposure in our patients.

Conclusion

This study expands the existing clinical and epidemiological data by reviewing the current practice of oxygen therapy in a pediatric intensive care set-up in Pakistan and implementing the current standard of care to optimize the risks and benefits of this therapy in the future. The findings of this study contribute to the body of knowledge on the use of oxygen therapy in critically ill children and inform clinical practice in resource-limited settings.

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ORIGINAL ARTICLE

Ultrasonographic assessment of hydronephrosis in adults and children: Experience from a tertiary care hospital

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A B S T R A C T

Introduction: Hydronephrosis (HN) refers to the dilation of the pelvicalyceal system. It is prevalent in both pediatric and old age. The etiology of HN in adults differs from that in neonates and children. The current study aims to evaluate various presentations and causes of HN in children and adults with the help of ultrasound (US) as the primary diagnostic modality.

Methodology: This cross-sectional prospective study was conducted in a tertiary care hospital in Lahore, Pakistan on patients between 0-70 years of age, who were diagnosed with HN in the US. Data was collected on a self-designed proforma including gender, age, symptomatology, and anthropometry. Percentages and frequencies were calculated for categorical data. The chi-square test was applied to compare urinary calculi in gender, age, BMI, and side.

Results: The total number of patients was 73. The mean age was 31 years. Adults were 74% (54) while 26% (19) were of the pediatric age group. Males were 67.6% (50) and 31.5%(23) were females. Lumbar pain was the commonest presenting complaint. Hydronephrosis was bilateral in 20.5%(15), 43.8% (32) in the left and in the right kidney (35.6%) 26. In adult patients, renal calculi were the commonest cause of 69.9%(51) of HN. In the case of children, PUJ obstruction and renal calculi were equally common 31.6%(6) each. The ureter was the most common site of calculi 35.6% (26). A significant association was found between HN with side of involvement (p-value < 0.001) and age of the patient (0.041).

Conclusion: Ultrasound imaging is helpful in the diagnosis, determination of etiology, and grading of hydronephrosis. Ureteric calculi is the most frequent cause of hydronephrosis followed by pelvic ureteric junction obstruction.

Keywords: *Hydronephrosis, Etiology, Ultrasound, Renal calculi, Pediatric.*

Introduction

Hydronephrosis (HN) refers to the distension and dilation of the pelvicalyceal system. It is quite common in both pediatric and adult populations. The prevalence of HN from neonates to old age is 3.1%.[1] HN is reported in 2-2.5% of pediatric population.[1] Both acute and chronic forms of HN are observed. In most cases, HN is secondary to obstruction of urine flow but it can be seen even without any obstruction. The underlying cause of HN can vary according to the age of the patient. Congenital urinary tract abnormalities like posterior urethral valves, PUJ obstruction, stenosis at the ureterovesical junction, and ureteric strictures are frequently encountered etiology of HN in children.[2] Renal calculi are frequently seen in adolescents and young adults, while prostatic hypertrophy

or carcinoma, retroperitoneal or pelvic malignancies, and renal calculi are the primary causes in older patients.[3, 4] This condition is frequently encountered by urologists, emergency medicine specialists, and primary care physicians. HN has various clinical presentations. Quite a number present in ER with severe pain while many present in OPDs. Flank pain is the main symptom of HN. Other presentations include decreased urination, urinary incontinence, dysuria, increased frequency, fever, and nausea.

Presenting symptoms depend on the cause and severity of urinary obstruction.[5] Severity of HN in infants and adults is assessed through grading systems like Onen, AP diameter, SFU, radiology, and UTD.[6] All these systems are ultrasound-dependent. According to the Society of Fetal Urology (SFU) classification system, HN has four severity grades;

Grade 1; and dilation of the renal pelvis. Grade 2; dilation of the renal pelvis and major calyces. Grade 3; grade 2 + minor calyces' dilation. Grade 4; grade 3+ thinning of the renal parenchyma. Ultrasound(US) remains the first-line imaging modality for diagnosis and grading of HN. US imaging is a non-radiation and non-invasive modality that is widely accessible and cost-effective. It is also available in portable form in most healthcare setups.[6, 7] It not only determines the severity of HN promptly but also prompts the necessity of other diagnostics.[8] Ultrasound adds a functional evaluation of the urinary tract when combined with clinical findings. Adequate data about the etiology of HN in children and adolescents, in Pakistan, is lacking.

The current study aims to evaluate various presentations and etiology of HN in children and adults. This study will especially be of value for radiologists, urologists, pediatricians, and emergency practitioners who have to find out the cause of HN as a frequent and important problem corresponding to their daily work. Quick diagnosis will assist in prompt treatment of the underlying condition and will be beneficial for better patient outcomes.

Methodology

This cross-sectional prospective study (IRB number 00-18-21) was conducted in the radiology Department of Lahore General Hospital Pakistan. Patients between 0-70 years of age, who were diagnosed as having HN based on US were included in the study, after taking verbal informed consent. Patients with prenatal HN were excluded. Standard protocol for ultrasound imaging of kidneys was followed. A 3.5 MHz curved transducer of Medison, Sono ex-model six color Doppler machine was used to perform ultrasound of study participants. Patients were scanned by the same highly experienced radiologist following the protocol of ultrasound imaging of the kidneys. Longitudinal and transverse sections of each kidney were acquired in supine, lateral, and prone positions.

Demographic data was collected on a self-designed proforma including gender, age, and symptomatology. Anthropometric measurements were recorded. Data was analyzed using SPSS version 23. Percentages and frequencies were calculated for categorical data. The chi-square test was applied to see the association of urinary calculi with gender, age, BMI, and side. A P <0.05 was taken as significant.

Results

The study involved 73 patients who were diagnosed as having HN based on abdominal ultrasound imaging. The mean age was 31 years (range was 4 months to 81 years). Adults were 74% (54) while 26% (19) were < 18 years of age. Males were 67.6% (50) and 31.5%(23) were females (Table 1).

Table 1: Symptomatology of Hydronephrosis

Symptom	Frequency n =73	Percentage
Bilateral lumbar pain	17	23.3
Right lumbar pain	18	24.7
Left lumber pain	22	30.1
Groin pains	6	8.2
Recurrent UTIs	3	4.1
others	7	9.8

HN was bilateral in (20.5%) 15, (43.8%) 32 in the left and in the right kidney (35.6%) 26. Regarding the BMI of our patients, 63% were healthy, 11% were underweight, 20.5 % were overweight and 3% were obese. Table 2

shows a significant association between HN with a side of involvement ($p < 0.001$) and the age of the patient (0.041) but no significant association with gender and BMI.

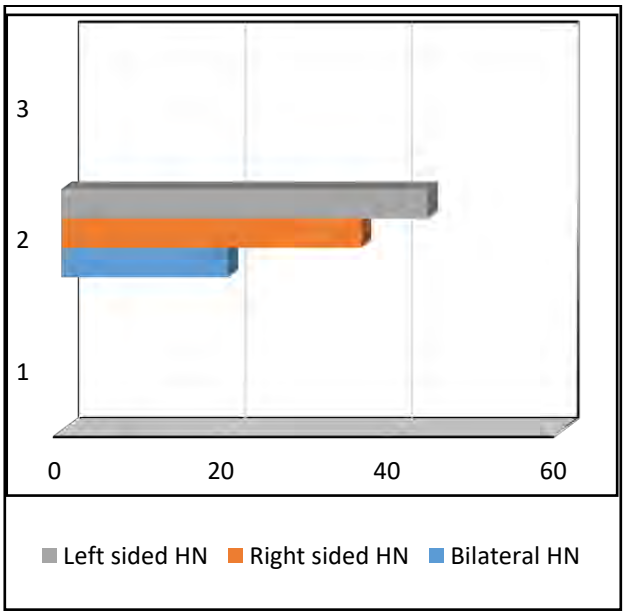

Figure 1: Kidney involvement with hydronephrosis

Table 2: Association of HN with a side of involvement, gender, and BMI

Values	Category	Number	%age	p -value
Gender	Male Female	50 23	67.6 31.5	0.651
Kidney	Unilateral Bilateral	58 15	79.4 20.5	0.651
Age	Child Adult	19 54	26 74	0.041
BMI	healthy Overweig ht/obese	45 19	63 23.5	0.273
Side	Right left bilateral	26 32 15	35.6 43.8 20.5	0.000

Regarding the severity of HN, the mild (Grade 2) form of Hn was the commonest 38 (52%), followed by moderate (Grade 3) HN 26 (36%) and gross (Grade 4) HN 9 (12%). We did not find any case of minimal HN (Figure 3). Renal calculi were the cause of HN in 69.9%(51) cases and pelvic ureteric junction obstruction was seen in 16.4% (12) cases, Table 4. In the case of children, PUJ obstruction and renal calculi were causing HN in an equal number of cases i.e. 6 (31.6%). Other causes are mentioned in Table 3.

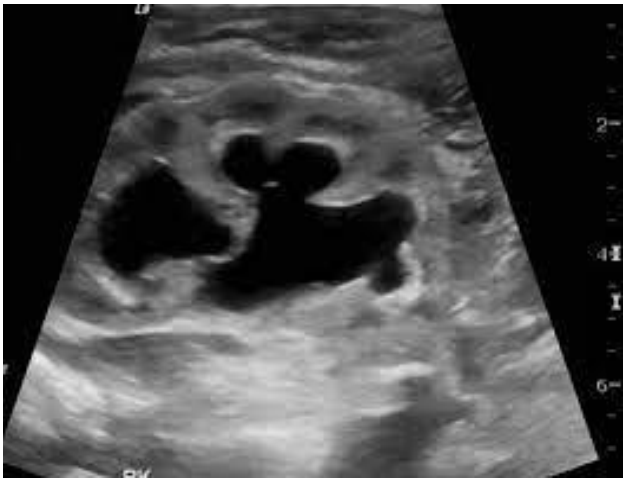

Figure 2: Ultrasound image of HN in children

Grade-1: (Minimal) Dilation of the renal pelvis.
Grade-2: (Mild) Grade-1+ dilation of major calyces.
Grade-3: (Moderate) Grade-2+ dilation of all calyces.
Grade-4: (Gross) Grade-3+ thinning of renal parenchyma

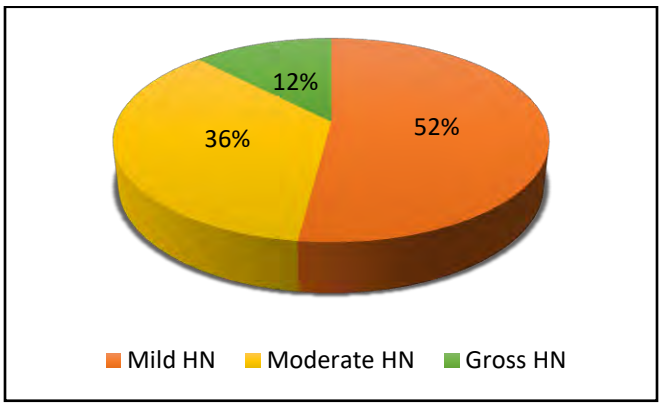

Figure 3: Percentage distribution of severity of HN

Renal Calculi were found throughout the renal tract. Calculi were found in Renal Pelvis in 21 (28.8%) cases. All parts of the ureter were found to have calculi. Lower ureter being the commonest site 18 (24.7%). Overall ureter was the site where calculi were most commonly found 26 (35.6%) Table 4.

Table 3: Causes of HN with division of age

Causes	Number /Percentage 73	N /%	
		<18 yrs. 19(26%)	>18yrs 54(74%)
Renal Calculi	51(69.9%)	6(31.5%)	45(83.3%)
PUJ obstruction	12(16.4%)	6(31.5%)	6(11.11%)
VUR	6(8.2%)	5(26.31%)	1(1.85%)
Prune belly syndrome	1(1.9%)	1(5.26%)	0
ureterocele	1(1.9%)	1(5.26%)	0
Ureteric stricture	1(1.9%)	0	1(1.85%)
Compression of the ureter by external LN	1(1.9%)	0	1(1.85%)

Table 4: Sites of Calculi causing HN

Categories	Numbers	Percentages
Renal pelvis	21	28.8
Upper ureter	5	6.8
Mid ureter	3	4.1
Lower ureter	18	24.7
Multiple sites	4	5.5
U Bladder	4	5.5

Discussion

Acute flank pain is a frequently encountered clinical scenario presenting in any emergency care facility. Ultrasound is the first diagnostic modality for instant and precise diagnosis in these cases. Incorporating renal ultrasound in emergency health care setups, can quicken the case management and shorten the hospital stay. As per our analysis, males (67.6%) were found to have HN more than females (31.5%). Akash et al report similar findings, female patients with 30% of and 70% of males with HN.[9] Sultan et al also have similar observations .[2]In contrast It is observed in certain studies that females are more likely than males to develop hydronephrosis (56%) because they have a lower threshold for renal effects.[3]

Literature reports that females of age 20-60 years, experience hydronephrosis more frequently. This is due to pregnancy or other gynecological problems.[10] In our cohort we did not have any females with pregnancy or gynecological malignancy. The pediatric age group was 26% while adults were 74% in our study. HN has a significant association with the age of the patient (p=0.041). Limited studies are comparing the effect of age on the incidence of HN.

In our cohort we had 23.5% obese /overweight patients having HN, which is a documented risk factor for renal calculi.[11] Others have reported even a higher figure in the adult population.[12] Obesity is linked with several risk characteristics contributing to the frequent occurrence of renal calculi. It is described in the literature that high body weight for age is related to low urinary pH and escalated excretion of uric acid, oxalate, and phosphate via the kidneys.[13,14]

It is crucial to point out and control the risk factors for the development of renal calculi because nephrolithiasis along with hydronephrosis increases the risk of acute kidney injury in patients having urinary tract infections (p=0.025).[15] Hydronephrosis can present with various symptoms. Pain was the most common presenting symptom in our cohort of patients. Similar to Marium et al in the adult population .[3]Others have observed hematuria and recurrent UTIs as one of the leading symptoms, in addition to pain.[5,16] Although in some cases it is completely asymptomatic without any significant complaints.[2] The severity of the presenting symptoms depends on the grade of HN and the underlying cause.

According to our results, Unilateral HN (79.4%) is commoner than bilateral HN (20.5%). We found left-sided HN to be more common than right-sided one. (43.8% Vs 35.6%. Similar findings are shared by Musab et al. They found left-sided HN in 42/71 cases.[17] Common occurrences of right-sided HN are also reported in the literature.[2] In the current study, mild and moderate HN were most commonly seen (Figure 3). Stephanie et al also have reported similar findings.[18] others also report similar findings HN 48.5% and 16.2%.[19] Gross HN was seen in 12% of our cohort and 4% is reported in the literature.[20]

Renal Calculi were the commonest cause of HN in adults (83.3%) as well as children (31.5%) Table 4. Renal calculi cause HN irrespective of its location. Literature supports our findings (Renal calculi p=0.0001) .[16]Ureteral stones (35.6%) are the commonest site of renal calculi observed as per our results followed by renal calculi

(28.8%) Table 5. Others have found the renal pelvis as the commonest site of calculi in adults.[16] There are scenarios where renal calculi do not cause HN at all. According to researchers, 11% of ureteric stones present without hydronephrosis, and 71% exhibit only mild hydronephrosis.[19]

In contrast to our results, Shafique et al report only 4.9% renal calculi in the pediatric population, in their study.[21] This difference might be due to our small sample size. In our cohort of children, PUJ obstruction along with renal calculi, (31.5% each) was found to be the most frequent determinant of hydronephrosis. PUJ obstruction can both be congenital and acquired in the pediatric age group. Without intervention, it can lead to irreversible renal damage. Rehman et al report 40.1% of cases of HN in children due to PUJ obstruction.[22] Regarding renal calculi, Literature reports renal calculi (69.1%) as the most common cause of acquired HN in children.[21]

Our study has certain limitations. First, it was a single-center study with a relatively small sample size. Secondly, we did not have a record of medical history so the data regarding underlying chronic medical conditions was lacking which could have given valuable information regarding the etiology of renal calculi. Third, we cannot comment on neonatal causes of HN as neonates were excluded from the study. Fourth, follow-up of the study participants was not done regarding the record of any further urographic studies performed. Furthermore, the sensitivity and specificity of ultrasound could not be calculated due to the limited availability of CT scan KUB in our center. Further research with a larger sample size, more elaborate medical history, and post-procedure follow-up of patients can give better results.

Conclusion

Ultrasound imaging is helpful in the diagnosis, determination of etiology, and grading of hydronephrosis. Ureteric calculi are the most frequent cause of hydronephrosis followed by pelvic ureteric junction obstruction. Ultrasound should routinely be used as a screening tool followed by other diagnostics, for patients with suspected HN.

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ORIGINAL ARTICLE

Prevalence of antibiotic resistance in patients with urinary tract infections

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A B S T R A C T

Introduction: Antibiotic resistance is a significant threat to the effective treatment of urinary tract infections (UTIs). The frequency of antibiotic-resistant UTIs is becoming increasingly concerning due to the possible consequences for patient health and healthcare expenses.

Methodology: A retrospective research at DHQ Hospital Mirpur AJK examined 225 patients with febrile UTIs from Dec 2023 to Feb 2024. Urine samples were collected and antibiotic testing were performed in accordance with Clinical and Laboratory Standards Institute standards.

Results: The study revealed alarming antibiotic resistance rates in urine isolates. Klebsiella spp. showed high resistance to Ceftriaxone (54%), Colistin (57%), and Cefuroxime (86%). Staphylococcus aureus exhibited significant resistance to Erythromycin (64%) and Doxycycline (81%). Escherichia coli displayed resistance to Ceftriaxone (23%) and Amoxicillin (25%). Notably, all species were susceptible to Vancomycin, with no observed resistance.

Conclusion: This study demonstrates significant antibiotic resistance among bacterial species that cause urinary tract infections (UTIs), with Klebsiella pneumoniae showing the highest resistance rates. Effective antibiotic stewardship are urgently required to address this issue and enhance UTI care.

Keywords: *Antibiotic resistance, Urinary tract infection, Antimicrobials, Klebsiella pneumoniae, Antibiotic Stewardship.*

Introduction

The discovery of antibiotics is among the biggest discoveries made by humanity in the 20th century. The antibacterial revolution revolutionized modern biomedicine and continues to define, shape, and expand its possibilities as well as limitations. Unfortunately, any medicinal agent's potential for resistance to develop restricts its efficacy.[1] Antimicrobial drugs that have been used to combat infections date back to ancient civilizations when natural extracts with therapeutic powers were used. Even before the name "antibiotics" was created, plant and mold extracts showed antibacterial activity.[2] American microbiologist Selman Waksman and his team's pioneering work resulted in the creation of the name "antibiotics." They successfully identified chemical compounds from bacteria that might prevent the development of other germs.[3]

However, Alexander Fleming's inadvertent discovery of penicillin in 1928 marked the beginning of modern antibiotic therapy. This discovery bridged the gap between ancient knowledge, like the Egyptians' use of moldy bread to cure ailments, and the age of antibiotics.[4] The post-World War

II period, known as the "golden era" of antibiotic development, saw the discovery of various antibiotic classes that are still in use today.[3] Antimicrobial resistance is posing an increasingly serious threat to global healthcare. This is resulting in increased patient care costs, longer hospital stays, and higher mortality rates. Almost all common infections observed in clinical practice have demonstrated significant resistance to traditional antibiotic therapy. Many organisms are multidrug-resistant.[5]

Urinary tract infections (UTIs) are one of the most prevalent infectious disorders affecting people, and the second leading cause of antibiotic prescriptions, trailing only respiratory tract infections.[6] Urinary tract infections (UTIs) are common infectious diseases that affect around 150 million people each year. They can harm the urethra, bladder, or kidneys, causing serious morbidity and significant medical costs. Recurrent UTIs cost over $5 billion in the United States alone each year.[7] UTIs can occasionally cause serious complications such as pyelonephritis, sepsis, and kidney abscesses.

UTI can lead to serious mortality and morbidity, especially in immunocompromised individuals and those who are older. If drug-resistant bacteria are present, any urinary infection in otherwise healthy people can have disastrous results. Women have a higher risk of UTIs than men. Male urinary infections, on the other hand, are typically problematic and require further treatment.[8] Each year, approximately 20% of women aged 20 to 56 years suffer from a urinary tract infection (UTI), and 40-50% will have at least one UTI in their lifetime. One out of every four patients who were affected had a recurrence, with 27% having one within 6 to 12 months. [9]

Uropathogenic Escherichia coli (UPEC) is the primary cause of both mild and complex urinary tract infections (UTIs). Klebsiella pneumoniae, Staphylococcus saprophyticus, Enterococcus faecalis, Group B Streptococcus (GBS), Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, and Candida spp. are other prevalent bacteria in mild UTIs. The most prevalent causes of complex UTIs include Enterococcus spp., Klebsiella pneumoniae, Candida spp., Staphylococcus aureus, Proteus mirabilis, Pseudomonas aeruginosa, and Group B Streptococcus (GBS).[10] Bacterial AMR is expected to directly cause 1.27 million deaths worldwide in 2019 and contribute to 4.95 million deaths.[9]

According to the analysis, AMR killed more people in 2019 than HIV or malaria combined, making it the leading cause of death globally. In 2021, the World Health Organization (WHO) identified AMR as one of the top 10 global public health threats to humanity.[9] A study found that data from the Global Burden of Disease Study 2019 were used to investigate the incidence, mortality, and Disability-Adjusted Life Years (DALYs) of UTIs in 204 countries and territories between 1990 and 2019. In 2019, there were estimated to be 404.61 million UTI infections worldwide, resulting in 236,790 deaths and 520,200 DALYs.[11]

The rationale for this study is the growing concern about antibiotic resistance in urinary tract infections (UTIs). UTIs are common infections that, if not addressed, can lead to major health consequences. Antibiotic-resistant bacteria have arisen and are spreading, making effective UTI treatment challenging. Understanding the prevalence of antibiotic resistance in different bacterial species in UTIs is crucial for developing personalized treatment plans and improving patient outcomes. This study aims to contribute to current knowledge by studying UTI patients' resistance patterns and demographic characteristics, consequently providing important insights for therapeutic decision-making and antibiotic resistance treatment in UTI.

Methodology

A retrospective research was carried out at DHQ Hospital Mirpur AJK to look at patients suffering from urinary tract infections. Between Dec 2023 and Feb 2024, the research planned to assess samples taken from both inpatients and outpatients with febrile UTIs. Permission was granted through ERB under Ref # 16/Academic Block/Trauma Center/ Surgery 2023. The study included 225 febrile UTI patients. A febrile UTI was defined as a temperature of 38°C or higher, at least 5 white blood cells visible under a high-power microscope, and at least 105 colony-forming units (CFU)/mL in urine culture. Urine samples were collected using techniques appropriate for the patient's age. For toilet-trained children, the midstream technique was employed to guarantee adequate hygiene prior to collecting the urine specimen.

Urine samples were collected in a sterile bag from children who had not been taught to use the restroom. The samples were labeled with unique patient IDs and stored correctly for future testing. The Clinical and Laboratory Standards Institute guidelines were followed while identifying microorganisms and testing for antibiotic resistance. To determine bacterial growth, urine samples were plated on sheep blood agar and MacConkey agar plates. Urine samples with more than 105 CFU/mL were found to have a urinary tract infection. The interpretation criteria for determining antibiotic resistance were determined according to the breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[12] Bacterial identification was performed on isolates from positive urine cultures to determine which uropathogens were present. The discovered isolates were also tested for antibiotic susceptibility.

This involved subjecting the isolates to a variety of medicines to determine their response and resistance patterns. The data was collected and then imported into IBM SPSS Statistics (version 23) for further analysis. Descriptive statistics were generated using SPSS, and the results were presented as tables and figures. To establish antimicrobial resistance trends, the number of resistant isolates was divided by the total number of isolates tested. The susceptibility of these uropathogens to different antibiotics was expressed as a percentage. We reviewed the data for quality and completeness during the collection process, as well as at the end and after entering the data into SPSS for statistical analysis. The hospital's Ethical Committee examined and approved the research protocol, ensuring that the study was carried out ethically. The committee thoroughly assessed the method to safeguard the participants' rights and safety. The study followed the committee's ethical rules and recommendations.

Results

A retrospective study was conducted at DHQ Hospital Mirpur AJK to investigate the prevalence of antibiotic resistance in patients with urinary tract infections (UTIs). The study included 225 febrile UTI patients with a diverse demographic profile. In terms of age distribution, the study found that 25% of UTI patients were under the age of 18, indicating a high occurrence of pediatric cases. The majority of instances (38%) were reported by those aged 18 to 40, with 22% in the 41-60 age range and 15% over 60. These findings highlight people's susceptibility to UTIs across age groups, as well as the importance of personalized treatment regimens.

In terms of gender, the survey discovered that 26% of UTI patients were male and 74% were female. This gender disparity emphasizes females' higher susceptibility to UTIs, which can be attributed to anatomical and hormonal differences. The study also included residency, which found that 30% of UTI infections occurred in rural areas and 70% in urban settings. The difference in UTI prevalence between rural and urban areas could be related to changes in healthcare availability, hygiene behaviors, or environmental factors.

Table 1: Sociodemographic and Clinical Characteristics of the Patients

Characteristics	Frequency	Percentages
Age		
< 18 years	57	25%
18-40 years	86	38%
41-60 years	48	22%
> 60years	34	15%
Sex		
Male	59	26%
Female	166	74%
Residence		
Rural	68	30%
Urban	157	70%
Clinical Feature		
Fever	178	79%
Dysuria	201	89.3%
Urgency	167	74.2%
Abdominal Pain	144	64%

The study further evaluated the clinical aspects of UTIs in individuals. Fever was the most common symptom, showing up in 79% of cases. Dysuria (painful urination) was reported by 89.3% of the patients, demonstrating that it is common in UTIs. 74.2% of cases reported urgency, which is defined as a strong desire to urinate. Sixty-four percent of the patients reported abdominal pain, indicating that the infection had spread to the kidneys or bladder. These thorough findings shed light on the distinct

characteristics and demographics of UTI patients, potentially informing targeted prevention, diagnosis, and treatment strategies.

Understanding the prevalence of antibiotic resistance in these populations is crucial for developing effective therapeutics and addressing the growing problem of antimicrobial resistance in UTIs (Table 1). Out of 225, a total of 141 cases of bacterial infections were identified in the study. Klebsiella pneumoniae was the most common of the bacteria detected, accounting for 32 cases (22.6%). Enterococcus faecalis was next with 14 (10%) instances, followed by Proteus mirabilis with 10 (7%). Escherichia coli was found in 37 cases (26.2%), Pseudomonas aeruginosa in 13 cases (9.2%), Staphylococcus aureus in 24 cases (17%), and Serratia marcescens in 11 (8%) cases. These findings provide significant information about the spread of bacterial illnesses in the research population (Figure 1).

The study's findings elucidate the levels of antibiotic resistance in several bacterial species isolated from urine samples. Notably, Klebsiella spp. exhibited the highest resistance to Ceftriaxone (54%), underscoring the challenges in treating infections caused by this bacterial species. Escherichia coli showed a lower but still significant resistance rate of 23%, whereas Serratia and Proteus spp. showed resistance rates of 12% and 7%, respectively. Pseudomonas aeruginosa had the lowest resistance rate (4%). Moving on to Ciprofloxacin, Klebsiella spp. exhibited a 34% resistance rate, Staphylococcus aureus 25%, and Escherichia coli 14%. Enterococcus spp. and Serratia spp. showed lower resistance rates of 9% and 7%, respectively, while Proteus spp. and Pseudomonas aeruginosa had even lower rates of 5% and 6%.

Klebsiella spp. showed 50% resistance to Cefalaxin, while Staphylococcus aureus showed 25% resistance. Enterococcus spp. showed a 9% resistance rate, demonstrating the wide range of resistance among bacterial species. Klebsiella spp. were 57% resistant to Colistin, whilst Staphylococcus aureus was only 43% resistant. Klebsiella spp. showed an 86% resistance rate to Cefuroxime, while Escherichia coli had a lower but still substantial resistance rate of 14%. Klebsiella spp. had a 45% ampicillin resistance rate, while Enterococcus spp. had 17%. E. coli showed a 25% resistance rate, while Proteus and Serratia spp. showed 5% and 5% resistance rates, respectively. The incidence of Amoxicillin resistance in Klebsiella spp. was 53%.

Proteus species showed a 3% resistance rate, whereas E. Coli showed a 32% resistance rate among other species. Pseudomonas aeruginosa and Serratia spp. had resistance rates of 5% and 7%, respectively. Compared to Enterococcus spp., which had a resistance rate of 36% to erythromycin, Staphylococcus aureus had a high resistance rate of 64%. Moving on to cefoxitin, 29% of Klebsiella spp. showed resistance, whilst 24% of Escherichia coli showed a minor increase in resistance. With a resistance rate of 47%, Staphylococcus aureus was the highest of the three species. While Escherichia coli only showed a 24% resistance rate to Gentamycin, Klebsiella spp. showed a significant 66% resistance rate.

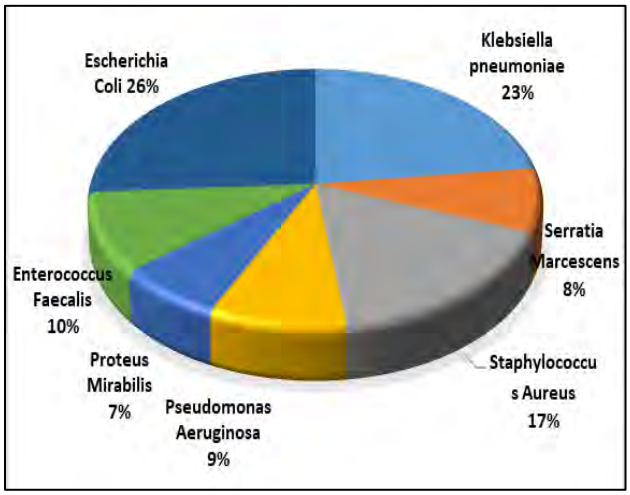

Figure 1: Distribution of significant uropathogenic microorganisms among patients with urinary tract infection.

A 10% resistance rate was found in Pseudomonas aeruginosa. Levofloxacin resistance was observed in 36% of Klebsiella spp. and 25% in Staphylococcus aureus. Lower resistance rates of 16% and 11% were observed in Escherichia coli and Enterococcus spp. The lowest resistance rate, 5%, was seen in Proteus species. According to the data, 53% and 51% of Klebsiella spp. were resistant to imipenem and meropenem. A study found that 28% of Escherichia coli were resistant to Meropenem and 19% to Imipenem. Meropenem (13%) and imipenem (5%), to which Proteus spp. exhibited decreased resistance rates. Resistance rates for Imipenem were 10%, and those for Meropenem were 15% and 6% for

Pseudomonas aeruginosa and Serratia spp. The percentage of Klebsiella spp. that were resistant to cefepime and linezolid was 59% and 60%, respectively. Staphylococcus aureus strains that were resistant to linezolid accounted for 40% of the total. With a resistance rate of 2%, Proteus species had the lowest rate of Cefepime. In contrast to Pseudomonas aeruginosa, Escherichia coli shown a 22% resistance rate to Cefepime. Cefepime resistance in Serratia spp. was 10%. The results also showed that some bacterial species were resistant to fosfomycin and nalidexic acid. 56% of Klebsiella spp., 33% of Escherichia coli, and 11% of Pseudomonas aeruginosa showed resistance to nalidexic acid. 50% of Staphylococcus aureus and Enterococcus spp. were resistant to fosfomycin. Moreover, Novobiocin proved to be 100% resistant to Staphylococcus aureus. The majority of bacteria, specifically Klebsiella spp., were resistant to Rifampicin (50%) more than Escherichia coli (30%) and Enterococcus spp. (20%). Proteus species displayed 8% resistance to sulfamethoxazole, Escherichia coli showed 18%, Staphylococcus aureus displayed 26%, and Serratia species displayed 3% resistance.

Klebsiella species demonstrated 45% resistance to sulfamethoxazole. It's interesting to note that none of the bacterial species under investigation—Klebsiella spp., Enterococcus spp., Proteus spp., Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Serratia spp.—exhibited resistance to vancomycin. Staphylococcus aureus showed a higher proportion of resistance to Doxycycline (81%), compared to 19% for Enterococcus spp. It was discovered that 44% of Staphylococcus aureus and 56% of Klebsiella spp. were resistant to tigecycline. Penicillin G resistance in Enterococcus spp. was 25%, but Staphylococcus aureus showed 75% resistance. Lastly, Staphylococcus aureus exhibited 76% resistance to clindamycin, compared to 24% resistance in Escherichia coli. The data analysis reveals Amikacin resistance rates in various bacterial species. Klebsiella spp. revealed a 42% resistance rate, whilst Proteus spp. showed an 8% resistance rate. Escherichia coli exhibited 21% resistance, Pseudomonas aeruginosa 8%, and Staphylococcus aureus 21%. The data demonstrate that none of the bacterial species identified were resistant to Polymycin B. Polymycin B was found to be effective against Klebsiella spp., Enterococcus spp., Proteus spp., Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Serratia spp.

The resistance rates to nitrofurantoin were 37% for Klebsiella spp., 4% for Proteus spp., 38% for Escherichia coli, and 21% for Staphylococcus aureus. In terms of Tetracycline resistance, Klebsiella spp. exhibited a 36% rate, Enterococcus spp. showed a 5% rate, Proteus spp. showed a 5% rate, Escherichia coli showed a 17% rate, and Staphylococcus aureus showed a 36% rate. Finally, in the instance of Tazobactam, Klebsiella spp. showed the highest resistance rate (73%), indicating a significant challenge in treating these infections. Proteus spp. showed a resistance rate of 9%, whereas Escherichia coli showed a resistance rate of 14%. Pseudomonas aeruginosa has a relatively low resistance rate of 4%.

The study reveals significant clinical implications regarding antibiotic resistance. High resistance rates in Klebsiella spp., particularly to Ceftriaxone, pose a challenge in treating infections caused by this bacterial species. This suggests the need for alternative antibiotics and targeted treatment strategies to combat infections caused by multidrug-resistant Klebsiella spp. In clinical practice, this may involve adjusting treatment protocols and implementing surveillance and infection control measures. The resistance rates in Escherichia coli, a common cause of urinary tract infections, suggest the need for judicious use of antibiotics. Intermediate resistance rates suggest that antibiotic treatment options for Escherichia coli infections may be effective but require careful consideration.

This highlights the importance of antimicrobial stewardship programs and appropriate prescribing practices to avoid further selection of resistant strains. Lower resistance rates in Serratia and Proteus spp. may provide more treatment options for infections caused by these bacteria. The study also highlights the importance of understanding local resistance patterns to tailor empirical therapy and ensure optimal treatment outcomes. Lastly, the absence of resistance to certain antibiotics, such as vancomycin, among the studied bacterial species is promising. These antibiotics can serve as important treatment options for infections caused by these organisms and provide valuable alternatives when other antibiotics are ineffective due to resistance.

The findings of this study demonstrate the varying levels of antibiotic resistance among different bacterial species. Certain pathogens, such as Klebsiella spp. and Staphylococcus aureus, are demonstrably resistant to a variety of medications, emphasizing the need for alternative treatment options and good antimicrobial stewardship programs. These findings emphasize the need to monitor antibiotic resistance trends to make sound treatment decisions and combat emergence of resistant bacterial strains. Additional research and surveillance are needed to develop effective approaches for minimizing and managing antibiotic resistance (Table 2).

Table 2: Antibiotic resistance pattern of different organisms isolated from the urine specimen of the patients

Antibiotic	*Klebsiella spp.*	*Enterococcus spp.*	*Proteus spp.*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Serratia spp.*
Ciprofloxacin	29 (34%)	8 (9%)	4 (5%)	12 (14%)	5 (6%)	22 (25%)	6 (7%)
Ceftriaxone	31 (54%)	NA	4 (7%)	13 (23%)	2 (3%)	NA	7 (12%)
Cefalaxin	16 (50%)	3 (9%)	2 (6%)	3 (9%)	NA	8 (25%)	NA
Colistin	4 (57%)	NA	NA	NA	NA	3 (43%)	NA
Cefuroxime	12 (86%)	NA	NA	2 (14%)	NA	NA	NA
Ampicilin	27 (45%)	10 (17%)	3 (5%)	15 (25%)	2 (3%)	NA	3 (5%)
Amoxicillin	31 (52.5%)	NA	2 (3%)	19 (32%)	3 (5%)	NA	4 (7%)
Erythromycin	NA	4 (36%)	NA	NA	NA	7 (64%)	NA
Cefoxitin	11 (29%)	NA	NA	9 (24%)	NA	18 (47%)	NA
Gentamycin	19 (65.5%)	NA	NA	7 (24%)	3 (10.5%)	NA	NA
Levofloxacin	29 (36%)	9 (11%)	4 (5%)	13 (16%)	1 (1%)	20 (25%)	5 (6%)
Meropenem	17 (53%)	NA	4 (13%)	9 (28%)	2 (6%)	NA	NA
Imipenem	21 (51%)	NA	2 (5%)	8 (19%)	4 (10%)	NA	6 (15%)
Linezolid	6 (60%)	NA	NA	NA	NA	4 (40%)	NA
Cefepime	24 (58%)	NA	1 (2%)	9 (22%)	3 (7%)	NA	4 (10%)
Nalidexic Acid	5 (56%)	NA	NA	3 (33%)	1 (11%)	NA	NA
Fosfomycin	NA	2 (50%)	NA	NA	NA	2 (50%)	NA
Rifampicin	NA	2 (20%)	NA	3 (30%)	NA	5 (50%)	NA
Sulfamethoxazole	28 (45%)	NA	5 (8%)	11 (18%)	NA	16 (26%)	2 (3%)
Tetracycline	20 (36%)	3 (5%)	3 (5%)	9 (17%)	NA	20 (36%)	NA
Vancomycin	NA	NA	NA	NA	NA	NA	NA
Doxycycline	NA	5 (19%)	NA	NA	NA	21 (81%)	NA
Tigecycline	5 (56%)	NA	NA	NA	NA	4 (44%)	NA
Penicillin G	NA	4 (25%)	NA	NA	NA	12 (75%)	NA
Amikacin	10 (42%)	NA	2 (8%)	5 (21%)	2 (8%)	5 (21%)	NA
Polymycin B	NA	NA	NA	NA	NA	NA	NA
Clindamycin	NA	NA	NA	4 (24%)	NA	13 (46%)	NA
Nitrofurantoin	9 (37%)	NA	1 (4%)	9 (38%)	NA	5 (21%)	NA
Novobiocin	NA	NA	NA	NA	NA	3 (100%)	NA
Tazobactum	16 (73%)	NA	2 (9%)	3 (14%)	1 (4%)	NA	NA

Discussion

Drug-resistant infections develop when organisms adapt in ways that render antimicrobial therapies ineffective. As a result, infections survive and spread. When infections are treatable with antimicrobials, people can be treated, and future transmission in the community is readily managed. This has saved hundreds of millions of lives since the widespread usage of these "miracle drugs" over 70 years ago. Antimicrobial resistance (AMR) is reducing treatment efficacy in both developing and industrialized nations. If this trend continues, the world will confront a situation in which numerous infectious diseases have "no cure and no vaccine".[12,13]

Hospital-acquired urinary tract infections (UTIs) are a major concern in healthcare settings because they are linked to drug resistance. Urinary tract infections (UTIs) account for 20-40% of all infections encountered in hospitals worldwide. Patients in the hospital with urinary system abnormalities (such as those in the urology unit) are more likely to get UTIs during their stay. It is responsible for up to 60-70% of all hospital infections.[14] Antibiotics are required for effective treatment of UTIs. Broad-spectrum antibiotics are commonly used to begin treatment. However, antibiotic abuse and widespread availability without adequate management have resulted in the worldwide establishment of antibiotic resistance among common bacteria associated with UTIs.[15] This study's findings provide a thorough assessment of antibiotic resistance trends in different bacterial species isolated from urine samples. The high levels of resistance to numerous antibiotics found in Klebsiella spp. and Staphylococcus aureus serve as a stark reminder of the difficulties in treating infections caused by these bacteria. These findings not only support but also reflect previous study findings, which have shown a steady increase in resistance among these specific bacterial species throughout time.[16, 17]

Klebsiella spp. were extremely resistant to several antibiotics, including Ceftriaxone, Ciprofloxacin, and Cefalaxin. This resistance trend is consistent with previous research, which has consistently reported higher resistance levels in Klebsiella spp. This disturbing development underscores the difficulties and problems that healthcare providers have while treating infections caused by this particular bacterial species.[18,19] Staphylococcus aureus also demonstrated significant drug resistance, including Ciprofloxacin, Cefalaxin, and Erythromycin. These findings are consistent with previous research that has demonstrated greater rates of resistance in Staphylococcus aureus, indicating a challenging terrain for treating infections caused by this bacterium. Escherichia coli showed varying resistance rates to various antibiotics, with some having very low resistance levels and others, such as Cefuroxime and Amoxicillin, having substantially higher resistance.

These findings are consistent with earlier research exposing the varied resistance rates observed in Escherichia coli, emphasizing the challenges of managing antibiotic resistance in this bacterial species.[20, 21] Compare the resistance rates of Proteus spp. to those of Klebsiella spp. and Staphylococcus aureus, and we noticed that the overall resistance is lower. However, despite lower overall resistance rates, Proteus spp. still shown considerable resistance to certain antibiotics such as Amikacin. This holistic perspective sheds light on the patterns in antibiotic resistance among many bacterial species.[22, 23] The overall reduced resistance rates observed in Pseudomonas aeruginosa are consistent with findings from earlier investigations. Despite this overall trend, certain medications, such as Ciprofloxacin, nevertheless showed significant resistance rates, emphasizing the significance of understanding Pseudomonas aeruginosa's resistance profiles to properly advise treatment options.[24, 25] Serratia spp. and Enterococcus spp. have varying resistance rates to various antibiotics, showing the complex and diverse landscape of antibiotic resistance patterns among these bacteria.

This variability underscores the significance of tailored and targeted treatment strategies that account for the various resistance profiles of Serratia spp. and Enterococcus spp. to improve therapeutic outcomes.[25, 26] The lack of resistance to Vancomycin and Polymycin B is remarkable, as these antibiotics are routinely used as last-resort treatments for multidrug-resistant infections. However, resistance to specific antibiotics has been found in some cases, emphasizing the significance of ongoing observation. According to this study, Vancomycin may still be an effective treatment for certain bacteria-related

disorders. However, the presence of Vancomycin-resistant bacteria in other studies emphasizes the importance of continued monitoring.

It should be emphasized that the data presented in this study are based on specific bacterial species isolated from urine specimens and may not include the entire range of resistance patterns. Additionally, resistance rates may vary geographically and over time, underscoring the importance of constant monitoring and surveillance. Overall, this study found frightening levels of resistance to commonly used antibiotics in several bacterial species.

Healthcare settings are a major source of antibiotic-resistant bacteria, with factors like multidrug-resistant organisms, invasive procedures, and exposure to antibiotics contributing to resistance. To prevent the spread of antibiotic-resistant UTIs, robust infection control measures, such as hand hygiene protocols and surveillance, are crucial. Antimicrobial stewardship programs promote the appropriate use of antibiotics, optimize treatment guidelines, and improve patient outcomes. Infection control measures include standard precautions, isolation strategies, and active surveillance. Public awareness about antibiotic use, its dangers, and the importance of completing prescribed treatment courses is also crucial.

Research into novel treatment approaches and antimicrobial agents is vital for addressing antibiotic-resistant UTIs. Factors such as antibiotic misuse, patient demographics, and healthcare settings influence antibiotic resistance patterns. A multifaceted approach, including antimicrobial stewardship programs, infection control measures, public awareness campaigns, and ongoing research and development efforts, can mitigate the impact of antibiotic resistance and preserve effective treatment options.

Conclusion

In coclusion, this study illustrates the diverse levels of resistance shown by different bacterial species to several antibiotics commonly used to treat urinary tract infections. Klebsiella spp. consistently showed the highest resistance rates across multiple drugs, emphasizing the crucial need for effective strategies in managing infections caused by these multidrug-resistant organisms. The findings further emphasize the importance of judicious antibiotic selection and ongoing surveillance in the treatment of infections caused by Escherichia coli and Staphylococcus aureus, which have significant resistance rates.

These findings highlight the need for antimicrobial stewardship programs, infection control measures, and continuous research in combating the global problem of antibiotic resistance. A multimodal strategy can help improve patient outcomes, keep existing therapies effective, and lead the development of new antibiotic-resistant bacterial infection treatments.

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ORIGINAL ARTICLE

A cross-sectional study to explore depression in postmenopausal women

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[1] Study concept, design, data interpretation, manuscript writing
[2] Data analysis
[3] Critical revision
[4] Drafting of article
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A B S T R A C T

Introduction: The impact of depression on postmenopausal women is a significant public health concern but remains largely unknown. Menopause signifies the cessation of a woman's reproductive ability, indicating the halt of ovarian activity and leading to permanent amenorrhea. This organic change is associated with various symptoms including physical, vasomotor, sexual, and psychological elements. This cross-sectional survey was conducted to investigate the severity of depression in postmenopausal women and the factors that influence that depression.

Methodology: This study examined 240 women from the Gynae department of DHQ Hospital Mirpur, AJK, Pakistan. Data on menopausal symptoms and demographic traits was collected via structured interviews and Menopausal Rating Scale (MRS) questionnaires.

Results: The study revealed that 57% of participants experienced physiological symptoms such as hot flashes, sweating, heart discomfort, insomnia, and sleep problems. Psychologically, 39% experienced depressive mood, irritability, anxiety, and exhaustion. Urogenital, 60% experienced sexual problems, bladder issues, and vagina dryness. The severity of symptoms varied, with 5% reporting no symptoms, 77% reporting mild to moderate symptoms, and 18% reporting severe to extremely severe symptoms.

Conclusion: The study reveals that postmenopausal women often experience mild to moderate depression symptoms, emphasizing the need for personalized support and interventions to enhance their overall well-being.

Keywords: *Menopause, Depression, Anxiety, Menopausal Rating Scale, Menopausal symptoms.*

Introduction

Depression and anxiety are two key types of mental illnesses that have become substantial public health concerns around the world. Women were more likely than men to suffer from depressive and anxiety disorders after menarche, and women may be at an increased risk of depression and anxiety throughout times of hormonal swings such as puberty, pregnancy and postpartum, and the perimenopause stage.[1] Every woman has had a significant experience with her quality of life after menopause. During menopause, a woman's life expectancy increases by around one-third.[2] Menopause is defined by the occurrence of a 12-month amenorrhea, and post-menopause is the period that follows the final menstrual cycle. According to the Stages of Reproductive Aging Workshop +10 (STRAW) guidelines, this phase is separated into two stages based on hormonal levels: early and late post-menopause.[3] According to studies, depressive symptoms increase dramatically in the early

stages of menopause as compared to pre-menopause. Factors driving this rise include age at menopause, vasomotor symptoms, socioeconomic status, obesity, and a history of depression. While the prevalence of sadness during perimenopause is widely recognized, research on postmenopausal depression is limited.[4, 5]

Menopausal symptoms such as hot flashes, night sweats, cognitive fog, and sleep problems differ in strength and duration. Effective management entails tailored measures such as seeking medical advice, adopting good lifestyle choices, and investigating treatment options, which improve women's well-being throughout this transitional stage.[6-8] According to the Fawcett Society's 2022 research, over 77% of women in the UK have at least one menopausal symptom throughout the transition. The most common of these symptoms were heat flashes. Furthermore, the survey revealed that 44% of women going through menopause reported experiencing three or more severe symptoms.[8] According to research, menopausal symptoms cost the world $150 billion in diminished work productivity each year, affecting one in every three women. This emphasizes the need for increased awareness, support, and workplace adjustments in improving women's well-being and contributing to a more inclusive workforce.[9]

Women with severe menopausal symptoms usually exhibit more presenteeism and report greater difficulty at work than those without similar symptoms.[9] Previous research has shown that the prevalence and severity of vasomotor (VMS) and sexual menopausal symptoms are highly related to the stage of menopause. VMS symptoms appear to grow in prevalence and frequency as menopause approaches, with a peak in the late perimenopausal and postmenopausal years.[10] This could be attributed to hormonal changes or biological aging since a recent study discovered a link between age and the intensity of vasomotor and sexual symptoms. Reduced oestradiol levels and increased follicle-stimulating hormone (FSH), two commonly used menopausal markers, have been associated with an increase in the prevalence and severity of vasomotor and sexual symptoms, independent of age. Hormone replacement treatment (HRT) is usually effective in treating menopausal symptoms in the vasomotor and sexual domains reported by postmenopausal women. Recently, the literature has mostly emphasized the variations in vasomotor and sexual symptoms between menopausal stages; nevertheless, there is an increasing emphasis on psychological problems associated with the menopausal transition.[11, 12]

Over half of British women feel anxiety and sadness throughout the menopausal transition, and the link between these symptoms and menopausal phases is unclear. Some believe these symptoms are related to midlife difficulties such as marital conflict and caregiving. Perimenopausal women had an increased incidence of psychological complaints, although it is unknown if these issues resolve following the perimenopausal period. Women who have a history of severe depressive illness are more likely to acquire MDD during menopause. Postmenopausal women experience more severe depressive symptoms, however, there is no substantial change in the prevalence of depressed mood.[13, 14]

In a 2022 poll, 69% of British women assessed anxiety as a "very" or "somewhat tough" symptom of menopause.[8] Research on the association between depression and menopause is frequently disregarded, and anxiety measurements are frequently inadequate. This study seeks to identify the stage of the menopausal transition at which women are most vulnerable, as knowing and accepting these concerns may be useful. It also assesses psychological complaints, perceived stress, resilience, and self-efficacy, which are all linked to protective psychosocial characteristics.[15-18] The purpose of the study is to ascertain the degree to which women's menopausal quality of life is impacted by memory loss, emotions of hopelessness, and anxiety, as well as the relationship between resilience, self-efficacy, and low perceived stress.

Methodology

The study used a cross-sectional approach to evaluate postmenopausal depression and its risk variables. It was conducted at DHQ Hospital Mirpur AJK, where a large number of patients seek treatment for gynecological diseases daily. Participants in the study were drawn from a pool of people seeking medical care at DHQ Hospital Mirpur AJK using a traditional sampling approach. This strategy yields a representative sample of the population under study. The study included 45-60-year-old hospital

visitors. Participants have to be able to speak effectively in Urdu and demonstrate a willingness to engage in the study. The institutional review board gave the study ethical approval IRB Ref # 16. Ethical considerations included obtaining informed consent from participants, maintaining the confidentiality and privacy of participant information, ensuring voluntary participation with no repercussions, and adhering to the ethical guidelines and standards established by the study's ethical committee.

Women with major medical issues confirmed psychological diseases, a lack of Urdu communication skills, or an unwillingness to engage were all excluded. Participants were informed about the research objectives, procedures, and potential risks. Each subject provided informed consent before participating in the study. Data gathering included organized interviews in which we administered a questionnaire. The Menopausal Rating Scale (MRS) was used as part of the screening questionnaire to assess the severity of depression symptoms and other menopause-related symptoms reported by participants. The MRS, coupled with demographic data, contributed to a more complete picture of the individuals' experiences and allowed for a more thorough examination of postmenopausal depression.

The Menopausal Rating Scale (MRS) is a widely used questionnaire in studies on menopause and postmenopausal symptoms. It is a self-report tool designed to assess the intensity and impact of menopausal symptoms experienced by women. The MRS is composed of several items that assess the presence and severity of certain symptoms commonly associated with the menopause transition. Participants are asked to rank each symptom on a scale of 0 to 4, with higher ratings indicating more severe symptoms. Some versions of the MRS may also include sections to assess how menopausal symptoms affect daily life and overall well-being.[19]

The MRS questionnaire has been proven reliable and valid through previous research, demonstrating internal consistency and test-retest reliability. It accurately measures menopausal symptoms over time, with content validity due to comprehensive coverage of relevant symptom domains and construct validity due to its ability to differentiate between individuals with varying degrees of symptom severity. The questionnaire was administered through structured interviews, ensuring standardized data collection and obtaining ethical approval. Participants provided informed consent before participation. The statistical analysis was performed with IBM© SPSS© Statistics version 20.0. Descriptive statistics were used to summarize study participants' characteristics, demographic variables, and symptom severity levels.

Inferential statistics were used to explore significant differences or relationships in the data. Correlation analysis was conducted to examine associations between menopausal symptoms, including depression, and other variables. This rigorous analysis provided a comprehensive understanding of the severity of menopausal symptoms and their relationship to demographic factors.

Results

The data offered provides important insights into the participants' demographic parameters for menopause. Individuals between the ages of 46 and 50 make up the majority of participants (49%). The 41-45 age group comes in second, accounting for 13% of the participants. Notably, participants aged 35-40 years, 51-55 years, 56-60 years, and 61-65 years contributed to the study at 8%,13%, 5%, and 1%, respectively.

With regards to menopause age, the majority of respondents (59%) reported having it between the ages of 45 and 50. Other age groups were 35-40 (8%), 41-45 (15%), and 51-55 (18%). The bulk of responders (84%) reported being married. On the other hand, 16% were recorded as unmarried. When considering parity, it is clear that 81% of the participants had given birth to more than one child, making them multiparous. Conversely, 19% of respondents were classed as nulliparous, which means they had not given birth to any children. In terms of residency, the results show that 63% of participants lived in cities, with the remaining 37% in rural areas. Considering education level, 52% of participants were uneducated, while 23% had completed basic education, 6% had secondary education, 13% had a graduate degree, and 5% had a postgraduate degree.

When it comes to employment status, the data shows that the vast majority (73%) of participants are unemployed. In addition, 18% were employed, while 9%

had retired. These findings shed light on the demographic characteristics of the individuals in connection to menopause (Table 01). Variations in age groups, age at menopause, marital status, parity, domicile, education, and employment help to better understand the elements that may influence the participants' menopausal experience. Furthermore, it is vital to remember that some females underwent total abdominal hysterectomy due to fibroids and other gynecological disorders, which led to the early beginning of menopause.

Menopausal symptoms were examined in the research samples using MRS. The 11 symptoms on this scale were divided into three categories: urogenital, psychological, and physical. There was a significant difference between the three study groups, with menopausal women performing better in all domains, including urogenital, psychological, and physical.

A variety of physical and psychological impacts were observed when investigating the participants' complaints (Table 02). Starting with the physical symptoms, 57% of participants reported hot flushes and perspiration, making it one of the most common complaints. Many women associate this physiological reaction with menopause. Heart discomfort came closely behind, with 56% of respondents reporting it, which might show as palpitations or chest discomfort. Sleep disturbances were common among participants, impacting 57% of those assessed. Insomnia and interrupted sleep patterns are typical complaints during menopause, and they can have a major influence on daily functioning and quality of life.

Moving on to psychological symptoms, 39% of people reported having a depressive mood. This emotional component is critical to address because mood swings can have a substantial impact on mental health. Irritability, indicated by 46% of participants, and anxiety, affecting 53%, are additional relevant psychological symptoms to consider when determining the overall impact of menopause on mental health. Physical and mental exhaustion were prevalent, with 51% of respondents reporting this symptom. This weariness can be debilitating, interfering with everyday tasks and general quality of life. In terms of urogenital symptoms, 60% of participants reported sexual issues, emphasizing menopause's impact on sexual health.

Table 1: Demographics of the Participants

Characteristics	Frequency	Percentage
Age		
35-40 years	19	8
41-45 years	32	13
46-50 years	118	49
51-55 years	57	24
56-60 years	11	5
61-65 years	3	1
Age At Menopause		
35-40 years	19	8
41-45 years	36	15
45-50 years	142	59
51-55 years	43	18
Marital Status		
Married	202	84
Unmarried	38	16
Parity		
Nulliparous	46	19
Multiparous	194	81
Residence		
Rural	89	37
Urban	151	63
Education		
Uneducated	126	52
Primary	56	23
Secondary	15	6
Graduate	31	13
Post Graduate	12	5
Employment		
Unemployed	176	73
Employed	43	18
Retired	21	9

Bladder issues, reported by 62% of those polled, and vaginal dryness, reported by 61%, are frequent urogenital concerns that can emerge after menopause and have an impact on everyday comfort and quality of life. Joint and muscular soreness, described by 40% of respondents, is a symptom that can have physical and psychological consequences since it can impair movement and overall well-being. Through the provision of an elaborate analysis of every symptom category and the related frequency associated with it, we acquire a thorough comprehension

of the many experiences that participants have described about menopause

Table 2: Menopause Rating Scale: Symptoms experienced by the participants

Symptoms	Frequency (%)	Mean	Standard deviation
Hot flushes, sweating (p)	57%	2.7	0.931
Heart discomfort (p)	56%	2.8	0.711
Sleep problems (p)	57%	2.7	0.980
Depressive mood (psy)	39%	3.4	0.849
Irritability(psy)	46%	3.1	0.900
Anxiety(psy)	53%	2.9	0.986
Physical and mental exhaustion(psy)	51%	3.0	0.869
Sexual problems (u)	60%	2.6	0.962
Bladder problems(u)	62%	2.5	1.109
Dryness of vagina(u)	61%	2.5	0.836
Joint and muscular discomfort (p)	40%	2.5	0.743

Menopause Rating Scale (MRS) (P=Physiological, PSY=Psychological, U=Urogenital)

Using the Menopause Rating Scale to assess the severity of menopausal symptoms, the data demonstrates a range of symptom intensity experienced by individuals. Among the 240 respondents, 5% reported having no symptoms ranging between 0 and 11 on the scale, indicating a relatively low symptom burden for this group. The majority of patients (77% of the sample) had mild to moderate symptom intensity, scoring between 12 and 35 on the Menopause Rating Scale. This shows that the majority of respondents had noticeable but treatable symptoms in their daily lives, which could have a moderate influence on their quality of life.

A lower but significant proportion of participants (18%) had severe to very severe symptoms (score 36 or higher scale). This group certainly had major obstacles as a result of the severity of their menopausal symptoms, which may have had a significant influence on their overall well-being and everyday functioning (Table 3).

Table 3: Severity of menopausal symptoms experienced by the participants

Severity level	Frequency N=240 (%)
No symptom (≤11)	12 (5%)
Mild to moderate (12-35)	185 (77%)
Severe to very severe (≥36)	43 (18%)

Researchers and healthcare providers can better understand the distribution of symptom intensity among surveyed individuals by categorizing menopausal symptoms using the Menopause Rating Scale. This allows for tailored interventions and support strategies to address the diverse needs of menopausal women.

Discussion

Menopause is a significant phase of a woman's life that can have a substantial impact on her general well-being and quality of life. Understanding the frequency and severity of menopausal symptoms is critical for offering appropriate support and therapies to middle-aged women as they transition. In postmenopausal women, we aimed to ascertain the frequency and intensity of menopausal symptoms. The data showed that women suffered symptoms in a variety of categories, including somatic, psychological, and urogenital. These symptoms were reported more frequently in post-menopausal women, reflecting the difficulties they may experience during this period of life.

A majority of individuals (57%) reported hot flushes and perspiration as physical symptoms. This is consistent with a prior study on menopausal women,22 which highlighted the prevalent occurrence of vasomotor symptoms during this era. Heart discomfort, such as palpitations and chest pain, was also common among individuals (56%). Sleep problems, such as insomnia and disrupted sleep patterns, were reported by 57% of individuals. These findings highlight the difficulties that women confront when managing their physical health throughout menopause. Psychological symptoms were also prevalent in the study participants. A sizable percentage of participants reported sad mood (39%), irritation (46%), and anxiety (53%). These psychological symptoms have been widely linked to

the hormonal variations and life changes that accompany menopause.[23]

The high incidence of these symptoms emphasizes the necessity of treating mental health concerns in menopausal women and providing appropriate support and services. Urogenital problems were commonly mentioned by the individuals. 60% of the women experienced sexual issues, underscoring the importance of menopause for sexual health and well-being. 62% of the individuals reported bladder issues, such as urine frequency and incontinence. 61% of women reported vaginal dryness, which can cause discomfort and agony during sexual intercourse. Urogenital symptoms can have a substantial impact on menopausal women's quality of life and interpersonal interactions.[24]

The study evaluated women's perceptions of depression, anxiety, impaired memory, stress, resilience, and self-efficacy throughout the menopause. The findings revealed that early postmenopausal women experienced higher levels of stress and anxiety than postmenopausal women. Although age did not influence perceived anxiety or stress levels, women with poorer educational backgrounds and income reported higher levels of stress.[19] According to research, older persons have more coping resources, higher life satisfaction, and advanced emotional regulation skills, resulting in a greater sense of optimism and fewer psychological distress symptoms than younger adults.[10]

The differences between our study and previous research findings can be attributed to several factors, including socio-cultural characteristics, racial and genetic differences, individual perceptions of menopause, sample size variations, study designs, and measurement instruments. Geographic location can also have a role, as demonstrated by our study, in which a higher incidence of joint and muscle problems in one area may have contributed to higher scores on the Menopause Rating Scale questionnaire's physical domain. These characteristics demonstrate the complex and multifaceted nature of menopausal experiences, underlining the importance of considering several factors when analyzing study findings and outcomes.19 Racial disparities have an impact on menopausal symptoms' prevalence and severity, menopause's average age of onset, and menopause's duration, which leads to variations in the features of the research sample and accounts for the variations in menopausal severity. Moreover, women in different regions of the nation suffer the symptoms of menopause brought on by insufficient estrogen in different ways.[21]

One limitation of this study is that it may lack generalizability due to its geographic location and sample size. The findings may not be representative of menopausal women in other locations or cultural situations, and the small sample size of 240 individuals may limit the data' generalizability. Furthermore, the use of self-report measures, as well as the subjective nature of symptom reporting, raises the likelihood of recall bias and heterogeneity in individual interpretation. The study's cross-sectional methodology makes it difficult to establish causal links between menopausal symptoms and demographic characteristics. Lastly, the study did not go into great detail about the impact of cultural or socioeconomic factors on menopausal experiences. These limitations should be noted when interpreting the results, and they highlight the need for larger, more diverse research with longitudinal designs that include a broader variety of contextual factors.

Future studies should focus on longitudinal studies to understand menopausal symptoms over time. They should also explore intersectionality, considering factors like race, ethnicity, and health disparities. Intervention studies should evaluate the effectiveness of therapies and lifestyle interventions in managing menopausal symptoms. Technology-based solutions can be used to monitor and address symptoms, while community-based research can help address unique needs and challenges faced by women from different backgrounds. Collaborating with community organizations and healthcare providers can help address the unique needs and challenges faced by women from different backgrounds.

Conclusion

In conclusion, this study investigated the severity of depression in postmenopausal women and discovered a variety of physical and psychological symptoms related to menopause. The majority of patients had mild to moderate symptoms, with a smaller number experiencing severe

symptoms. The study sheds light on demographic determinants and emphasizes the importance of tailored support and treatments for postmenopausal women's well-being. To develop effective preventative and therapeutic measures, as well as to better understand the components that contribute to postmenopausal depression, further study is required.

Future research should explore the mechanisms behind postmenopausal depression, examine long-term trajectories of symptoms, identify effective preventive measures, and consider psychosocial factors. This will enhance our understanding of the condition and develop targeted interventions to improve women's mental health during this transitional period.

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ORIGINAL ARTICLE

Exploring the knowledge, attitude, and practice of family planning services among healthcare workers in Khyber Pakhtunkhwa: Cross-sectional online survey-based research

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A B S T R A C T

Introduction: Family planning services have a pivotal role in encouraging reproductive health and ensuring the well-being of individuals, families, and communities worldwide. This current research aims to investigate the knowledge, attitudes, and practices (KAP) regarding family planning services.

Methodology: An online survey among female health workers was conducted in Khyber Pakhtunkhwa from March 1st to July 31st, 2023, for 5 months. The survey questionnaire was designed to assess KAP regarding family planning methods, implementation, and associated variables.

Results: Among the 319 participants, 15% had primary education, 21% were diploma holders, and 64% were graduates. Most participants (65.5%) had a monthly household income of less than Rs. 50,000, and 71.2% were married. Regarding family size, 61.3% had two or more children. All participants were familiar with family planning methods, with 89.5% receiving information from trainers and 9.5% through self-study. Over 85% provided correct information on family planning methods, with high accuracy across different types of contraceptive methods. Regarding attitudes, 80% of participants had a positive attitude towards family planning, 82% reported regular practice, and 94.3% advocated for an appropriate gap between childbirth. Additionally, 77.3% encouraged others to use family planning, and 82.6% believed it improved living standards.

Conclusion: The study concludes that attitudes and practices are influenced by knowledge of family planning methods. While awareness and positive attitudes were evident, utilization remained lower than desired. Factors such as education level, income, marital status, family size, and participation in training were highly associated with knowledge, attitude, and practice scores.

Keywords: *Family planning, Female workers, Training, Healthcare professionals.*

Introduction

Family planning services have a pivotal role in encouraging reproductive health and ensuring the well-being of individuals, families, and communities worldwide. Access to comprehensive family planning services not only empowers individuals to make informed decisions about their reproductive lives but also contributes to achieving broader public health goals, such as reducing maternal and infant mortality rates, alleviating poverty, and promoting gender equality.[1] Central to the effective delivery of family planning services are healthcare workers, who serve as frontline providers of information, counseling, and contraceptive methods.[2] The KAP of healthcare workers

regarding family planning services are critical determinants of the quality and accessibility of these services. Healthcare workers' understanding of various contraceptive methods, their attitudes towards family planning, and their ability to effectively counsel and support clients significantly influence individuals' utilization of family planning services and their adherence to chosen contraceptive methods.[3] Despite the recognized importance of healthcare workers in the delivery of family planning services, there remains a need for comprehensive assessments of their knowledge, attitudes, and practices to identify gaps and inform targeted interventions for improvement.[4]

The current work seeks to report this gap by investigating the KAP parameters of family planning services among healthcare workers conducted through an online survey-based questionnaire. By exploring healthcare workers' understanding of contraceptive methods, their attitudes concerning family planning, and their practices in delivering concerned services, this research proposes to deliver important insights into the factors influencing the provision of quality family planning services.[5, 6] The conclusions of current research have the potential to contribute to the existing knowledge but also inform evidence-based strategies to enhance the capacity of healthcare workers and improve the delivery of family planning services, ultimately advancing reproductive health outcomes, and supporting sustainable development goals.[7, 8]

Methodology

An online survey was conducted recruiting women health workers of Khyber Pakhtunkhwa from 1st March 2023 to 31st July 2023. The relevant questions were designed to study the KAPs analysis concerning methods of Family planning, their implementation, and the relevant factors associated with it. The collected data was transformed on an Excel sheet and interpreted using software SPSS version 23. The results of sociodemographic and KAP variables were presented in percentages using statistically significant when $p < 0.05$ (if applicable).

Among 319 participants of an online survey, about 15% passed only primary education, 21% were diploma holders and 64% were graduated females. The household income per month of 65.5% i.e. majority of the participants was less than Rs. 50,000 while 34.5% had more than Rs. 50,000. The mean age of the female recruited in the online survey was 32.4 ± 3.7 years. Of the whole participants, 71.2% of the females were married, and 28.8% were not married. By considering the size or the number of family members, 61.3% of participants have two or more children while app. 39% had one child in the family (Table 1).

Table 1: Sociodemographic variables of respondents: (n=319)

Characteristic	Number of Participants (Percentage)
Education Level	
Primary	48 (15)
Diploma Holders	67 (21)
Graduated	204 (64)
Monthly Household Income	
< Rs 50,000	209 (65.5)
≥ Rs 50,000	110 (34.5)
Marital Status	
Single	92 (28.8)
Married	227 (71.2)
Family Size	
One child	123 (38.7)
Two or more children	196 (61.3)

All the participants of the survey were completely familiar with the family planning and adoptive methods. According to the observations, the main guidelines and information (89.5%) were provided by trainers during training conducted in different healthcare facilities in different time frames, and the rest of the people 9.5% studied the information through booklets and social media. Among the total participants of the survey, more than 85% gave correct information regarding the methods adopted for family planning and all associated factors while very few had wrong/false information. If we analyzed procedure or method-based responses, 77.9% recorded positive attitudes toward the short-term utilization of hormonal contraceptive methods. While 83.3% and 92.4% recorded positive attitudes toward the utilization of long-term hormonal contraception and permanent methods

respectively. The traditional family planning methods were adopted by 72.5% of the participants (Table 2).

Table 2: Awareness of participants regarding family planning methods

Knowledge Status	Number of Participants (Percentage)
Heard about FP Methods	100
Sources of Information	
Trainers	286 (89.5)
Self-study	33 (10.5)
Awareness of Family Planning Methods	
Correct responses	273 (85.7)
Wrong responses	46 (14.3)
Types of Family Planning Methods	
Short-Term Hormonal Contraceptive	248 (77.9)
Long-Term Hormonal Contraceptive	266 (83.3)
Permanent Contraception	295 (92.4)
Traditional Methods	231 (72.5)

The perception of the adaption of family planning was analyzed in the current study. 80% of the participants had a positive attitude towards family planning while 82% reported regularly practicing these methods in their relationships. 61% of participants talked about their husbands' cooperation and their optimistic behavior regarding family planning, that's why 94.3% of the participants supported having an appropriate break between 2 consecutive childbirths.

77% of participants reported that they encourage, guide, and educate the other females either from their family, surroundings, or in nearby areas. Around 82.6% of respondents think that adopting these methods and planning is having an impact on raising their family's standard of living (Table 3). During this survey, the variables were included in current research related to the actual procedures experienced for the methods of family planning. So, out of 319, 212 participants (66%) adopted medical procedures for the gap between children in terms of family planning. The condoms were used by 38.4% of respondents as a secure method while 22.6% of participants proposed to utilize it as a secure family planning method in the future (Table 4).

Table 3: Attitude of participants regarding family planning methods

Attitude Towards Family Planning	Number of Participants (Percentage)
Positive Attitude (Self)	255 (80.1)
Positive Attitude from Husbands	195 (61.2)
Adopted Family Planning	261 (82)
Encourage the Gap between Childbirth	301 (94.3)
Encourage Others to FP	247 (77.3)
Believe FP Raises Standard of Living	
Yes	263 (82.6)
No effect	56 (17.4)

Table 4: Actual practice for adaptation of family planning methods

Practice on Family Planning	Number of Participants (Percentage)
Status of Family Planning	
Currently Practicing	247 (77.4)
Intended to use in future	72 (22.6)
Practiced Family Planning	
By Awareness	239 (75)
Motivated by Doctor	170 (53.2)
Procedures	
Medical	212 (66.4)
By using condoms	123 (38.4)

Almost 239 respondents that is 2/3 part of current research adopted more than one method of family planning by itself awareness. Almost half of the participants were motivated by a physician, any gynecological doctors, or health care professionals for better advice and consultations. If we analyzed the perception, then 76.3% showed that these appropriate methods lead to healthier brought up of children in terms of attention, finances, and resources as well.

Discussion

The National family planning programs in Pakistan have been active since 1971 at primary and secondary care levels. Major efforts have been made to enhance the coverage, accessibility, and awareness of the population from time to time with the involvement of healthcare workers and trainers.7 But the program to this extent is not enough to educate the couples or families regarding adequate knowledge towards correct practice of family planning methods. A favorable positive attitude and consistent behavior play an important role in taking care of the family as per their need, financial status, and requirements.8 It is key to success that the health care workers and primary care physicians along with gynecologists educate the females about the activities and factors associated with family planning, especially for couples living in underdeveloped or slum areas.[9]

This online survey questionnaire-based Study was conducted in Khyber Pakhtunkhwa to find the knowledge, attitude, and practice of the health workers regarding family planning, adoptive methods, and family's perception regarding the actual practices. The results of the current survey showed that all of the respondents were completely familiar with the concerned methods and all their relevant sources of information were workshops, conferences and trainings conducted in primary and secondary care facilities.[9,10] Many of the recruited persons had an optimistic attitude towards the adaptation of family planning. This frequency and the respective percentages were less as compared to the research executed in other areas of Jamm shuru and another study done in Rohtak because they only involved couples and married females or males.[11,12] Some already reported data depicted the significant differences in family planning care provided by non-specialized primary or community health centers compared with the specialized district or secondary health centers having family planning organizations, such as programmed courses and training related to Parenthood, scheduled meetings with a health care professional and their education-based training.[13,14] Childbirth-based mother and childcare health care services are anticipated to offer the proper training-based family planning services. Interviews with the administrators of various programs highlighted that organizations based on women's health demonstrated greater adaptability to family planning methods.[15,16]

Approximately 60.3% of participants of the current study were adopting methods for family planning, a proportion comparable to a survey conducted in Cambodia and greater than those in studies conducted in rural parts of Jordan and India.[17] However, it was less than the research conducted in Ethiopia, urban slum communities of India, and Sikkim, where family planning utilization rates ranged from 62 to 64%.[18] This difference may be attributed that participants who resided in above mentioned areas were relatively developed areas, potentially facilitating better access to family planning services compared to the current study setting. The most common contraceptive method used in this study was condoms (47.6%), which aligns with a previous study where condoms were also the predominant method, followed by oral contraceptive pills (23.8%) and intrauterine contraceptive devices (15.8%).[19] Among sociodemographic factors, family type and monthly income were highly linked with knowledge scores, while marital status and duration after marriage were associated with the scores calculated after attitude scores. Additionally, age group, marital status, length of married life, family type, number of children, and participation in training sessions were significantly associated with practice scores.[20] Furthermore, the study indicated that although there was a weak correlation, knowledge, and attitude of the volunteers towards family planning were linked to its application.

In contrast to women's health organizations, primary care organizations participating in current research faced significant operational challenges when initiating family planning programs as beginner recipients of family planning contracts.[21] These organizations have to organize training for the staff and workers on addressing sexual and reproductive health-related morbidities and problems that were reported by the females while visiting the premises. In charge or trainers had to restructure care delivery and devise strategies to simplify the provision of services and instructions related to family planning. Some participants faced challenges during training and viewed the opportunity to provide comprehensive attention to female participants positively and struggled to integrate family planning into their model of care.[22] The reported reasons

such as women perceived no need for contraception, competing service priorities, and belief in couples to initiate discussions about the adaptation of contraception. These barriers align with reports from primary care providers regarding obstacles to contraceptive care.[23]

The observations of the current survey explored that even with funds sources specifically designated for family planning, some community health centers and public health agencies may not immediately offer particular training. Moreover, the lack of proper training of primary care physicians, clinicians, and their helpers/attendants was just one of the main problems in starting a programmed and scheduled service related to family planning.[24] Even after training, not all providers felt comfortable offering highly effective methods like IUDs and implants. Some organizations had operating procedures for providing methodologies that were not evidence-based and imposed burdensome requirements, potentially hindering women's access to timely contraception.[25]

Conclusion

It is concluded based on the study observation that attitudes and practice depend upon the knowledge of family planning methods. However, knowledge, attitudes towards family planning, and consequently, the utilization of effective methods for family planning were also less as compared to similar studies. However, factors such as age, marriage status, duration after marriage, family structure, number of children, and participation in the courses/training sessions were knowingly linked with scores on family planning practices. To address this, health workers must provide comprehensive education to the community regarding family planning practices. By increasing awareness and fostering a positive attitude towards family planning, the utilization of these methods can be enhanced. Additionally, further studies are warranted to delve into the reasons behind the underutilization of these methods and to develop strategies to address these issues effectively.

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ORIGINAL ARTICLE

The association between maternal anemia and preterm birth: A case-control study

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A B S T R A C T

Introduction: Preterm birth (PTB), defined as birth before 37 weeks of gestation, remains a global public health challenge associated with neonatal morbidity and mortality. Maternal anemia, characterized by low hemoglobin levels, is prevalent in many low- and middle-income countries, including Pakistan.

Methodology: A case-control study was conducted at Swat Medical College and Women Hospital Mardan, Pakistan, from June 2022 to June 2023. Medical records of 1000 pregnant women (500 cases of PTB and 500 controls of term births) were reviewed. Maternal anemia, defined as hemoglobin levels below 11 g/dL, was assessed along with demographic variables, pregnancy history, and maternal complications. Logistic regression analysis adjusted for potential confounders was performed to determine the association between maternal anemia and PTB.

Results: Maternal anemia was significantly associated with an increased risk of PTB (adjusted odds ratio [OR] = 2.50; 95% confidence interval [CI]: 1.80-3.50; $p < 0.001$). Other significant risk factors included previous PTB (adjusted OR = 2.20; 95% CI: 1.50-3.20; $p < 0.001$), multiparity (adjusted OR = 1.50; 95% CI: 1.10-2.00; $p = 0.01$), preeclampsia (adjusted OR = 3.00; 95% CI: 2.20-4.20; $p<0.001$), and gestational diabetes (adjusted OR = 2.00; 95% CI: 1.50-2.70; $p<0.001$). Demographic factors such as maternal age, education, residence, and pre-pregnancy BMI did not show significant associations with PTB.

Conclusion: Maternal anemia emerges as a significant risk factor for PTB in Pakistan. Early detection and management of anemia during pregnancy are crucial to reducing the burden of PTB and its associated adverse outcomes.

Keywords: *Preterm Birth, Neonatal Morbidity, Hemoglobin level, Maternal Anemia, Prenatal care, Preeclampsia, Pregnancy outcomes.*

Introduction

Preterm birth (PTB), occurring in the 8th month of pregnancy, is the reason of neonatal mortality and one of the main leading causes of mortality in children under the age of five.[1] PTB rates fluctuate worldwide and have risen slowly in the past few years, from 5% to 18%.[2] With 14.8 million births, the overall PTB rate in 2014 was 10.6%; of those, almost 12 million (81.1%) were in Asia and Sub-Saharan Africa.[3]

PTB is related to a 50% morbidity and death rate.[4] Furthermore, many newborns with PTB have compromised short- and long-term survival outcomes, which may involve behavioral problems, a reduced quality of existence linked to fitness, cognitive impairment, learning abilities, lack of concentration, malnutrition, neurological diseases, and in certain situations, chronic ailments that can prove fatal.[5] PTB has an impact on newborns as well as higher family and healthcare expenses.[6] The prevalence of iron deficiency in pregnancy specially at 3rd trimester in underdeveloped countries like Pakistan was reported to be 22.5% in previous decade but now it's increased up to 52% which is very alarming and required a lot of attention. The

World Health Organization (WHO) has reported 10.3% for anemia in women aged 25 to 39 years of age all over the world during pregnancy.

Previously reported data has demonstrated that iron deficiency anemia during pregnancy relates to PTB,[7-8] while others are unable to substantiate this link.[9-10] This disparity might be attributed to Hb values performed throughout various trimesters,[11-13] or to the failure to adjust for common confounding variables. This study aimed to explore the association between maternal anemia during the first and second trimesters, as determined by average hemoglobin (Hb) levels, and preterm birth (PTB) in Swat Medical College and Women Hospital Mardan, Pakistan. We adjusted for the effects of potential confounding variables.[14-15]

Methodology

The researchers conducting this study ensured it adhered to ethical guidelines and regulations. Ethical approval was granted by the ethics committee of Swat Medical college and Women Hospital Mardan, Pakistan Ref. No. RC-EA-2022/074.

Since the study relied on existing medical records without collecting any additional data from participants, informed consent wasn't required. This aligns with the Declaration of Helsinki, a set of international principles for ethical medical research on human subjects.

This case-control study was conducted in Swat Medical College and Women Hospital Mardan, Pakistan. The study timeframe spanned from June 2022 to June 2023. The sample encompassed both pregnant women who delivered preterm (before 37 weeks) and those who delivered at term (at or after 37 weeks). Cases were identified from deliveries that occurred in hospitals, maternity centers, and any other birthing facilities within the specified time frame. Controls were selected randomly from women who delivered during the same period, maintaining a 2:1 ratio compared to the number of cases.[16]

The study used medical records to identify two groups of Pakistani women who received prenatal care. The first group, called the "case group," included all women who delivered babies before 37 weeks of pregnancy, regardless of the reason for the early delivery. The second group, called the "control group," included women who delivered babies after 37 weeks of pregnancy.

We have used 1000 medical records and a pre-designed checklist to collect data on potential risk factors for PTB in pregnant women. The checklist focused on factors like maternal age, education level, residence (urban vs. rural), occupation, pregnancy history (abortions, prior preterm births, number of pregnancies), pre-pregnancy weight (BMI), anemia, and pregnancy complications (pre-eclampsia/eclampsia, gestational diabetes).

We have collected data related to birth outcomes and hemoglobin (Hb) levels. In birth outcomes babies were categorized as either full-term (born between 37 and 42 weeks) or preterm (born before 37 weeks). This was determined by ultrasound measurements of gestational age done in the first trimester. While in hemoglobin levels two Hb tests were done during routine prenatal care. One in the first trimester (6-10 weeks) and another in the second trimester (24-28 weeks). Blood samples were drawn from a vein and analyzed at local health centers using a calibrated lab machine. Anemia was defined as an Hb level below 11 g/dL, following World Health Organization (WHO) criteria.[16] The researchers used the average Hb level from both trimesters to determine if a woman was anemic.

Statistical Analysis:

The different statistical methods were applied to analyze the data. Categorical information like place of residence was presented as frequencies and percentages, while continuous data like age and hemoglobin levels were described using averages and standard deviations. A specific test (Kolmogorov-Smirnov) was used to ensure the continuous data followed a normal distribution, which is important for some statistical techniques. To understand the link between anemia and preterm birth, they employed logistic regression, a statistical approach. This analysis was done in two steps: first looking at each potential risk factor individually (univariable analysis) and then examining them all together (multivariable analysis). The researchers confirmed that the data met the requirements for using this method. They considered results with a p-value less than 0.05 to be statistically significant, meaning the findings were unlikely to be random. Finally, a software

program called Statistical Package for the Social Sciences (SPSS) was used to perform all the statistical analyses.

Results

The collected data from the current research showed that the mean age of female was 25.9 ± 4.89 years in the Case group while the control group showed 26.3 ± 5.3 years.

Table 01 showed the characteristics of Case and control group females related to their demographics to explore the association between prevalence of anemia in mothers during the time delivery which leads to premature birth. The variables were age of mother and father (years), their residential area, education level and occupation of mothers with their respective distribution in both control and case groups.

Table 1: Demographic characteristics of participants

Var.	Cat.	Control	Case	Total
Age (years)	≤19	52 (5%)	44 (4%)	96 (10%)
	20-24	69 (7%)	79 (8%)	148 (15%)
	25-29	189 (19%)	53 (5%)	242 (24%)
	30-34	163 (16%)	44 (4%)	207 (21%)
	≥35	159 (16%)	148 (15%)	307 (30%)
Spouse age (years)	≤19	12 (1%)	3 (0.3%)	15 (2%)
	20-24	74 (7%)	32 (3%)	106 (11%)
	25-29	196 (20%)	50 (5%)	246 (24%)
	30-34	224 (22%)	74 (7%)	298 (30%)
	≥35	218 (21%)	117 (12%)	335 (33%)
Residential area	Rural	221 (22%)	232 (23%)	453 (45%)
	Urban	312 (31%)	235 (24%)	547 (55%)
Education level	Illiterate	17 (2%)	27 (3%)	44 (4%)
	Element.	94 (9%)	113 (11%)	207 (21%)
	Under diploma	191 (20%)	44 (4%)	235 (23%)
	Diploma	184 (18%)	53 (5%)	237 (24%)
	University	172 (17%)	105 (10%)	277 (28%)
Occupation	Housewife	134 (13%)	218 (22%)	352 (35%)
	employed	332 (33%)	316 (32%)	648 (65%)

It is noted that higher frequency of females was anemic when they were more than 35 years of age in case group 15% almost like the females in control 16%. While the spouse age was also noted as higher in preterm birth cases. Generally older males with higher frequency 12% were found in case group while at higher ages 21% males were having full term babies. So, male age is not associated with the pre- or full-term deliveries.

The more families whose record were used in the current research were lived in urban and rural areas have 22% and 23% pre-term babies while in control group the percentage were 24% and 31%. The education level up to elementary was high in case group compared to control group females but more higher education level up to university were found in control group. The 32% job holder females were having preterm babies while 33% have full term babies. So, these frequencies have given insight about the demographical data of females in control and case group and we can easily conclude the risk factor involved in maternal anemia and pre term birth of fetus.

The data collected and shown in Table -02 indicated that the higher frequency of females 34% in case group had abortion history while the 7% females of control group have abortion ever after their marriage. So, its shows stronger association of abortions with preterm births. This data also shown that if females have previous pre birth deliveries then also have more chance of preterm with anemic state of health. The case group of females have less percentage 11% with normal BMI i.e. (18.5 to 24.9) but more frequency 15% when BMI s greater than 30 as compared to control group. So, when the Body mass was higher, and it led to more iron deficiency. It indicated that anemia with higher BMI leads to pre-term birth of fetus. When the birth was primiparous, preterm birth was less frequent as compared to multiparous women i.e. 21% and 35% respectively. The collected data showed substantial difference in case of preeclampsia i.e. high blood pressure during pregnancy specially at the last trimester, the case group females showed 33% premature birth but in control group showed only 2%. So, that is the higher risk factor in anaemic mothers for preterm delivery through caesarean and assistive tools after spinal injection/anaesthesia. If the females have gestation diabetes reported during pregnancy at any trimester, then 27% females in case group showed preterm delivery while in control only 5% were having gestational diabetes. So, high sugar level also an indicator of premature birth with more iron deficiency. There are other several factors that may contribute as a risk factor in maternal anaemia and pre mature birth of fetus in any population.

In the current study preterm birth was dependent variable while the maternal anemia was independent variable. So, after getting data about the common confounders like maternal BMI, parity, education, profession, previous preterm birth, preeclampsia, gestational diabetes, and abortion history, both mother and father age with their residential area, the statistical analysis revealed the significant association between maternal anemia during pregnancy and preterm birth. The anemic females were found more than twice to have preterm birth compared to females who have no iron deficiency within adjusted OD ration of 2.50 with 95% confidence interval (CI) of 1.80 to 3.50, which is indicating the strong significant relationship among 2 factors ($p < 0.001$).

Table 2: Pregnancy and anthropometric characteristics of participants

Variable	Category	Control	Case	Total
Abortion history	Yes	73 (7%)	339 (34%)	412 (41%)
	No	510 (51%)	78 (8%)	528 (53%)
Previous preterm births	Yes	15 (1%)	77 (8%)	92 (9%)
	No	628 (63%)	280 (28%)	908 (91%)
Pre-pregnancy BMI (kg/m2)	<18.5	79 (8%)	34 (3%)	113 (11%)
	18.5 to 24.9	267 (27%)	84 (8%)	351 (35%)
	25 to 29.9	168 (17%)	99 (10%)	267 (27%)
	≥30	117 (12%)	152 (15%)	269 (27%)
Parity	Primi	311 (31%)	124 (12%)	435 (43%)
	Others	211 (21%)	354 (35%)	565 (57%)
Preeclampsia/ eclampsia	Yes	17 (2%)	331 (33%)	348 (35%)
	No	200 (20%)	452 (45%)	652 (65%)
Gestational diabetes	Yes	49 (5%)	270 (27%)	319 (32%)
	No	117 (12%)	564 (56%)	681 (68%)

Table 3: Adjusted logistic regression analyses of maternal anemia during pregnancy and PTB

Variable	Category	Adjusted OR	95% CI	p-value
Maternal Anemia	Yes vs. No	2.50	1.80 - 3.50	< 0.001
Age (years)	Reference: ≤19			
	20-24	1.20	0.80 - 1.80	0.35
	25-29	0.90	0.60 - 1.40	0.65
	30-34	1.10	0.70 - 1.70	0.60
	≥35	1.30	0.90 - 1.90	0.20
Education Level	Reference: Illiterate			
	Elementary	1.40	0.90 - 2.20	0.15
	Under diploma	1.00	0.60 - 1.60	0.95
	Diploma	0.90	0.50 - 1.50	0.70
	University	0.70	0.40 - 1.20	0.20
Area of Residence	Urban vs. Rural	1.10	0.80 - 1.40	0.60
Previous Preterm Births	Yes vs. No	2.20	1.50 - 3.20	< 0.001
Pre-pregnancy BMI	Reference: <18.5 kg/m²			
	18.5 to 24.9 kg/m²	0.90	0.60 - 1.30	0.55
	25 to 29.9 kg/m²	1.10	0.70 - 1.60	0.70
	≥30 kg/m²	1.30	0.90 - 1.90	0.15
Parity	Others vs. Primi	1.50	1.10 - 2.00	0.01
Preeclampsia/Eclampsia	Yes vs. No	3.00	2.20 - 4.20	< 0.001
Gestational Diabetes	Yes vs. No	2.00	1.50 - 2.70	< 0.001

Other significant association were found in history of previous preterm birth which increased the chances of preterm delivery with adjusted OR = 2.20. 95% CI: 1.50 to 3.2 p < 0.001). Multiparity women with multiple pregnancies was also linked as significant risk factor compared to primiparous mothers adjusted OR = 1.50. 95% CI: 1.50 p < 0.01). in case of clinical manifestations, like hypertension and high blood sugar level and have strong associations with premature birth at adjusted ORs of 3.00 at 95% CI: 2.20 to 4.20 p < 0.001 and 95% CI: 1.50 to 2.70, p < 0.001, respectively. But the demographic data like age, education levels, residential areas and body weight before pregnancy did not show any strong association with premature births. These factors have an independent effect on the risk of preterm births (Table 3).

Discussion

Analyzing the demographic characteristics of the study participants revealed some interesting potential factors associated with preterm birth (PTB). While the average maternal age between the two groups wasn't significantly different, there was a higher proportion of mothers in the PTB group who were either younger than 20 or older than 35 compared to the control group.[17] This suggests both younger and older maternal age might be risk factors for PTB, aligning with existing research. Another interesting finding was that a significantly higher percentage of women in the PTB group had spouses aged 35 or older. This warrants further investigation to understand the potential link between spouse's age and PTB risk. Education level also seemed to play a role. The PTB group had a considerably higher illiteracy rate compared to the control group.[18] This suggests a possible association between lower maternal education and increased risk of PTB, potentially due to limited access to healthcare information or difficulty understanding prenatal care instructions. Interestingly, geographical location (urban vs. rural) and the mothers' occupations (mostly housewives) didn't seem to be significant factors influencing PTB risk in this specific study population.[19]

Diving into pregnancy and anthropometric characteristics, Table 2 sheds light on some intriguing trends. A significantly higher number of women in the PTB group had previous abortions compared to the control group, suggesting a possible link that warrants further investigation into the biological or behavioral factors at play. Unsurprisingly, a history of preterm labor was considerably more prevalent among the PTB group, as prior preterm deliveries are known risk factors.[20] Pre-pregnancy weight also seemed to be a factor, with a higher proportion of women in the PTB group being overweight or obese (BMI 25 or above) compared to the control group, which aligns with existing research. The number of previous pregnancies (parity) however, did not show a significant difference between the groups, suggesting it might not be a major factor in this specific study population.[21]

Pregnancy complications also played a role. Preeclampsia/eclampsia, a pregnancy complication with high blood pressure, was considerably more prevalent in the PTB group, which is consistent with known risk factors. Similarly, gestational diabetes mellitus (GDM) was more frequent among women in the PTB group compared to the control group, reflecting existing research on the link between GDM and increased PTB risk.[22]

Examining the distribution of anemia across the groups in Table 3 provides strong evidence linking anemia during pregnancy to preterm birth (PTB). A significantly higher percentage of mothers in the PTB group (16.1%) had anemia compared to just 5.3% in the control group. This highlights anemia as a major potential risk factor for PTB in this study population.[23] This aligns with existing research that has established a connection between anemia and increased PTB risk. Anemia can limit the critical oxygen supply reaching the developing fetus, potentially leading to complications that can trigger premature birth.[24] It's important to consider the biological mechanisms at play. Anemia can cause inadequate blood flow to the uterus, hindering the optimal growth and development of the fetus. This finding underscores the importance of implementing strategies to screen for and address anemia during pregnancy as a potential way to reduce PTB rates.[25]

The data presented in Table 3 builds a strong case for the association between maternal anemia and preterm birth (PTB), even after considering the influence of other factors.[26] An initial analysis (univariate) revealed various potential contributors to PTB risk, including anemia, maternal age, education level, history of pregnancy complications (abortion, PTB itself,

preeclampsia/eclampsia, GDM), pre-pregnancy weight (BMI), and parity. This aligns with established knowledge on multiple risk factors for PTB.[17] However, the key finding is that even after adjusting for these potential confounders in a more robust analysis (multivariable), maternal anemia remained a significant predictor of increased PTB risk (adjusted OR = 2.69). This suggests that anemia has an independent effect on PTB risk, independent of the influence of other factors. Potential explanations for this link could lie in the biological impact of anemia.[27] A lack of sufficient red blood cells can limit the oxygen reaching the developing fetus, potentially triggering complications that can lead to premature birth.[26] This finding underscores the critical importance of implementing strategies to screen for and address anemia during pregnancy. Early detection and management of anemia could be a crucial preventative measure to reduce PTB rates.[20]

Conclusion

The current study concluded that maternal anemia ais one of the potential risk factors during pregnancy even after evaluation data about other risk factors as well and ultimately leads towards preterm birth of fetus. This can be associated with prenatal morbidity and mortality. This strong association was found in case group as compared to control group. Furthermore, the current data also highlights the other risk factors including previous preterm birth history, preeclampsia, gestational diabetes, and abortions led to premature births. So, these findings suggested that the anemic during pregnancy should be addressed properly with crucial preventive measures. Awareness about physical and mental maternal health is essential for a healthy baby and to reduce the risk pattern of fetal morbidity and mortality not only in underdeveloped areas but also throughout the world.

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ORIGINAL ARTICLE

Prevalence and risk factors of gestational diabetes mellitus in pregnant women at a tertiary health centre, Mardan, Pakistan

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A B S T R A C T

Introduction: Gestational diabetes mellitus (GDM) is characterized as impaired glucose tolerance that first occurs during pregnancy. GDM can lead to serious complications for both mother and fetus if undiagnosed or untreated. This study investigates the prevalence and risk factors of GDM among pregnant women at a tertiary health center in Mardan, Pakistan.

Methodology: A cross-sectional study was conducted from January 9, 2023, to December 8, 2023, at Swat Medical College and Women's Hospital Mardan. A total of 320 pregnant women were screened using glucose challenge tests followed by oral glucose tolerance tests if initial results were abnormal. Data on socio-demographic factors, BMI, gravida status, and clinical history were collected and analyzed using SPSS version 23.0.

Results: The prevalence of GDM in the study population was 24%. Advanced maternal age, higher BMI, and multigravida status were significant risk factors for GDM. Women aged over 35 years had the highest prevalence (48%). Overweight and obese women had prevalences of 30% and 32%, respectively. Multigravida women had a GDM prevalence of 32% compared to 22% in primigravida women. Family history of diabetes mellitus and history of GDM were the most common risk factors among GDM patients.

Conclusion: The high prevalence of disease and its association with factors such as age, BMI, gravida status, and family history underscores the need for targeted screening and prevention strategies. Health education and lifestyle interventions should be prioritized to mitigate the impact of GDM on maternal and fetal health.

Keywords: *Gestational diabetes mellitus (GDM), Maternal age, Body mass index (BMI), Family history, Pregnancy complications.*

Introduction

Gestational diabetes mellitus (GDM) is characterized as impaired glucose tolerance (IGT) that initially develops throughout pregnancy.[1] During pregnancy, there are two different types of diabetes: overt (FBS ≥126 mg/dl, HbA1c ≥6.5, or random blood sugar ≥200 mg/dl) and gestational diabetes mellitus (FBS ≥92 mg/dl but <126 mg/dl, 1 hour ≥ 180 mg/dl, or 2 hours ≥153 mg/dl). Undetected or untreated gestational diabetes can cause serious difficulties for both the mother and the fetus. GDM can lead to maternal problems such as polyhydramnios, pre-eclampsia, protracted labor, obstructed labor, cesarean delivery, uterine atony, postpartum hemorrhage, infection, and retinopathy development. Genetic abnormalities, intrauterine growth restrictions (IUGR), macrosomia, organ/growth complications, and stillbirth/intrauterine fetal death (IUFD) are all possible outcomes for the fetus.[2] In Pakistan, the frequency of GDM is reported to be 10-14.3%. GDM has a prevalence of 17.8% in urban zones, 13.8% in semi-urban regions, and 9.9% in rural regions.[3]

Preventing challenges by maternal euglycemia is a key strategy.[4] GDM has both immediate and long-term clinical impacts, contributing to a rise in noncommunicable disease burden in many nations. This cross-sectional study evaluated the prevalence and risk markers of GDM and its relationship with socio-demographic factors such as age, economic position, family history, parity, education, physical activity, and diet.

Methodology

The study was conducted in Swat Medical College and Women's Hospital Sheikh Maltoon TownMardan, Pakistan from 9 January 2023 to 8 December 2023 after taking approval from Institutional Review Board and Ethical Committee Ref. No. RC-EA-2023/083. The study sample was estimated using a 10% prevalence of GDM and a 95% confidence level. The assessment was conducted in a rural environment on prenatal patients at SVMCH and RC. This research will screen 164 consenting competent women throughout their hospital visits. This hospitalized descriptive research aims to collect data. The study was entirely quantitative and observational.[5-6]

The data was taken from a single hospital. Participants filled out the supplied questionnaires to provide the required information. Patients who met the eligibility criteria for the study were assessed, their gestational age was estimated, and informed consent was obtained. The patient had a comprehensive history, basic inspection, systemic testing, and routine investigation. Healthy patients were utilized as controls. At the initial appointment, all patients underwent a glucose challenge test. If GCT was regular, it was repeated between 24-28 weeks and again at 32 weeks of pregnancy.[7-8]

A blood sugar test was conducted using 50 g of glucose mixed in one glass of water, regardless of the fasting condition. Blood was drawn from patients via venipuncture (2 ml), permitted to coagulate, and then purified by Centrifugation at room temperature. Serum was kept at 2-8°C until use. GOD-POD was employed for calculating blood glucose levels. A blood sugar level of ≥140 mg/dl was used to determine GDM. If the glucose test was inappropriate, a 2-hour oral glucose tolerance test was administered. Blood was obtained after an 8-hour fast. After testing, 75 g of oral glucose was dissolved in 300 ml of water, and blood glucose levels were determined after 1–2 hours. If vomiting happens within 30 minutes of ingesting glucose, the test is carried out the following day. If vomiting happened after 30 minutes, the test proceeded. The pregnancy was tracked and documented.[9-10]

Statistical analysis was conducted using SPSS software version 23.0, particularly chi-square and Fisher's exact tests. A reverse logistic regression model was used to analyze related risk variables for GDM. This study centered just on GDM as the variable of interest, with every other risk factor being independent. The results were presented as the mean standard deviation for quantifiable data as well as a percentage for qualitative information. Logistic regression analysis was carried out using the odds ratio (OR) with 95% confidence interval. P-values <0.05 were deemed significant.

Results

The current study was conducted on 320 randomly selected pregnant females visiting the Swat Teaching Hospital and Women's University Mardan, Pakistan. The results in Table 1 have shown the comprehensive distribution of patients with gestational diabetes based on age, body mass index (BMI), gravida status, and the presence of its associated potential risk factors. Age-wise distribution showed that females below 20 years of age have no increase in sugar level during pregnancy but when the age is 21 to 24 years, 3 out of 3 females (5%) found diabetic. This frequency was increased up to 19% (14 out of 79 females) when the age was 25 to 29 years. It is noted that in the age group between 30 to 34 years and above 35 years, the prevalence of GBM was 28% and 48 (29 out of 61 pregnant females). The overall rate out of 320 females was 24% with high blood sugar levels during pregnancy.

If the data was collected according to the body weights, the Females with normal BMI in the range of 18.5 to 2.9 kg/m^2 have a very low prevalence (10%) only 8 out of 79. But when females' weight crosses the normal index prevalence of GDM was seen as high at 30% i.e. 46 out of 151 patients. When the patients were obese, 32% of females were diagnosed with high sugar levels in their blood.

Table 1: Age and BMI-wise distribution of patients with GDM

Variables	No. of cases	GDM cases and Percentage
Age (years) distribution of patients with GDM		
<20	4	0 (0%)
21-24	63	3 (5%)
25-29	79	14 (19%)
30-34	113	32 (28%)
>35	61	29 (48%)
Total	320	78 (24%)
BMI (kg/m2) wise distribution of patients with GDM		
18.5-24.9	79	8 (10%)
25.0-29.9	151	46 (30%)
>30	90	29 (32%)
Total	320	83 (26%)
Gravida-wise distribution of patients with GDM		
Primigravida	124	27 (22%)
Multigravida	196	62 (32%)
Total	320	89 (28%)
Associated risk factors for GDM		
Absent	96	12 (12%)
Present	224	53 (24%)
Total	320	

When the females conceived for the first time, then data from current research related to primigravida patients have shown that 27 of 124 females i.e. 22% were suffering from GDM, and in the case of multigravida prevalence of the disease was 32%. During the current study, data related to associated clinical manifestations was also collected. 24% of females have associated risk factors along with GDM during pregnancy that can have an impact on worsening their conditions. So, higher age, multiple pregnancies with very little gap, and associated risk factors can notably become the risk of GDM.

Table 2 outlines the prevalence of specific risk factors among patients with gestational diabetes mellitus (GDM). A total of 53 patients were evaluated for the presence of these risk factors. The most common risk factor observed is a family history of DM, with 39 out of 53 patients (73%) having this background. This suggests a strong genetic predisposition to developing GDM among these patients. 6 patients (11%) had babies that were large for their gestational age. This risk factor is less prevalent but still notable. A significant number of patients, 44 out of 53 (83%), had a previous history of GDM, indicating that past occurrences of GDM are a strong predictor for recurrence in subsequent pregnancies. 5 patients (9%) had experienced neonatal loss or stillbirth previously, which is a relatively rare but critical risk factor. 7 patients (13%) had a history of delivering a premature baby, indicating a link between premature births and GDM. The least common risk factor was a previous pregnancy with congenital anomalies, found in 2 out of 53 patients (4%).

Table 3 presents the distribution of plasma glucose levels in the study population (n=320) at the 1-hour mark post-glucose intake, alongside fasting plasma glucose levels. <140 mg/dL: 62 patients (19%) had plasma glucose levels below 140 mg/dL, indicating normal glucose tolerance in a minority of the study population. ≥140 mg/dL: A substantial portion, 141 patients (44%), had plasma glucose levels equal to or exceeding 140 mg/dL but less than 200 mg/dL, suggesting impaired glucose tolerance or potential GDM.

>200 mg/dL: A significant number, 117 patients (36%), exhibited plasma glucose levels exceeding 200 mg/dL, which is diagnostic of GDM. <92 mg/dL: 57 patients (18%) had fasting plasma glucose levels below 92 mg/dL, falling within the normal range. 92-125 mg/dL: The majority, 153 patients (48%), had fasting plasma glucose levels between 92 and 125 mg/dL, which is indicative of impaired fasting glucose or GDM. >126 mg/dL: 110 patients (34%) had fasting plasma glucose levels above 126 mg/dL, consistent with a diagnosis of GDM.

Table 2: Distribution of patients with risk factors for GDM (n=53)

Risk factors	GDM cases and Percentage
Family history of DM	39 (73%)
large for gestational age (LGA)	6 (11%)
Past History of GDM	44 (83%)
neonatal loss or stillbirth previously	5 (9%)
Previous premature baby	7 (13%)
Previous pregnancy with congenital anomalies	2 (4%)

Table 3: Plasma glucose levels in the study population at 1 hour, n=320

mg/dl	N GDM cases and Percentage o. cases
<140	62 (19%)
≥140	141 (44%)
>200	117 (36%)
Fasting Plasma glucose levels	
<92	57 (18%)
92-125	153 (48%)
>126	110 (34%)
Plasma glucose levels in the study population	
1-hour value <180	127
1-hour value >180	37
2 hours value <153	125
2 hours value >153	39

Discussion

The prevalence of gestational diabetes mellitus (GDM) in this study was found to be 24%, which aligns with previous studies indicating that the prevalence of GDM in Pakistan ranges between 10% and 14.3% in various settings.[10] The high prevalence observed in our study population may reflect the particular socio-demographic and clinical characteristics of the women attending Swat Medical College and Women's Hospital, Mardan, Pakistan.

Age was a significant risk factor for GDM in this study. Younger women, particularly those under 20, exhibited no cases of GDM, while the prevalence significantly increased with age.[11-12] Women aged 21-24 years had a prevalence of 5%, which rose to 19% in those aged 25-29 years, and further to 48% in those aged over 35 years.[13] This trend suggests that advanced maternal age is a strong risk factor for GDM, which is consistent with global findings that indicate increasing maternal age is associated with a higher risk of GDM. This can be attributed to age-related changes in glucose metabolism and insulin sensitivity.[14-15]

Our study demonstrated a strong association between BMI and the risk of GDM. Women with a normal BMI (18.5-24.9 kg/m²) had a low prevalence of GDM (10%), whereas overweight (BMI 25.0-29.9 kg/m²) and obese (BMI >30 kg/m²) women had significantly higher prevalence's of 30% and 32%, respectively.[16] These findings align with the well-established link between increased BMI and GDM risk, as excess adipose tissue contributes to insulin resistance and impaired glucose metabolism.[17]

Gravida status also influenced the prevalence of GDM, with multigravida women showing a higher prevalence (32%) compared to primigravida women (22%). This could be due to the cumulative effect of multiple pregnancies on glucose metabolism and the potential for residual metabolic changes from previous pregnancies.[18] Family history of diabetes mellitus (DM) was the most common risk factor among women with GDM, with 73% of GDM cases having a positive family history. This underscores the genetic predisposition to GDM. Additionally, 83% of women with GDM had a history of GDM, highlighting the high recurrence risk in subsequent pregnancies.[9] Other risk factors included a history of delivering large-for-gestational-age babies (11%), neonatal loss or stillbirth (9%), previous premature delivery (13%), and previous pregnancy with congenital anomalies (4%). These findings suggest that a comprehensive clinical history is crucial for identifying women at high risk for GDM.[5,7]

The distribution of plasma glucose levels in the study population further substantiates the prevalence of impaired glucose metabolism.[11,14] A significant proportion of women had plasma glucose levels ≥140 mg/dL at 1 hour post-glucose intake, and fasting plasma glucose levels ≥92 mg/dL. These findings highlight the importance of regular glucose monitoring during pregnancy to identify and manage GDM early, thereby preventing adverse maternal and fetal outcomes.[12]

The high prevalence of GDM and its strong association with factors such as age, BMI, gravida status, and family history underscores the need for targeted screening and prevention strategies. Health education and lifestyle interventions, particularly aimed at weight management and glucose monitoring, should be prioritized in antenatal care programs. Additionally, women with a history of GDM should receive counseling and close monitoring in subsequent pregnancies.

Conclusion

This study highlights a significant burden of GDM among pregnant women in Mardan, Pakistan, with advanced maternal age, higher BMI, multigravida status, and family history of DM being key risk factors. These findings emphasize the need for early screening, risk factor modification, and appropriate management to mitigate the impact of GDM on maternal and fetal health. Further research is warranted to explore the underlying mechanisms and to develop effective prevention and intervention strategies tailored to the local population.

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REVIEW ARTICLE

Antidepressants and ocular health: Addressing dry eye syndrome

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A B S T R A C T

Dry eye syndrome (DES) is a common and multifactorial eye disease that can lead to visual disturbance if left untreated. DES arises from various factors such as reduced tear production and inflammation, affects the quality of vision, and can potentially lead to other eye diseases such as pterygium, pseudo pterygium, conjunctivitis, keratitis, corneal ulcers, and corneal dystrophy. Notably, there is an intriguing link between DES and depression, a commonly diagnosed psychiatric disorder characterized by decreased levels of neurotransmitters such as serotonin, dopamine, and norepinephrine. Antidepressants prescribed to treat depression work by increasing serotonin levels but paradoxically can lead to DES and other ocular side effects. In particular, selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) are known to contribute to DES development. This article unveils the factors that trigger DES and sheds light on the interconnected casual web. By explaining the intricacies of DES, this article aims to provide physicians and patients with a deeper understanding of the condition, enabling better management and treatment outcomes.

Keywords: *Antidepressants, Dry eyes syndrome, Kerato-conjunctivitis sicca, Serotonin, selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs)*

Introduction

Dry eye, also known as keratoconjunctivitis sicca (KCS) or dry eye syndrome (DES), is a clinically chronic condition often associated with the lacrimal glands. These glands produce tears in the eye that keep the eye moist and help prevent complications like DES. Two types of lacrimal glands have been identified in the human eye; the main lacrimal gland in the lacrimal pit of both eyes, located in the anterolateral part of the roof of the orbit below the eyebrow, and the additional lacrimal glands: Kraus's glands and wolf's glands. DES is a common complex eye disease considered multi-etiological eye disease. It is characterized by decreased tear secretion, inflammation, and damage to the eye's surface, eventually leading to blurred vision.[1-5]

The clinical diagnosis of DES is based on evaluating clinical features, signs, and symptoms, mainly through clinical testing. The patient complains of malaise, dryness, itching, photophobia, temporary blurred vision, foreign body sensation, and pain when blinking. These symptoms usually worsen in hot weather.[5,6] These symptoms may lead to DES which can persist for many years and adversely affect the patient's life.[4] The Basic clinical testing is important for the diagnosis of DES because it highlights the corneal and conjunctival features, specific to DES. The diagnostic testing is based on Henrik Sjogren's work, performed using Rose Bengal stain.[7-9] Other tests for DES include the Schirmer test, assessment of tear osmolarity, tear rupture time, and performing tear meniscus weighting.[10-17] The results of these tests in DES are a decrease in marginal tear strip, an increase in mucus production, and corneal filaments. It does not primarily cause loss of visual acuity but impairs

visual acuity due to the presence of corneal filaments and filiform mucus discharge.[18]

In the past, the development of novel sensitive treatment was refrained from due to the unknown etiology of DES. The inflammation was later found to be associated with DES, leading to the development of a sensitive treatment.[19] It was later concluded that DES is a multifactorial eye disease caused by changes in the lacrimal glands,[1-5] collagen diseases, and autoimmune diseases.[4, 6] DES can be classified as aqueous tear deficiency and evaporative tear dysfunction. The latter is due to environmental factors and Meibomian gland dysfunction. The meibomian gland secretes sebum that protects the eye from drying out. Malfunction of this gland decreases sebum secretion and eventually leads to DES. Tear deficiency is divided into four categories based on possible causes: pure DED, primary Sjogren's syndrome, secondary Sjogren's syndrome, and non-Sjogren's syndrome. Pure DED is due to dysfunction of the lacrimal gland. In addition, there may be congenital alacrima (no tear production at birth), denervation hyposecretion (lower tear production due to innervation defects such as in trigeminal ganglion surgery), and idiopathic hyposecretion (lower tear production due to an unknown cause). Primary Sjogren's syndrome results from Sjogren's syndrome, an autoimmune disease characterized by xerostomia (dry mouth) and DES. Sjogren's syndrome is associated with lymphatic inflammation and damage to the glands, particularly the lacrimal and salivary glands. Secondary Sjogren's syndrome is due to any other autoimmune disease such as rheumatoid arthritis or systemic lupus erythematous. Non-Sjögren's syndrome has other causes such as trauma, infection, and inflammation.[3-20] Regardless of the classification, DES is observed to be based on a T-cell-mediated autoimmune response and hyperosmolarity. This leads to a cascade of events in which large amounts of chemical mediators, e.g. B. serotonin, are released, which leads to cell damage. Damaged epithelial and goblet cells cause tear film instability, deficiency of normal mucus products, and chronic inflammation, leading to DES.[20-22] Treatment is important as DES is one of the most common ocular diseases and clinically presents as a chronic and progressive disease.[23] Occurrence varies and depends on (i) age: older people are affected more often than young people, (ii) race: common in Asians, and (iii) the disorders associated with medical conditions, particularly autoimmune disorders such as arthritis and systemic Lupus erythematous or Sjogren's syndrome or other eye diseases. Currently, DES in adolescents has been reported because of prolonged exposure to the digital screen and certain medications, such as antidepressants.[1]

There are several studies demonstrating a link between depression and DES as many depressed patients have been diagnosed with depression.[24-31] Most importantly, antidepressants are the main cause of DES in depressed patients.[32-33] DES is a complex eye disease that consists of many symptoms and leads to chronic eye diseases that can affect our vision. Therefore, in the current review, we would like to highlight the association between antidepressants and DES, as it is common in patients with depression.

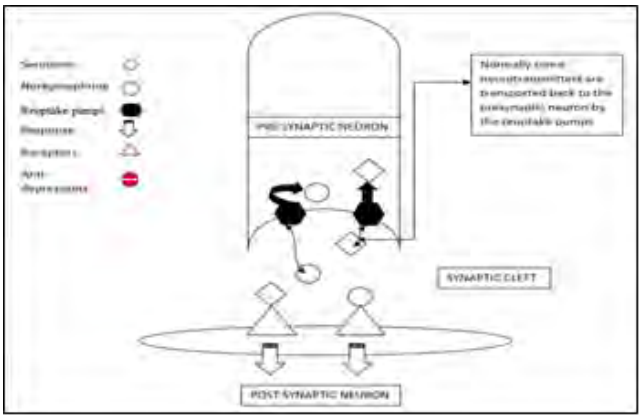

Figure 1: Normal reuptake mechanism keeps in check the neurotransmitter concentration in the synaptic cleft

Association Between DES and Depression

Depression as a Psychiatric Disorder

Depression is an idiopathic cognitive disorder caused by a longstanding condition, substance abuse, or a combination of social, economic, and genetic factors.[34,35] It is one of the most common mental disorders, if left untreated it can lead to suicide in the worst case.[36] The exact etiology of depression and its pathophysiological basis need to be elucidated, hence it can be considered simply as a multi-etiological disorder.[34-38] Studies of the

brain have found that the hippocampus, which is a crucial part of the brain responsible for both memory and learning, is primarily affected by stress and depressive states. Therefore, it is a crucial target for antidepressants.[39-41] The biochemical origin of depression is due to the depletion of the monoamine neurotransmitters serotonin, norepinephrine, and dopamine in the brain.[36-42] This is consistent with the primitive monoamine hypothesis based on the mechanism of action of first-generation antidepressants.[43,44] According to the monoamine hypothesis, low monoamine concentration is the most important biochemical factor leading to depression.[36] The monoamine hypothesis was later discarded and replaced by the monoaminergic receptor theory, which held that depression was due to a defect in the postsynaptic monoamine receptors that made them unresponsive to monoamine neurotransmitters. In the 1980s, the monoaminergic receptor hypothesis was developed, which suggested that depression is due to decreased sensitivity of the postsynaptic receptors, which are supposed to bind to the monoamines produced by the presynaptic neuron.[45,46]

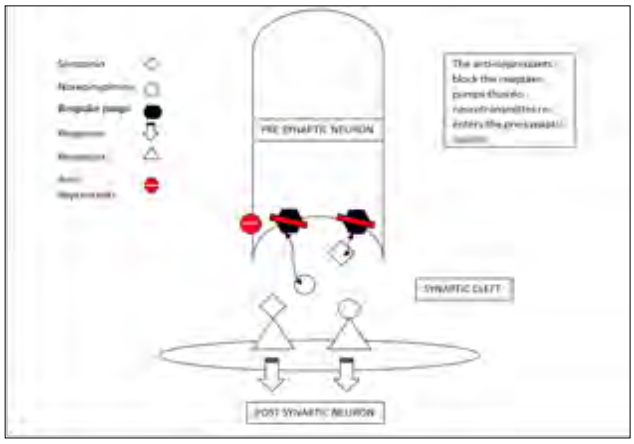

Figure 2: Blockage of reuptake mechanism in presence of antidepressants leads to increase of neurotransmitter concentration in the synaptic cleft

An Overview of Antidepressants

Antidepressants, as the name suggests, are used for the treatment as well as the management of depression.[47] The most prescribed antidepressants are selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressant agents (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and atypical antidepressants. Among these antidepressants, TCAs and MAOIs are prescribed less frequently, and SSRIs and SNRIs are most prescribed to treat depression.[48]

Antidepressants have been divided into three groups: first-generation antidepressants (FGAs), second-generation antidepressants (SGAs), and third-generation antidepressants (TGAs). First-generation antidepressants include TCAs and MAOIs, which were used in the 1960s. Although MAOIs have been extremely influential drugs, however, lack of selectivity and significant adverse effects limited their prescriptions.[49,50] As an alternative, TCAs were introduced which have been used to treat various mental illnesses. However, due to their antagonistic effect on the muscarinic, adrenergic, and histaminergic receptors they have various systematic side effects.[51]

The second-generation antidepressants are jointly known as SGA and include drugs that were primarily developed between the 1980s and 1990s. SGAs include SSRIs, SNRIs, noradrenergic and specific serotonergic antidepressants (NaSSAs), 5-HT2A antagonists-reuptake inhibitors (SARIs), and noradrenaline reuptake inhibitors (NARIs). Due to their minimal systematic side effects, SSRIs are clinical substitutes for TCAs.[52,53] These drugs are used as first-line treatment for depression in both children and adults due to their improved drug safety profile and efficacy.[54] They are prescribed to one in six adults [55,56] and are the most commonly prescribed antidepressants SNRIs, NaSSAs, and NARIs are used as the primary drugs of choice to treat depression. The third-generation antidepressants are called TGAs, and their mechanism of action is based on the non-monoaminergic mechanism.

Mechanism of Action of Antidepressants

Drugs used to treat mental illness significantly affect the nervous system and the release of neurotransmitters.[56] At the synapses of the brain, antidepressants target neurotransmitter pumps and the presynaptic receptors. They regulate the concentration of neurotransmitters at these synapses, altering the signal transduction and downstream secondary signaling pathways, which subsequently leads to long-term

transcriptional changes in enzymes and receptors.[57] Several hypotheses have been proposed about the mechanism of action of antidepressants: (i) monoamine hypothesis-biogenic amine hypothesis, (ii) monoaminergic receptor hypothesis, (iii) signaling adaptation hypothesis, and (iv) neuroplasticity hypothesis. According to the monoamine hypothesis, antidepressants currently on the market act on the principle of inhibition of the reuptake mechanism and affect the concentration of neurotransmitters at the synapses or in the presynaptic neurons.[58] Depression is due to low levels of monoamine neurotransmitters, among which serotonin is one of the most important neurotransmitters targeted by antidepressants.[36] Antidepressants increase serotonin concentration by blocking the reuptake pumps or serotonergic receptors (SERT) in presynaptic neurons.[56] Figure 1 and 2, thereby increasing serotonin levels in the CNS,[56] making it available to postsynaptic receptors for signaling.

The monoamine hypothesis cannot explain the delayed therapeutic effect of antidepressants. The increase in monoamine concentration should have been achieved within a few hours but took longer, so this hypothesis was rejected.[43] The monoaminergic receptor hypothesis has been developed, and according to this hypothesis, antidepressants affect the sensitivity of presynaptic receptors rather than the reuptake mechanism.[45] However, the delayed therapeutic effect could not be understood and this mechanism could not explain the mode of action of all antidepressants, although the mechanism of action of SSRIs and TCAs was consistent with this hypothesis.[32]

The post-synaptic signaling mechanism is based on the signaling adaptation hypothesis which was developed to understand the delayed therapeutic effects of antidepressants. This hypothesis assumes that antidepressants induce adaptive changes in the post-receptor signaling cascades and that these changes occur slowly, leading to the observed delayed therapeutic response.[52] As neuroscience advanced in the 2000s, a more advanced hypothesis emerged the neuroplasticity hypothesis. According to this hypothesis, antidepressants affect neuroplasticity, cellular flexibility, and synaptic plasticity.[39] The neuroplasticity hypothesis explains the multiple mechanisms of the anti-depressant effects.

Regardless of the mechanism of action, antidepressants affect monoamine neurotransmitters. Serotonin is not the only neurotransmitter affected. Other neurotransmitters affected are acetylcholine, dopamine, and norepinephrine/noradrenaline.[37] SSRIs such as direct effect on the serotonergic and cholinergic systems and therefore indirectly affect the dopaminergic and noradrenergic systems.[51] For example, SSRIs such as fluoxetine have an antagonistic effect on one of the serotonergic receptors, thereby indirectly increasing norepinephrine and dopaminergic transmission.[51] Similarly, through its direct anticholinergic effect, paroxetine blocks norepinephrine reuptake and sertraline blocks dopamine reuptake.[56] These drugs have 300- to 3000-fold higher selectivity for the serotonin transporter compared to the norepinephrine transporter, and thus block serotonin reuptake, resulting in an increase in serotonin concentration in the synaptic cleft without blocking activity at the alpha-adrenergic receptors.[60,68] Therefore, they have minimal systemic side effects. SNRIs and TCAs are not SERT specific and can directly block norepinephrine reuptake pumps by a similar mechanism,[49] thus TCAs have more severe ocular side effects compared to SSRIs. TCAs are associated with xerostomia, urinary retention, and constipation which are part of Sjogren's syndrome and thus can lead to DES due to Sjogren's syndrome.[30]

The eye is the second most frequently affected organ by drug poisoning after the liver.[31,32] The eye is susceptible to drugs because of its anatomical or embryological structure. Although relatively small in mass, the eye is blessed with a large and rich blood supply, allowing any chemical in the blood to reach any part of it.[42] Another reason for its medical vulnerability is the eye's visual system, which is made up of multiple tissues lineages. The innermost layer of the eye, the retina which is responsible for vision, is an embryological derivative of the brain ectoderm.[37] Another factor that makes the eye vulnerable to medical side effects is the high rate of metabolism in the eye particularly in the retina and optic disc.[55] The side effects of medicine on the eye can vary in severity. It can range from complete absence to

devastating consequences, and from transient and reversible to completely irreversible.[56]

Antidepressants can cross the blood-brain barrier and enter the central nervous system (CNS), where they enhance their therapeutic effect. They also affect the peripheral nervous system and smooth muscle fibers.[33] Because the eye is an embryonic derivative of the CNS, any psychiatric drug can harm it. All antidepressants have various side effects on the eye.[41] These include DES, decreased accommodation (accommodation is the ability of our lens to change shape depending on our distance from the observed object), blurred vision (mainly with paroxetine), mydriasis (dilated pupils), cycloplegia (ciliary muscle paralysis), ocular dystonia (rarely), optic neuropathy (rare), maculopathy (with sertraline), retinopathy, lid enlargement, and angle-closure glaucoma are most common.[34] Antidepressants that play an important role in triggering DES include TCAs [33,] and SSRIs.[34-38] Error! Reference source not found. lists all drugs that belong to these anti-depressant classes.

SSRIs are known to cause and exacerbate depression due to their impairment of watery and mucous secretion.[29] SSRIs have a direct effect on the serotonergic and cholinergic systems and therefore indirectly affect the dopaminergic and noradrenergic systems.[31] These drugs compete with acetylcholine, a parasympathetic neurotransmitter, for the postsynaptic muscarinic receptors. Since the nervous innervation for tear flow is only parasympathetic and thus competes with acetylcholine, SSRIs interfere with its signaling. This leads to tear film instability caused by decreased signaling to tear secretion.[20] Another possible reason for the occurrence of DES could be the increased serotonin level in the eye.[56] Serotonin in the tear film influences corneal nociceptor sensitization, high serotonin levels decrease corneal sensitivity and tear flow.[25] Elevated levels of serotonin contribute as an ocular surface inflammatory agent and therefore lead to apoptosis in the corneal epithelium, which is a clear clinical sign of DES.[5, 13] To assess the significant changes in ocular structure, tear films of patients consuming SSRIs were examined. Approximately 75% of patients taking SSRIs had tear breakup times of less than 10 seconds and more discoloration of superficial corneal epithelial dots. However, no significant difference was observed in the Schirmer 1 test. These results showed that serotonin largely affected the ocular surface by reducing corneal sensitivity but had no effect on tear production. Elevated levels of serotonin can decrease tear film sensitivity, tear reflexes, and corneal nerve sensitivity, causing DES.[29]

The TCAs have an anticholinergic effect, a serotonergic effect, and an antihistaminic effect, all of which together contribute to DES.[31] TCAs most commonly cause mydriasis and cycloplegia along with blurred vision and/or presbyopia. TCAs antagonism to the noradrenaline\norepinephrine uptake and its effects on alpha-adrenergic receptors stimulate DES and other ocular side-effects. SSRIs have a significantly higher propensity for dry eye syndrome than TCAs.[36]

Preventing Antidepressants-Induced DES

Precaution is the key to avoiding DES, especially when it occurs due to medication. Antidepressants are the only therapeutic indication for the treatment or management of not only depression but other mental health conditions such as anxiety and stress. Patients who are about to start taking SSRIs or other antidepressants should be well-informed about all the details of the drug. Likewise, the psychiatrist should always point out the possible side effects of the drugs and instruct the patient to be aware of any noticeable changes in normal bodily function.[34] A routine ophthalmologic examination to clarify possible ocular side effects is also required. If psychiatrists, optometrists, and patients are aware of all potential side effects of the drugs used and take early precautions, most serious and potentially irreversible eye damage can be prevented.[31-33]

Healthy communication with the patient is the duty of a healthcare professional and is essential to the treatment of the patient.[23] Studies suggest that the behavior of patients and psychiatrists toward each other leads to an increase in the unhealthy use of antidepressants. When taking medication over a long period, psychiatric patients often fail to reveal and explain their visual symptoms in detail.[22-26] This can either be due to patient discomfort towards the psychiatrist or substance abuse or overuse on the part of the patient.[84] But the delayed recognition of

DES makes it chronic and the prognosis is usually delayed, mostly leading to other chronic eye diseases.[18-21]

The ocular side effects mostly vanish by stoppage of the medicines in use but in clinical practice, artificial tears are usually prescribed.[25] Newer antidepressants like SSRIs and SNRIs should be preferred and in the case of TCAs desipramine and nortriptyline should be preferred as they have less anticholinergic side effects.[27] SSRIs are known to cause DES and since SSRIs are the most effective drugs against depression and are used as a drug of choice for the treatment of depression, therefore, their use cannot be discontinued. So, to overcome the anticholinergic side effects of either TCAs or SSRIs it is recommended to use pilocarpine 1% solution 1 drop almost four times daily, cholinergic agents such as bethanechol chloride which is used 10–30mg/day and contact lenses.[26]

But if the complications still exist it is recommended to use other classes of antidepressants like SNRIs which can also inflict DES but to a lesser extent as compared to SSRIs. NaSSAs, SARIs, NARIs, MAO inhibitors, TGAs, and other atypical antidepressants can also be brought into application in case of chronic DES.

Discussion

DES is an ocular syndrome that can lead to other ocular disorders if left unchecked.[1,3] This condition is increasing in developed countries though it is considered multifactorial, and its proper etiology is still not understood.[4] DES is linked with xerostomia, mainly in Sjogren syndrome, which is an inflammatory disorder marked by decreased glandular secretions.[20-22] This association is owing to etiological reasons.[2] DES is managed by tear gel or artificial tears but to treat DES the etiological cause should be eradicated.[19] DES is also an adverse effect associated with the application of antidepressants.[34-38] Depression is one of the most common mental disorders. In scientific language, it is a deficiency of monoamine neurotransmitters such as serotonin, norepinephrine, and dopamine in certain areas of the brain.[42] Depression is treated or combated with antidepressants.[47] The primary mode of action of these drugs, as suggested by the monoamine theory, is to increase the levels of neurotransmitters such as serotonin and norepinephrine.[28]

Researchers in recent years have found that depression is usually followed by DES and that most depressed patients are likely to be diagnosed with DES as an associated eye disease.[29] There are reports of the association between psychiatric disorders and DES.[24-30,31] In research DES in patients with depression has been diagnosed as a subjective symptom rather than an objective symptom.[6] It has been hypothesized that DES symptoms are more severe in patients with more severe depressive symptoms since somatic disorders tend to worsen when depression occurs.[13]

Therefore, it was hypothesized that the prognosis of DES in depression patients would be slow. However, research has not observed a significant difference between the prognosis of DES in healthy patients and that in patients with depression.[16] Hence, it could not be understood why depression was associated with DES. Studies showed that the level of serotonin in the tear film was elevated, eventually leading to DES. This showed that antidepressants were a cause of DES in patients with depression,[14] since serotonin level increased is the main function of these drugs to treat depression.[18]

Many studies suggest that DES is related to antidepressant use,[19] however, the link between DES and antidepressants could not be confirmed because only two of the studied population used antidepressants, and even after their removal the test results were not changed since the test was performed on a small number of patients it can be assumed that the results might have been different in a larger number of patients.[3-9] It is not necessary that DES be followed by depression but that depression can lead to DES its biological and pathological components.[6]

DES patients experience lifelong discomfort in their eyes, giving them a constant sense of grief and discomfort, leading to depression.[36] Depression is a common finding in eye patients as it can have a major impact on the patient's life.[37] However, more research is needed to understand the association between depression and antidepressants in DES.

Table 1: List of medicines used for the treatment of depression, leading to dry eyes syndrome

Drug Class	Drug name	Ocular side-effect	Therapeutic indication	Action mechanism	References
TCAs	Clomipramine (Anafranil, Placil), Doxepin (Deptran, Sinequan), Nortriptyline (Allegron, NortriTABS), Imipramine (Tofranil, Tolerade) Dosulepin/dothiepin (Dothep), Amitriptyline (Endep, Entrip), Chlorpromazine	Decreased lacrimation and dry eye, mydriasis, cataracts, blurred vision, corneal edema, corneal epithelial keratopathy, abnormal pigmentation of the eyelids/ conjunctiva or cornea or peripheral retina, and acute angle closure glaucoma due to pupil block.	Neuropathic pain, post-traumatic stress disorder, obsessive-compulsive disorder (OCD), phobias, panic disorders, and generalized anxiety.	Inhibit reuptake of both serotonin (5HT) and nor-adrenaline/nor-epinephrine into pre-synaptic nerve terminals by acting on serotonergic receptors (SERT) and alpha-adrenergic receptors.	(34-38, 42, 52, 53, 56)
SSRIs	Escitalopram (Lexapro), Fluoxetine (Fluotex, Lovan, Prozac, Prozet, Zactin), Fluvoxamine (Facerin, Luvox, Movox, Voxam), Sertraline (Eleva, Sertra, Sertracor, Setrona, Xydep, Zoloft), Paroxetine (Aropax, Extine, Paxtine, Roxet, Roxtine), Citalopram (Celapram, Celica, Cipramil, Talam)	Dry eye, mydriasis, intraocular pressure elevation, acute angle closure crisis Rare: ocular dystonia, oculogyric crisis, diplopia, optic neuropathy, maculopathy (sertraline), eyelash loss (escitalopram)	Generalized anxiety disorder, bipolar depression, OCD, panic disorders, post-traumatic stress disorder, and social phobia	Inhibit reuptake specifically of 5HT by binding to SERT	(34-38, 42, 52, 53, 56)

Conclusion

Systemic side effects can also occur during therapy in people suffering from depression. Disorders such as DES, in particular, are common in people with depression and are often associated with the use of antidepressants. To mitigate these issues, raising patient awareness and maintaining a strong patient-physician relationship are vital to not only combat depression without relying solely on antidepressants but also to prevent potential side effects such as DES. Physicians must carefully evaluate patients prescribed antidepressants and educate them about potential visual effects to allow for timely detection and treatment. Emphasizing a proactive approach, avoiding depression altogether, and adopting a healthy lifestyle are important steps in protecting against associated pathologies. By recognizing the complex relationship between mental health and eye health, one can empower patients to take responsibility for their well-

being and embark on a journey of individual healing and resilience. Together, we can envision a future where comprehensive care and patient-centered strategies lead to better, healthier, and more fulfilling lives for those struggling with depression and its complexities.

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SHORT COMMUNICATION

Development of clinical reasoning skills through strategic questioning

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A B S T R A C T

Introduction: The ability of healthcare professionals to use clinical reasoning skills effectively is essential for making decisions in clinical settings. It is a general observation that nursing graduates possess adequate knowledge, but they lack clinical reasoning skills. This study aimed to assess the effectiveness of strategic questioning in improving the clinical reasoning skills of nursing students.

Methodology: A quasi-experimental study was conducted at a private-sector university in Islamabad, Pakistan. In total, 24 students were included in the study who were enrolled in the Medical and Surgical Nursing course in the undergraduate nursing program. The students were allocated to an experimental (12) and a control (12) group. The experimental group was provided with strategic questioning developed based on Bloom's taxonomy and the comparison group was taught through traditional questioning methods. The intervention was done for two weeks and post-intervention scores of clinical reasoning were compared in both groups.

Results: After the intervention, the mean score on the Nurse Clinical Reasoning Scale (NCRS) for the experimental group was 63.50 to the comparison group which had a mean score of 57.25 and the mean difference was statistically significant.

Conclusion: Strategic questioning is an effective teaching-learning strategy that improves the clinical reasoning skills of nursing students in the clinical areas.

Keywords: *Clinical reasoning, strategic questioning, quasi-experimental.*

Introduction

The scope of nursing has expanded during the last decades which has brought huge responsibility as well.[1] Nurses make decisions that can affect patients' health. These decisions must be evidence-informed to ensure patient safety and quality care. To connect the dots and make the links to understand the patient's condition, and make the right clinical decisions, nurses must possess clinical reasoning. It is a unique dynamic process that facilitates a deeper analysis of patient's health issues thus enabling safe nursing care. Nurses develop these skills during their studies in nursing schools and colleges Therefore, the responsibility of developing clinical reasoning skills among the students is on the nursing educators.[1] Nurses with clinical reasoning skills can provide timely individualized care which is vital for patient safety therefore they need to possess these skills before entering the clinical field.[2, 3] Nurse educators play an important role in developing clinical reasoning skills among students through the effective utilization of teaching-learning strategies in their teaching practices.[4] A focused

approach to nursing education on clinical reasoning skills can improve the ability to deal with complex clinical situations.[5] Clinical reasoning is defined as the thinking processes related to making a judgment or a decision.[5]

Clinical reasoning models in medical education elaborate clinical reasoning into three different contexts that are as a cognitive skill, knowledge formation, and a complex process.[6,7] Similarly, in nursing education clinical reasoning is viewed as a logical thinking process to analyze a clinical situation and the application of the thinking process in clinical situations.[8] These concepts of clinical reasoning are utilized by educators in their teaching and learning practices to develop clinical reasoning skills in students. Hence, a focused approach to nursing education on clinical reasoning skills can improve the ability of nurses to deal with complex clinical situations.[9]

Table 1: Strategic Questions

1.	What significant findings did you find on interviewing/history taking?
2.	What are your assumptions about the medical diagnosis of this patient based on history findings?
3.	What additional assessment considerations are required to confirm your assumption about the medical diagnosis of this patient?
4.	What lab investigations are required to monitor the overall functional status of a patient with liver disease?
5.	Why spironolactone is being administered to this patient?
6.	The dietitian has advised 3 egg whites daily for breakfast to your patient. What type of diet it is?
7.	Your patient's serum albumin is 3. What dietary interventions are required to improve albumin levels?
8.	What will be the priority patient education point?
9.	How these functions of normal kidneys are affected as a result of renal failure?
10.	How dialysis will help to manage a patient's clinical manifestations of renal failure?
11.	Your patient's Hb is 10. What interventions are required to improve the Hb level?
12.	The consultant has ordered to monitor the daily weight and intake output of this patient. Do you agree with this order /what could be the outcome?

Strategic questioning involves the purposeful and deliberate formulation of questions to stimulate the critical thinking of students.[9] The effective use of this strategy not only facilitates students' engagement in learning but also inculcates curiosity and critical thinking in them.[10] Use of memorization questions in teaching can hinder the clinical reasoning skill of the students and educators are suggested to use strategic questioning as a strategy to develop higher-order thinking among the students.[11] Therefore, this research aimed to study the effectiveness of strategic questioning based on Bloom's Taxonomy in improving the clinical reasoning skills of nursing students during clinical teaching.

Hypothesis

Ho: There is no significant difference in mean clinical reasoning between the groups.

H1: There is a significant difference in mean clinical reasoning between the groups.

Methodology

A post-test-only quasi-experimental method was used to conduct the study. The sample size included 24 students and was calculated using open epi, using CI 95%, Power of 80, and difference in group mean of 5. The students were doing medical-surgical clinical rotations in two groups and two clinical facilitators were supervising a group of 12 students. The group was selected conveniently. The 12 students rotating in Unit A were considered as the experimental group and the 12 others rotating in Unit B were considered as the comparison group. PI accompanied the clinical facilitator of the intervention group to implement a strategic questioning strategy, whereas other clinical facilitators used a questioning strategy without any preparation.

As shown in Table 1, the PI developed strategic questions keeping in mind the potential clinical cases and learning objectives by utilizing Bloom's taxonomy. These questions were asked by the students in the interventional group during clinical teaching. This intervention lasted for two weeks. After two weeks, through a self-administered

clinical reasoning scale, each clinical facilitator received students' responses in their post-conference. The clinical reasoning scale is an adapted 15-item scale with a Likert scale 1- strongly disagree, to 5-strongly agree. The score on the scale ranges from 15-75, higher score shows a high level of clinical reasoning. This scale was opted for since the items were relevant and applied in clinical teaching of the Adult Health Nursing course in year II. Furthermore, it is a valid and reliable tool with a Cronbach's alpha of 0.94.[12] The data obtained from the two groups were analyzed with the help of SPSS.

Approval was obtained from the head of the department. Written consent was taken from the study participants and verbal consent was obtained from one clinical facilitator. In addition, codes were used to maintain the confidentiality of the participants. All data were kept in locked files to ensure the privacy of the participants.

Results

The participants were second-year nursing students, twenty (20) of them were female and only four (4) were male with a mean age of 20. The data on clinical reasoning was analyzed using SPSS. A T-test for two independent samples was applied to compare the mean scores of clinical reasoning. The mean score for the experimental group was 63.50 with the total score being 80, with a standard deviation of 4.52. On the other hand, the comparison group had a mean score of 57.25 with a standard deviation of 5.66.

Table 2: Group Statistics

	Grouping	N	Mean Score	Standard Deviation
Clinical Reasoning	Interventional Group	12	63.50	4.52
	Comparison Group	12	57.25	5.66

The t value is 2.89 with a Standard Error Difference of 2.0 at the confidence interval (CI) of 95%. The p-value is 0.007 which is less than 0.05 which means that the mean difference in NCRS core between the experiment group and comparison group is statistically significant, therefore we reject our null hypothesis.

Discussion

Nurses need to make bedside decisions for patients that can be critical for their health outcomes. These clinical decisions require sound clinical reasoning. Bedside nurses must have clinical reasoning skills to provide safe and quality care to their patients. This skill must be learned by every nursing student at the nursing college and it is the educators' responsibility to instill this skill in them.

However, nursing educators in Pakistan are rarely equipped with the nuances of teaching and learning. Most of the educators have switched to teaching without any additional degrees in education. On top of it, continuous faculty development programs are non-existent. Therefore, nursing educators aren't aware of the importance of strategic questions in enhancing critical thinking and clinical reasoning skills. The results of this study depicted that strategic questioning can be instrumental in developing clinical reasoning among students. Our results correspond with other findings in the literature.[9-11]

It is recommended that the universities and colleges must develop their faculty members through diploma and certificate courses in education and teaching-learning exclusively to instill essential skills into the students. It is the only way to produce nurses with sound clinical reasoning to ensure safe nurses and safe patient care to the minimum.

Limitations

Self-administer scale was used to evaluate the clinical reasoning skills of the nursing students whereas, more objective assessment tools can be utilized from the educator's end as well. Approval from the ethical review committee was not obtained, however, approval from the head of the department was taken. The sample size was small and the study was limited to a single setting and course, thus the results are far from generalization.

Conclusion

In conclusion, this research project found that strategic questioning improved the clinical reasoning scores of the students. However, large-scale multi-setting studies are required to establish its effectiveness.

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Table 3: Independent Samples Test

		Levene's tests for equality of variances		t-test for quality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error. Difference	95% Confidence interval of difference	
									Lower	Upper
Clinical Reasoning	Equal variances assumed	0.279	0.603	2.989	22	0.007	6.25000	2.09120	1.91312	10.586
	Equal variances not assumed			2.989	20.980	0.007	6.25000	2.09120	1.9008	10.5991

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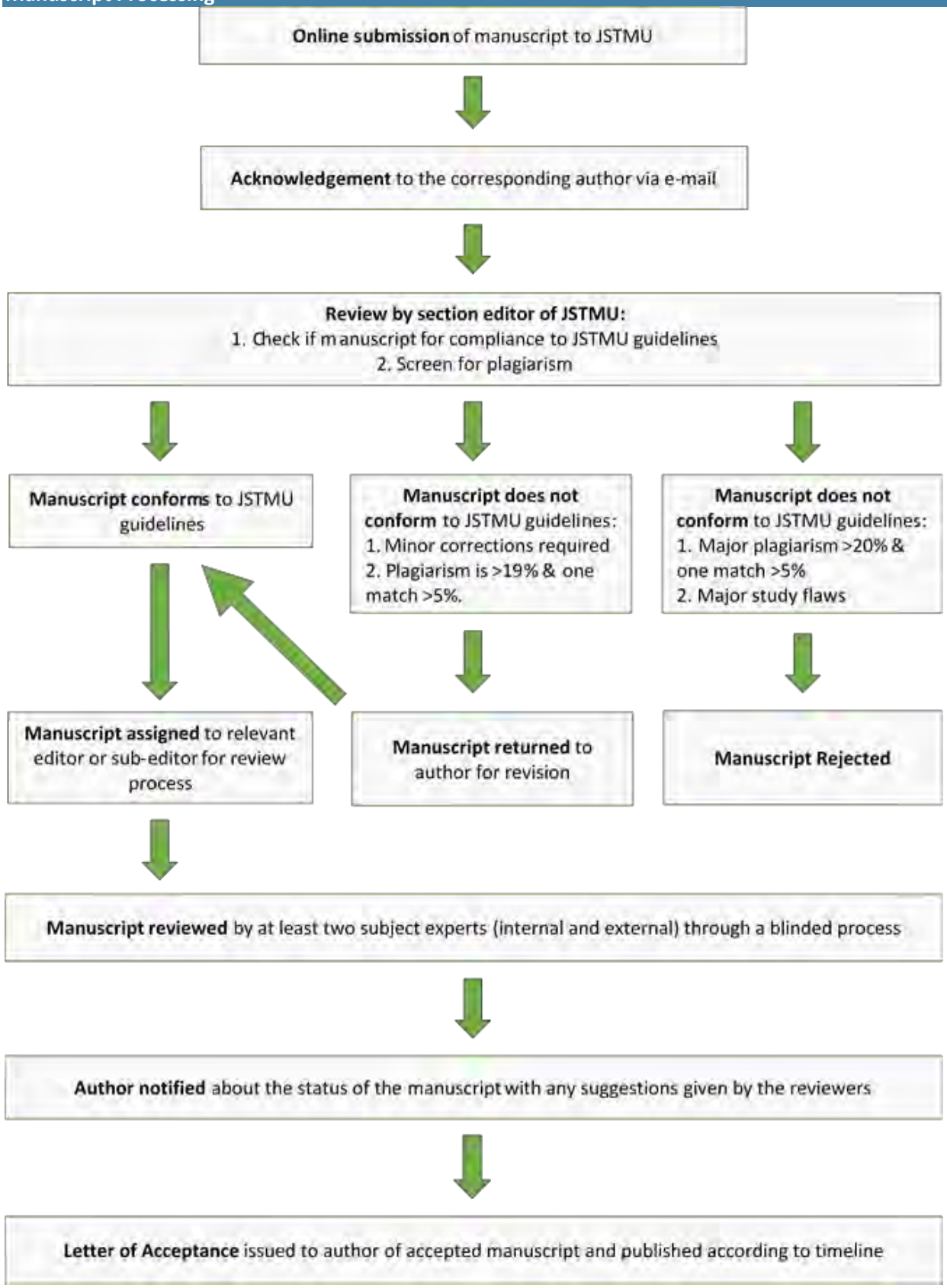

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Reproducibility and Robustness

We believe that the research we publish should adhere to high standards of transparency and robustness in their methods and results. This, in turn, supports the principle of reproducibility, which is a foundation of good research, especially in natural sciences. We achieve this by developing editorial processes and checklists to provide clarity for authors and supporting authors in the reporting of their work. We support the Transparency and Openness Promotion guidelines.

Conflict of Interest

Conflict of interest statement for Authors:

All manuscripts for articles, original research reports, editorials, comments, reviews, book reviews, and letters that are submitted to the journal must be accompanied by a conflict of interest disclosure statement or a declaration by the authors that they do not have any conflicts of interest to declare. All articles that are published in the journal must be accompanied by this conflict of interest disclosure statement or a statement that the authors have replied that they have no conflicts of interest to declare. To facilitate this policy, all authors must disclose 'ALL their potential conflicts of interest' to the editors of the journal at the time of submission. These include all financial and non-financial interests and relationships (see definitions provided a little later in the text), direct employment with a private sector entity (whether full or part-time), and service on private sector and non-profit Boards and advisory panels, whether paid or unpaid. Authors should also disclose any conflict of interest that may have influenced either the conduct or the presentation of the research to the editors, including but not limited to close relationships with those who might be helped or hurt by the publication, academic interests and rivalries, and any personal, religious or political convictions relevant to the topic at hand. In the article, the authors must include a draft statement that discloses all relevant conflicts of interest and affiliations. The relevance of financial conflicts of interest with private firms is defined as a relationship of any value with a firm that has a stake in the subject of the manuscript or its competitors. Relevance for patents is defined as any invention or pending invention connected in any way to the subject.

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We all know that scholarly manuscripts are written after thorough review of previously published articles. It is therefore not easy to draw a clear boundary between legitimate representation and plagiarism. However, the following important features can assist in identifying different kinds of plagiarized content. These are:

Reproduction of others words, sentences, ideas or findings as one's own without proper acknowledgement.

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Poor paraphrasing: Copying complete paragraphs and modifying a few words without changing the structure of original sentences or changing the sentence structure but not the words.

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Authors should avoid citing work solely from one country.

Authors should not use an excessive number of citations to support one point.

Ideally, authors should cite sources that have undergone peer review where possible.

Authors should not cite advertisements or advertorial material.

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Initial decision to review	1-2 weeks after submission
Decision after review	6-8 weeks after submission
Anticipated timeframe for suggested revisions	3-4 months (with flexibility if needed)
Time to online publication	1-2 months after acceptance
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A. Original Research Articles

The Journal considers original articles that are, cohort study, case-control study, clinical trials, intervention study, epidemiological assessment, cross-sectional study, meta-analysis, cost-effective analysis, decision analysis, study of screening and diagnostic test, other observational studies, and qualitative studies such as focus group discussions, in-depth open-ended survey etc. Articles based on thesis maybe submitted provided the data is not more than three years old.

Each original article must contain:

Title page *

Title page should contain the following information:

1. Complete title of the article
2. Name(s) of author(s)
3. Department(s)
4. Institution(s) at which work was performed
5. Official phone/fax number, mobile phone number, personal e-mail address of the corresponding author, and institutions address.

Abstract

The abstract should be structured and NOT more than 250 words. The abstract must be written under the following subheadings:

1. Introduction
2. Objectives
3. Methodology
4. Results
5. Conclusion

Text

Text must be arranged under the following headings:

1. Introduction
2. Methods
3. Results
4. Discussion
5. Conclusion(s)
6. Acknowledgements (if any)

Introduction: Should provide brief review of relevant literature in such a way that it highlights the importance of the study and that the purpose of the study should be clearly stated. The articles used in the review of literature should be properly referenced by Vancouver Style.

Methods: Should include the setting(s), the subjects (participants), sampling methods and sample size, if used, type of study design used, and other procedures that were conducted. The Methods section should be brief, crisp and detailed enough to enable the reader to replicate the study in another setting. Commonly used procedures and methods need not be described but require a reference to the original source.

Results: Should include the factual findings of the research study done and, presented in the form tables or figures. Each table and figures should be properly labelled with headings and numbers (e.g. Table

No. 1, Figure No. 1) on separate pages. The write-up of results in the text should highlight the important findings without duplication of presentations displayed in the tables or figures. *Explanation of the findings should be reserved for the Discussion section.*

Discussion: Should highlight the important findings comparing and contrasting the study's results with that of other similar researches published and it should be appropriately referenced. Discussion should be concise and supported by the presented data.

Conclusion: Is restricted to the study and is drawn from the results and discussion.

Acknowledgements: If any, should be placed at the end of the text and before references.

References: *

References should be cited consecutively in SUPERSCRIPT as NUMERICAL without parentheses and should appear AFTER the punctuation marks (. , ; : ? ! " etc.) in the text/sentence. The final bibliography should be in the order in which they are quoted/cited in the text and written in *Vancouver Style*.

Citation Example:

Equal amounts of dietary carbohydrates have variable blood glucose response considerably as a function of specific food ingested.[1]

Bibliography/References Example:

1. Wolever TMS, Yang M, Zeng XY, Atkinson F, Brand-Miller JC. Food glycemic index, as given in Glycemic Index tables, is a significant determinant of glycemic responses elicited by composite breakfast meals. *Am J Clin Nutr* 2006; 83(6):1306–12.
   DOI: https://doi.org/10.1093/ajcn/83.6.1306

B. Meta -Analysis/ Systematic Reviews

Meta-analysis are systematic, critical assessments of literature and data sources pertaining to clinical topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention, and that includes a statistical technique for quantitatively combining the results of multiple studies that measure the same outcome into a single pooled or summary estimate. All articles or data sources should be searched for and selected systematically for inclusion and critically evaluated, and the search and selection process should be described in the manuscript. Inclusion and exclusion criteria must be mentioned. Details of searching articles and search engines used should be clearly stated. The specific type of study or analysis, population, intervention, exposure, and tests or outcomes should be described for each article or data source. These should be described in the Method section. The data sources should be as current as possible, ideally with the search having been conducted within several months of manuscript submission. Authors of reports of meta-analyses of clinical trials should submit the PRISMA flow diagram and checklist. Authors of meta-analyses of observational studies should submit the MOOSE checklist. Follow EQUATOR Reporting Guidelines. The text **should NOT exceed 6000 words** excluding abstract, references, tables and figures.

Each of the sections of these articles should include specific sub-sections as follows:

Structured Abstract: (Not exceeding 250 words):

1. Objectives
2. Methodology
3. Results
4. Conclusion

Text should be organized under the following headings:

Introduction:

1. Rationale
2. Objectives
3. Research question

Methods:

1. Study design
2. Participants, interventions, comparators
3. Systematic review protocol
4. Search strategy
5. Data sources, studies sections and data extraction
6. Data analysis

Results:

1. Provide a flow diagram of the studies retrieved for the review
2. Study selection and characteristics
3. Synthesized findings

Discussion:

1. Summary of main findings
2. Risk of bias
3. Limitations
4. Conclusions

** For all other information including title page, typing and reference style, please follow the original articles instructions.*

C. Systematic Review (without meta-analysis): Review articles

Systematic Reviews/ review article are critical evaluation and assessments of scientific literature and other sources of data relating to health sciences topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention. Systematic Reviews without meta-analysis are published as Review articles; those with meta-analysis are published as Original Investigations.

Systematic Reviews should include the following:

1. Abstract (Unstructured abstract of no more than 350 words)
2. Introduction (150-250 words)
3. Methods (150-250 words)
4. Results (1000-1250 words)
5. Discussion (1000 words)
6. Conclusions (2-3 sentences)

Maximum length: **Should NOT exceed 3500 words of text** (not including abstract, tables, figures, acknowledgments, references), with no more than a total of 5 tables and/or figures and no more than 50-75 references.

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The journal will consider only those case report/series that represent very rare case(s), or epidemic diseases that are new or emerging, or first observation(s) of some emerging phenomenon or disease. They should have clinical significance and may also include observation of new adverse effect(s) of a drug, vaccine, or procedure or other unique observations, etc. Informed written consent of the patient or next of kin (if patient is not alive or comatose/disabled) should be obtained before submission of the manuscript. A covering letter from the authors that convincingly describe the merits of the case in the light of the mentioned criteria and it's educational or scientific merits should be sent along with the manuscript.

Case Report /case series should contain a single paragraph abstract and text **should NOT exceed 1000 words** (excluding abstract, references, tables and figures) with maximum 10 bibliographic references and either three figures or three tables. Each case report must contain:

1. Abstract (unstructured - should not exceed 120 words)
2. Introduction
3. Case Presentation
4. Discussion
5. Conclusion
6. Competing interest
7. Patient consent

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E. Rapid/Special /Short Communications

Rapid/Special/Short communication should be complete work, such as COMPLETE results of a short RESEARCH study, NOT a preliminary report and **should NOT exceed 1500 words** with one figure and/or one table. An editorial decision will be provided rapidly without reviews.

F. Letters to Editor

Letters should only be written on a specific article in the most recent publication of journal. The letter should be objective and provide constructive opinions offer some academic or clinical interest to the readers.
Letters **should NOT exceed 400 words** of text and 5 references, 1 of which should be to the recent article. It should not have more than 3 authors. The text should include the full name, academic degrees, and institutional affiliation for author and the email address for the corresponding author. Letters considered for publication shall be forwarded to the author of the cited article for possible response. The editor reserves the right to shorten these letters, delete objectionable comments, make other changes, or take any other suitable decision to comply with the style and policies of the journal. For writing and references style, follow the same instructions listed above.

Letter in Reply

Replies by authors should not exceed 500 words of text and 6 references. They should have no more than 3 authors.

G. Editorial

The topics of the editorial are decided by editorial board and/or Editor-in-Chief. Editorial is written either by one member of the editorial board or some expert on that topic invited by the Editor-in-Chief. As a convention, the editorial addresses relevant areas of interest that may pertain to a range of areas influencing health and health care sciences.

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