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EDITORIAL

Research in Undergraduate Medical Education, Why, How, and How Much?

Azhar Rashid

The application of knowledge in medicine requires sound, evidence-based justification for patient care.[1] The rapid and unstoppable evolution of knowledge and ever-changing technologies have created a colossal challenge for medical professionals every day.[2]

The evidence comes from research, and research in turn generates new evidence. It is imperative for the medical practitioner not only to understand research methodologies but also to critically evaluate the existing evidence to confirm its validity and to generate new insights.[3] A study conducted in Germany involving 165 hospitals showed that the survival rate in research-active hospitals is higher than in those that are not.[4]

The realization of the significance of this matter has led to the inclusion of the word 'scholar' in the definition of a 'competent physician'.[5] The Association of Medical Education in Europe (AMEE) includes student research as a component in its Award for Excellence in Medical Education in the category of 'Student Engagement'.[6] Many medical schools have now started teaching research in their undergraduate programs, and it is an integral part of their curriculum in an environment where there is already a dearth of clinical scientists.[7]

Many medical institutions have been imparting education in research for a long time. In the USA, 83.9% of students are engaged in research, while in China and Brazil the figures are 55.1% and 44%, respectively.[6] However, there is a gross difference between high-income countries and low–middle-income countries (LMICs). The USA has 3867 researchers per million, whereas Colombia and Venezuela have 190 and 200 per million researchers, respectively.[3] Publications also increase at the student level when research is taught.[7] Research indicates that individuals who begin publishing earlier in the day produce 1.7 times more publications than those who start later.

There are still few learning opportunities, especially in LMICs. The dearth of clinical scientists indicates that, to ensure patient safety, early research training should be made mandatory for all medical schools.

Apart from early adoption of evidence-based practice and research publication, there are many other advantages to engaging in research. For example, increased publications can facilitate entry into preferred residency programs and may enhance the likelihood of completing Masters and Doctorate degrees in a shorter time frame.[3] Communication skills, teamwork, and leadership abilities are enhanced. [8] Self-efficacy, critical thinking, and reflective skills improve further.[4]

The question of why research should be taught at the undergraduate level is self-explanatory. The more challenging issues are how to teach research and how much should be taught.

It is clear from the literature that early research education is a need of the hour. Different medical institutions adopt various approaches: in some, research is offered as part of electives or as a Student Selective Component (SSC), while others have made it a mandatory, short- or long-term component of the core curriculum.[2]

These programs either teach only basic research via didactic methods with assessments such as Multiple-Choice Questions (MCQs) and quizzes or they offer vertical and longitudinal modules that culminate in the practical application of research skills.[2]

The application of research skills may take the form of projects, poster presentations, conference presentations, or even journal publications.[2,7] Modules that emphasize the application of research skills are far more productive than those relying solely on didactic teaching. For instance, at the University of Free States (UFS) in South Africa, research publications increased significantly,[7] while at Stanford University School of Medicine in the USA, 90% of students participated in research and 75% published at least one article. [3] All these tasks are guided by faculty supervisors and mentors.[1,7]

Undoubtedly, research skills are essential at the undergraduate level in medical schools and should

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ultimately lead to publications. However, all prerequisites for effective research application must be addressed. Although exposure to research modules motivates most students, many remain unaware of its benefits,[8] and some even consider it irrelevant to clinical practice.[6] While mentors and supervisors are crucial, their support alone is insufficient. Students face a high cognitive load and limited time, leaving little room for additional learning. Moreover, a lack of adequate funds and resources especially in LMICs further hinders progress.[3]

Although Pakistan recognizes the need for undergraduate research, its full depth and significance remain underappreciated. The Pakistan Medical & Dental Council (PM&DC) has incorporated research methodology into the curriculum; however, practical application of research is still lacking.[9]

In conclusion, the inclusion of vertical research modules in the core curriculum is imperative. Every medical student should participate in a research project and aim to publish an article either individually or as an active member of a group. Although challenges such as limited resources, funds, time, and space persist, neglecting this critical aspect will adversely affect patient safety and impede the advancement of new knowledge.

We must recognize the significance of undergraduate research and its clinical and practical applications. As the saying goes, difficult things take a long time, and impossible ones take a little longer.

REFERENCES

1. Mahomed S, Ross A, Wyk JV. Training and assessing undergraduate medical students' research: Learning, engagement and experiences of students and staff. *Afr. J. Prim. Health Care Fam. Med.* 2021 Jan 15;13(1):2559. doi:10.4102/phcfm. v13i1.2559.
2. Lee GS, Chin YH, Jiang AA, Mg CH, Nistala KR, Iyer SG et al. Teaching medical research to medical students: a systematic review. *Med. Sci. Educ*. 2021 Apr; 31:945-62. doi: 10.1007/s40670-020-01183-w.
3. Mass-Hernández LM, Acevedo-Aguilar LM, Lozada-Martínez ID, Osorio-Agudelo LS, Maya-Betancourth JG, Paz-Echeverry OA et al. Undergraduate research in medicine: A summary of the evidence on problems, solutions and outcomes. *Ann. Med. Surg.* 2022 Feb 1;74:103280. doi: 10.1016/j.amsu.2022.103280.
4. Burney AA, Burney IA, Dherwani K. Undergraduate research in medical schools in Pakistan: Relevance, Needs, and Importance. *Pak. J. Med. Sci.* 2023 Sep;39(5):1542. doi: 10.12669/pjms.39.5.7137.
5. Council GM. Tomorrow's doctors: outcomes and standards for undergraduate medical education. Manchester, UK: General Medical Council. 2009 Sep.
6. Zhang G, Wu H, Xie AN, Cheng H. The association between medical student research engagement with learning outcomes. *Med. Educ. Online.* 2022 Dec 31;27(1):2100039. doi: 10.1080/10872981.2022.2100039.
7. Joubert G, Steinberg WJ, van Rooyen FC. Twenty-one Years of Undergraduate Medical Student Research Training at the University of the Free State (UFS), South Africa. *Med. Sci. Educ.* 2024 Dec;34(6):1343-51. doi: 10.1007/s40670-024-02107-8.
8. Burgoyne LN, O'Flynn S, Boylan GB. Undergraduate medical research: the student perspective. *Med. Educ. Online.* 2010 Jan 1;15(1):5212. doi: 10.3402/meo.v15i0.5212.
9. Pakistan Medical & Dental Council. Guidelines for Undergraduate Medical Education (MBBS) Curriculum.– 2024. Available from URL: https://pmdc.pk/Documents/Others/ PM&DC%20GUIDELINES%20FOR%20UG%20M.EDUCATION-06242024035407.pdf

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EDITORIAL

Artificial Reproductive Technology (ART) in Pakistan: A Need for Shariah Compliant Medico-Legal Framework

Muhammad Faeq[1], Saadia Sultana[2]

Introduction

Artificial Reproductive Technology has proved to be the medical technological solution to infertility. As defined by World Health Organization (WHO) "**Infertility** is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse". The global percentage of infertility has risen to 17.5% approximately, that pushed practitioners to introduce a viable solution to surmounting conceptional challenges. However, the application of ART raises complex dilemmas in Pakistan, where people are culturally family oriented, and religiously more sensitive to the susceptibility of new medical intervention that challenges progeny (lineage) and sanctity of marriage. In this editorial, I will reflect on Artificial Reproductive Technology (ART) with other associated procedures from Islamic jurisprudential aspect to ensure transparency between the religious misconceptions and established rulings.

Artificial Reproductive Technology

The American Centre of Disease Control (CDC) confined ART to handling embryo or egg for fertility treatment. Hence, handling only sperm for treatment does not fall under the ART category such as intrauterine insemination (IUI) technique. Nevertheless, ART in normative concepts among patients and in clinical practices, extends to all modalities of treating infertility.

The most common type of ART is **in vitro fertilization (IVF)** where eggs are retrieved from ovaries, fertilized with sperm in a laboratory and the resulting embryos are transferred to the uterus. The Islamic law does not frown on the simple technique used for conceiving, if it is performed between the wed-locked couple under Islamic law. On the other hand, situations where the wife (female) or the husband (male) seeks help from third-party sperm, ovum, or uterus, lead to certain important Islamic questions in context of the permissibility of ART and its associated modalities. The handling of gametes for treatment, with or without wedlock, comes under ART-IVF, whereas the commissioning of third-party uterus known as Surrogacy.

Surrogacy:

The surrogacy classifies into partial and complete. In partial surrogacy, the husband's semen is used to impregnate a commissioned or solicitous woman artificially to form a single parent child. In complete surrogacy the couple undergo IVF followed by commissioning a surrogate mother for embryo transfer.

The probabilities of the use of gametes and uterus can be found under Table I, II and III Below:

Table I:

Male Sperm Fused with Female Egg by IVF Method			
(a)	Donor Sperm	Wife Egg	wife womb
(b)	Husband Sperm	Donor Egg	
(C)	Donor Sperm		

Table II:

Male Sperm Fused with Female Egg by IVF Method			
(a)	Husband sperm	Wife Egg	Womb of Surrogate Mother
(b)	Husband Sperm	Donor Egg	
(C)	Donor Sperm	Wife Egg	

Table III:

Male Sperm Fused with Female Egg Single Parent/Couple			
(a)	Father Sperm	Partial Surrogate mother egg	Womb of Surrogate Mother
(C)	Donor Sperm	Mother Egg	

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Shariah Verdict on ART and Surrogacy

Islam encourages to have children and considered them adornment of this world. In the prophetic tradition *(Hadith)* the Holy Prophet (PBUH) said: "Marry the kind and fertile women who will give birth to many children for I shall take pride in the great numbers of my ummah"

Most Islamic Fiqh Councils and prominent Islamic jurists around the globe, including Mufti Muhammad Taqi Usmani, from Pakistan, are of the position that, in necessity with complete abidance by Islamic rulings, undergoing the ART procedures:

1. Using Islamically married couple's **own gametes** with Embryo Transfer into the **wife's uterus** is permissible, provided that the treatment is performed on the medical grounds by an expert physician.
2. Using IUI technique for administering **husband's semen** into the **wife's uterus** during Islamically valid marriage contract is permissible.

All other probable modalities or circumstances, that involve **third-party gametes,** or **uterus**, mentioned in Table 1, 2, and 3 are strictly **impermissible** *(Haram)***.** If a couple still choses partial or complete surrogacy despite its prohibition *(Hurmah)*, the motherhood of the child belongs to the **"Surrogate Mother"** as mentioned in the verse of the Holy Quran "None can be their mothers except those who gave them birth". The Federal Shariat Court of Pakistan opted the same stance in 2015 by usurpation the right of custody of the surrogate child from the zygotic parents.

With regards to zygote intrafallopian transfer (ZIFT), gamete intrafallopian transfer (GIFT), and artificial insemination (AI), the Islamic ruling remains akin to IVF despite their minor procedural changes for medical purposes.

Cryopreservation

As, Centers for Disease Control and Preservation (CDC) considers cryopreservation as part of ART, it is appropriate to mention its purpose and Islamic findings.

Cryopreservation technology is the freezing of gametes, pre-embryos and zygotes and it injunct no of Islamic ruling in itself. Egg-freezing technology is permissible for medical reasons, such as chemotherapy and radiotherapy, that preponderantly effect gonads from its exposure to it. **In all medically assisted permissible conceptions, use of frozen or unfrozen egg or sperm falls into prohibition right after the end of valid Islamic marriage contact *(Nikah)* either by death or divorce of any of the two from couples**, let alone the impermissible modalities that are already forbidden.

Contrary to medical purposes cryopreservation, the social use of this technology is highly discouraged for the prevention of contamination and gametes trading. That is also because egg or sperm banks are a risk to lineage preservation, a key objective of Islamic law (*Maqasid Al-Shariah),* therefore establishment of cryopreservation banks (sperm banks or egg banks) are strictly forbidden.

Islamic Viewpoint on Preimplantation Genetic Diagnosis (PGD) in IVF

Gender prioritization has always been the challenge from centuries and Islam discourages it ever since the females were buried alive.

That being said, the gender selection in IVF for non-medical reason is rendered impermissible due to the interference in the decree of Allah SWT and tampering its creation. Similarly, opting abortion after post-pregnancy parental screening is forbidden (*Makrooh- e-Tehreemi*)

The **permissible use** of PGD in sex-selection is a preponderant conference to a high-risk of a severe genetic condition. If a particular disorder invades X chromosome more than Y, or vice versa, the removal of one or two cells from an embryo at the third day of IVF developmental stage can be performed after blastomeres biopsy for genetic testing. Therefore, there is a leeway for medically necessitated sex-selection, hence PGD is permissible for that purpose alongside.

Integrated Islamic Medical Frame Working for Patient Centered Care

In Pakistan, patients seeking ART procedure are predominantly Muslims. While there are various avenues of patient-centered care, holistic care stands out as a Muslim from the outset to the conclusion. For that reason, there is a need of Islamic medical holistic approach to form a shariah-compliant, patient centered guidelines for ART clinics and hospitals.

Malaysian authors have collected several key questions that were posed by the Muslim patients while undergoing ART procedures. Although those

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questions were originally planned for survey, nonetheless, they have revealed a promising direction towards commencing integrated framework by fostering collaboration between doctors and Islamic jurists. Below are the areas yet to be covered comprehensively by keeping the medical opinion, procedure, and its viability unchanged.

Question Regarding Family Law

1. In what conditions are couples allowed to take fertility treatment?
2. Is the presence of the female/male chaperone mandatory during medical procedure and IVF/ICSI insemination process?
3. Is masturbation for derive seminal fluid sample permissible?
4. What are the implications of masturbation for seminal fluid sampling in Ramazan?
5. Is it allowed to freeze excess seminal fluid samples in Muslims and Non-Muslims cryopreservation banks?
6. Is husband's permission necessary for wife to have contraceptive pills to regulate menses before ART

Questions Regarding Social Law

1. What is Islamic perspective for women opening private parts *(Aurah)* for male doctors during consultation, ultrasound scan, and vum pick-up?
2. Is sharing a husband's infertility issues with the doctors without his consent permissible?

Questions about Acts of Worship *(ibadah)*

1. To perform ibadah after vaginal scan, ovum pick-up, and embryo transfer (RT), Is ablution (wudu) be mandated or complete body wash *(ghusl)*
2. Does undergoing vaginal scan, OPU and IUI invalidate fast?
3. Can patients pray after OPU despite bleeding?
4. Does taking non-halal infertility drugs permissible and

Questions about Systemic Flaws

1. What is the fate of the accidental mixing of the seminal fluids of different patients?
2. What could be the Islamic injunction on accidental sample switching during IUI?

After precisely mentioning the above questions, the importance of drawing guidelines becomes evident. **ART clinics are encouraged to collect questions from their patients considering all areas of Islamic teachings and prepare question bank to form reliable patient-centered Islamic guidelines**

Four Domains of Framework

1. Legislation and Governance is required for the enactment of laws regulating ART to ensure Shariah Compliance on a national level.
2. Ethical Oversight Committee on a national level must be formed comprising medical professionals, Islamic scholars and legal experts to monitor ART practices.
3. Public Awareness to eliminate misunderstandings of ART procedurally (such as IUI considered as pregnancy injection specially in the rural area) and clarify the Islamic status of the technology.
4. Establishment of the Medical Accountability stringent policies on ART to prevent commercial exploitation, genetic modification abuse and unislamic use of ART.

Conclusion

Artificial Reproductive Technology (ART) stands to be the promising solution in alleviating the suffering of infertility. To yield legitimate *(Halal)* results in the form of newly born human-being, the procedure must be restricted to the married couple during the marital period without the help of third-party gametes or uterus.

With the established tenets of Islamic law, extrapolated from the Holy Quran and Prophetic Tradition (Hadith), there is a pressing need for a comprehensive shariah compliant medico-legal framework for ART. Such a framework will play a crucial role not only in safeguarding progeny *(*lineage*)* but also ensure the standardization of the clinical practices that covers all areas of Islamization, coupled with patient-centered approach in Pakistan.

REFERENCES

1. Holy Qur'an 58:2.
2. Abu Dawood. Sunan Abi Dawood. Riyadh: Maktibt Al Maaref; Hadith 2050.
3. World Health Organization. Infertility Prevalence Estimates, 1990-2021. Geneva: World Health Organization; 2023. ISBN 9789240068315.
4. Al-Bar MA, Chamsi-Pasha H. Contemporary Bioethics: Islamic Perspective [Internet]. Cham(CH):Springer;2015. Chapter11,AssistedReproductiveTechnology:IslamicPerspe

ctive.2015May28. Availablefrom:https://www.ncbi.nlm.nih.gov/books/NBK500175/ doi:10.1007/978-3-319-18428-9_11.

5. Resolution No. 16 (4/3). Test-Tube Babies (In Vitro Fertilization). The Council of the International Islamic Fiqh Academy of the Organization of the Islamic Conference; 1986 Oct 11-16; Amman, Jordan.
6. Z, A. M., Y, . Z. S., S, . M. ., IH, A. I. ., & L, A. (2014). Is Assisted Reproductive Technique Shari'aa-compliant? A Case Study at a Fertility Centre in Malaysia *IIUM Medical Journal Malaysia*, *13*(2). doi.org/10.31436/imjm.v13i2.473.
7. Federal Shariat Court of Pakistan. Shariat Petition No. 2/l of 2015. [Judgement].
8. Usmani MM. Fatawa Usmani. Vol 4. Karachi (Pakistan): Quranic Studies Publisher; 2016 Nov. p. 238-326.

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ORIGINAL ARTICLE

Migraine Prevalence and Productivity Impact in Healthcare Professionals: A MIDAS Assessment

Maheen Asim[1], Rabbia Aslam[2], Sadaf Nasir[3], Khawar Shabbir[4], Mehdi Naqvi[5], Safeena Hameed Qureshi[6]

ABSTRACT

Objective: To detect the frequency of migraine headaches among healthcare professionals and to determine the associated triggering factors and level of functional disability using the Migraine Disability Assessment Score (MIDAS).

Study Design: Descriptive Cross-sectional study design.

Place and Duration of Study: Federal Government Polyclinic Hospital, Islamabad, from 1st July 2023 to 30th December 2023.

Materials and Methods: After obtaining informed consent, 283 healthcare professionals experiencing headaches were included using convenience sampling, regardless of their gender or department. The demographic details were documented on a proforma, and migraine was diagnosed according to the International Classification of Headache Disorders (ICHD-3) criteria.

The disability due to migraine was then determined by calculating the migraine disability assessment score (MIDAS) score. The data analysis was done using the Statistical Package for the Social Sciences (SPSS) version 24.0. The descriptive statistics were expressed using frequency/percentage and mean/standard deviation.

Results: Based on the ICHD-3 criteria, 84 (29.7%) respondents were found to have migraine. The most common triggering factor was stress (73.8%) followed by sleep disturbances (56%), noise (39.3%) and fatigue (35.7%). Most of the respondents with migraine had Grade IV MIDAS score (32.1%) - indicating severe disability followed by Grade III (29.8%), indicating moderate disability.

Conclusion: The prevalence of migraine in healthcare workers is very high, and it is associated with significant disability that negatively impacts our healthcare system. The majority of healthcare workers experience moderate to severe disability due to migraine, with stress and sleep disturbances being the most common triggering factors.

Key Words: *Migraine, Headaches, Migraine Disability Assessment Score, MIDAS, Healthcare Professionals.*

Introduction

Migraine, a primary headache disorder marked by recurring episodes of moderate to severe intensity, is a prevalent health condition. Globally, its estimated prevalence is 14–15%, and in terms of burden, migraine contributes to 4.9% of global ill health measured as years lived with disability.[1] In Pakistan, a study was done to assess the prevalence of migraine in the general population. Out of 986 participants, 393 individuals were diagnosed as migraine. Notably, most of these individuals were young females, indicating a higher prevalence of migraines in this demographic within the sampled population.[2] Migraine greatly affects the quality of life leading to significant disability, impaired work at home & workplace and disrupted family & leisure activities. It is also a major cause of depression, anxiety and sleep disturbances in people experiencing migraine.[3] Another study from Korea also showed increased migraine related disability over time due to missed days from work or education.[4] In addition, migraine is also a contributor to significant financial burden for the individual and the healthcare system. It includes consultation fees, drugs, hospital stays and absence/impaired work.[5]

There are many known trigger factors for migraines such as weather changes, intense physical exertion, sensory stimuli such as strong smells or flashing

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lights, alcohol, caffeine, menstruation, menopause, pregnancy, medications such as oral contraceptive pills, salty foods, food additives and cheese. But of all these triggering factors, sleep deprivation, emotional & physical stress and skipping meals are among the most frequent causes.[6] Migraine triggers extend beyond biological factors, with occupational elements playing a substantial role. The demanding nature of healthcare professionals, such as those of doctors and nurses, heightens stress levels, creating an environment conducive to migraine onset. Moreover, irregular sleep patterns and infrequent meals, consequences of the demanding work schedules and on-call hours inherent in healthcare roles, further amplify these challenges.[7]

In Pakistan, studies have been conducted addressing migraine in the general population and medical students. However, one study conducted in Faisalabad determined the prevalence of migraine among physicians and medical students. But it didn't include nurses and failed to address the impact of migraine on their productivity. Migraine can affect individuals from all aspects of life, but healthcare professionals are particularly susceptible to develop migraine.

Our study was designed to detect the frequency of migraine among healthcare professionals including consultants, resident doctors and nurses in Pakistan and determined its triggering factors and impact on their productivity. By understanding how migraines affect the productivity of doctors and nurses, we could gain insight into their broader effects on the healthcare system. This study might set the foundation for future research, fostering awareness about migraine-related disabilities, and contributing to the development of effective treatments and preventative measures. It might have implications for stress management, and public health interventions tailored to address the needs of the healthcare workers.

Materials and Methods

This cross-sectional descriptive study was conducted at Federal Government Polyclinic Hospital, Islamabad, from 1st July 2023 to 30th December 2023. The study was approved by the Hospital Ethical and Research Committee (Ethical Approval Number: FGPC.1/12/23). A sample size of 283 healthcare professionals was estimated using a 24.4% prevalence of migraine among doctors and medical students and a 5% margin of error.[8] The participants were recruited using convenience sampling. After obtaining informed consent, healthcare professionals experiencing headaches were included, regardless of gender or department. Healthcare professionals unwilling to participate or those who did not experience headaches were excluded. The demographic details of the participants were recorded on a proforma, and migraine was diagnosed according to the International Classification of Headache Disorders (ICHD-3) criteria. The disability due to migraine was determined by calculating the Migraine Disability Assessment Score (MIDAS). A score of 0–5 was classified as little or no disability (Grade I), 6–10 as mild disability (Grade II), 11–20 as moderate disability (Grade III), and >20 as severe disability (Grade IV). The participants provided information on the frequency of headaches during the three months preceding the study, and headache intensity was evaluated using a visual analogue scale (VAS). Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 24.0. Descriptive statistics were expressed as frequencies/percentages and means with standard deviations.

Results

Among 283 participants, 174 (61.5%) were female and 109 (38.5%) were male. There were 43.1% (122) respondents from the department of Internal Medicine, 15.9% (45) were from General Surgery, 7.8% (22) from Obstetrics & Gynaecology and 33.2% (94) from other specialties. Mean age of the respondents was 29.8$\pm$ 7.7 years. Based on the ICHD-3 criteria, 84 (29.7%) respondents were found to have migraine. The average daily working hours of those with migraines were calculated as 7.5 $\pm$ 2.1 hours. 4.8% of those with migraines were smokers. 38.1% of them had positive family history for migraines as well.

The most common triggering factor of migraine was stress (73.8%) followed by sleep disturbances (56%), noise (39.3%) and fatigue (35.7%). The triggering factors of migraine are shown in Table I.

Among these, the disability due to migraine was then determined by calculating the MIDAS score. Most of the respondents with migraine had Grade IV MIDAS

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Table I: Frequency of Different Triggering Factors for Migraines among The Respondents

Triggering Factors for migraines	Frequency (N)	Percentage (%)
Stress	62	73.8
Sleep disturbances	47	56.0
Loud noise	33	39.3
Fatigue	30	35.7
Travelling	24	28.6
Excess screen time	23	27.4
Dieting or missed meals	22	26.2
Dehydration	21	25.0
Menstrual periods	19	22.6
Certain smells	8	9.5
Bright sunshine	7	8.3
Certain foods (chocolate / caffeine)	4	4.8
Weather change	4	4.8
Exercise	2	2.4
Pregnancy	2	2.4
Oral Contraceptive pills	1	1.2
Other hormonal medications	1	1.2
Sexual activity	1	1.2

score (32.1%) showing severe disability followed by Grade III (29.8% indicating moderate disability) (Table 2).

Table II: MIDAS Score of Respondents with Migraines

MIDAS Grading	Frequency (N)	Percentage (%)
Grade I (0-5)	18	21.4
Grade II (6-10)	14	16.7
Grade III (11-20)	25	29.8
Grade IV (21+)	27	32.1

Discussion

Our results revealed a high frequency of migraine (29.7%) among healthcare professionals. This prevalence underscores the importance of understanding the specific challenges faced by healthcare professionals grappling with migraines. Our results are similar to another study conducted in Faisalabad in which the prevalence of migraine among physicians and medical students was found to be 24.4%.[8] Evers *et. al*.,[10] found that chronic migraine has a higher prevalence among doctors with the highest frequency in headache specialists (53.0%) and neurologists (43.0%). In another Egyptian study, migraine was reported in 17.9% of medical students.[11] In Pakistan, most of the studies are conducted on medical students. Jamali *et. al*.,[12] found that migraine prevalence is significantly high among the Pakistani population, especially among doctors and medical students as compared to university students. Two studies conducted in Karachi among medical students reported 17.84% and 52.3% frequencies of migraine.[13,14] This wide variation may be attributed to the difference in study population, diagnostic criteria, gender ratio and academic stress levels of the study participants. In our study, the most common triggering factor of migraine was stress (73.8%) followed by sleep disturbances (56%), noise (39.3%) and fatigue (35.7%). Stress and sleep deprivation were the most common contributing factors of migraine in medical students in two other studies.[13,14] A cross-sectional study in Saudi Arabia found a significant link between increased weekly working hours and the prevalence of migraines among healthcare professionals.[15] It was also observed in our study that 22.6% of the individuals suffered from migraines triggered by menstrual periods. Vetvik *et. al.,*[16] reported that menstrual migraine manifests in approximately 20–25% of women in the general population who experience migraines.

Our study showed that 29.8% of the respondents suffered from moderate disability and 32.1% suffered from severe disability. These results indicate a significant amount of disability associated with migraine headaches and consequently affecting the productivity of the healthcare system. Another study showed many individuals exhibited moderate to severe disability, underscoring the substantial

impact of migraines on their overall functional capacity and quality of life.[17] Another study from Egypt found that among medical students with migraines, 19.9% experienced moderate disability, while 56.9% suffered from severe disability.[18] According to another study conducted among physiotherapists from Lahore, significant number of participants experienced severe migraine disability, leading to reduced work productivity and quality of life.[19] Another study from Spain demonstrated that increasing the number of migraines per month is not only associated with severe disability but also increases the risk of anxiety and depression.[20] Similarly, another study in KSA showed not only increased prevalence of migraines among health care professionals but also demonstrated significant disability and consequently affecting the quality of life.[21] Alkahtani *et. al*.,[22] also found that migraine had a substantial negative impact on the quality of life and ability to work. Thiagarajan *et. al*.,[23] conducted a study among medical students of Malaysia and found that those with migraines reported significantly higher levels of functional disability compared to students suffering from non-migraine headaches.

Conclusion

The prevalence of migraine in healthcare workers is very high, and it is associated with significant disability that negatively impacts our healthcare system. The majority of healthcare workers experience moderate to severe disability due to migraine, with stress and sleep disturbances being the most common triggering factors.

Recommendations of the Study

As migraine frequently affects healthcare professionals, we recommend that healthcare institutions should address this issue by promoting workplace wellness programs, providing resources for stress management, and creating environments that support the overall well-being of their staff.

Limitations of the Study

Our study recruited healthcare professionals from a single institute and did not investigate different migraine subtypes. But as the frequency of migraine was high in our study, a multicentre study should be conducted in the future with a large sample size and documenting the types of migraine.

REFERENCES

1. Steiner TJ, Stovner LJ. Global epidemiology of migraine and its implications for public health and health policy. *Nat Rev Neurol*. 2023; 19(2):109-17. doi: 10.1038/s41582-022-00763-1.
2. Athar F, Zahid A, Farooq M, Ayyan M, Ashraf M, Farooq M, et al. Frequency of migraine according to the ICHD-3 criteria and its association with socio-demographic and triggering factors in Pakistan: A cross-sectional study. *Ann Med Surg (Lond*). 2022 Sep 17; 82:104589. doi: 10.1016/j.amsu.2022.104589.
3. Awaki E, Takeshima T, Matsumori Y, Hirata K, Miyazaki N, Takemura R, et al. Impact of migraine on daily life: results of the observational survey of the epidemiology, treatment, and care of migraine (OVERCOME [Japan]) study. *Neurol Ther.* 2024 Feb; 13(1):165-82. doi: 10.1007/s40120-023-00569-3.
4. Kim KM, Cho SJ, Shin HJ, Yang KI, Kim D, Yun CH, et al. Prevalence, Disability, and Management Patterns of Migraine in Korea: Nationwide Survey Data from 2009 and 2018. *J Clin Neurol.* 2021 Jan; 17(1):77-85. doi: 10.3988/jcn.2021.17.1.77.
5. Eltrafi A, Shrestha S, Ahmed A, Mistry H, Paudyal V, Khanal S. Economic burden of chronic migraine in OECD countries: a systematic review. *Health Econ Rev*. 2023 Oct 25; 13(1):49. doi: 10.1186/s13561-023-00461-8.
6. Kesserwani H. Migraine triggers: an overview of the pharmacology, biochemistry, atmospherics, and their effects on neural networks. *Cureus.* 2021; 13(4):e14243. doi: 10.7759/cureus.14243.
7. Xie W, Li R, He M, Cui F, Sun T, Xiong J, et al. Prevalence and risk factors associated with headache amongst medical staff in South China. *J Headache Pain*. 2020 Jan 14; 21(1):5. doi: 10.1186/s10194-020-1075-z.
8. Choudry H, Ata F, Alam MN, Ruqaiya R, Suheb MK, Ikram MQ, Chouhdry MM, Muaz M. Migraine in physicians and final year medical students: a cross-sectional insight into prevalence, self-awareness, and knowledge from Pakistan. *World J Methodol.* 2022 Sep 20; 12(5):414-27. doi: 10.5662/wjm. v12.i5.414.
9. Togha M, Seyed-Ahadi M, Jafari E, Vahabi Z, Naderi-Behdani F, Nasergivehchi S, et al. Estimating quality of life in a headache referral population based on Migraine disability assessment scale and headache impact test. *Curr J Neurol*. 2020 Apr 3; 19(2):76-84. doi: 10.18502/cjn. v19i2.4944.
10. Evers S, Brockmann N, Summ O, Husstedt IW, Frese A. Primary headache and migraine in headache specialists – Does personal history of doctor's matter? *Cephalalgia*. 2020 Jan; 40(1):96-106. doi: 10.1177/0333102419873671.
11. Oraby MI, Soliman RH, Mahmoud MA, Elfar E, Abd ElMonem NA. Migraine prevalence, clinical characteristics, and health care-seeking practice in a sample of medical students in Egypt. *Egypt J Neurol Psychiatry Neurosurg*. 2021; 57:26. doi:10.1186/s41983-021-00282-8.
12. Jamali YA, Khan HS, Channa R, Khuhro AB, Shaikh AS, Chandio ZH. Prevalence of migraine headache in Pakistan–a narrative review. *JHRR*. 2024 Jan 8; 4(1):23-7. doi:10.61919/jhrr.v4i1.275.
13. Bakhshi SK, Naim H, Salman A, Imran M, Ashraf J. The

 https://doi.org/10.57234/jiimc.march25.2081

frequency, classification and characteristics of headache among medical students of Karachi, Pakistan. *J Pioneer Med Sci.* 2016 Jul 1; 6:78-83.
14. Anwar F, Sheikh AB, Taher T, Khan MI, Masoom A, Khursheed A, et al. Prevalence and predictors of migraine among medical students in Karachi. *J Bas Res Med Sci.* 2021 Jan 10; 8(1):19-27.
15. Al Maqwashi LS, Sufyani AM, Bichara MM, Rajikhan YT, Albishri M, Hamood NA, et al. The association between shift work and migraine attacks among healthcare workers in the Kingdom of Saudi Arabia. *Cureus*. 2024 Jan; 16(1): e53315. doi: 10.7759/cureus.53315.
16. Vetvik KG, MacGregor EA. Menstrual migraine: a distinct disorder needing greater recognition. *Lancet Neurol.* 2021 Apr 1; 20(4):304-15. doi: 10.1016/S1474-4422(20)30482-8.
17. Pradeep R, Nemichandra SC, Harsha S, Radhika K. Migraine disability, quality of life, and its predictors. *Ann Neurosci.* 2020 Jan; 27(1):18-23. doi: 10.1177/0972753120929563.
18. Ragab S, Zaitoun N, Elrafie A, El-Ansarey H, Srour A, Nabil N, et al. Migraine among Egyptian medical students: prevalence, disability and psychological distress-cross sectional study. *The Egyptian J Neurol, Psychiatry Neurosurg*. 2023 May 8; 59(1):62. doi:10.1186/s41983-023-00665-z.
19. Saeed M, Latif K. Association of work productivity and quality of life with migraine related disability among physiotherapists. *J Rehabil Clin Res*. 2024 Apr 9; 2(1):18-22. doi:10.61776/jrcr.v2i1.2911.
20. Irimia P, Garrido-Cumbrera M, Santos-Lasaosa S, Aguirre-Vazquez M, Correa-Fernandez J, Colomina I, et al. Impact of monthly headache days on anxiety, depression and disability in migraine patients: results from the Spanish Atlas. *Sci Rep*. 2021 Apr 15; 11(1):8286. doi:10.1038/s41598-021-87352-2.
21. Alfaifi FJ, Qasim MY, Al-Harban AM, Alqahtani SS, Alshahrani NM. Prevalence, determinants and impact of migraine on quality of life of healthcare workers at primary healthcare centers in Abha City, Saudi Arabia. Middle East. *J Fam Med.* 2021 Aug 1; 7(10):122.
22. Alkahtani RF, Alrumaih SS, Algezlan SS, Almutairi RR, Alturki BA, Alanazi RM, et al. The impact of migraine disease on work productivity and quality of life among the adults in Riyadh, Saudi Arabia. *Cureus*. 2022 Aug; 14(8):e27733. doi: 10.7759/cureus.27733.
23. Thiagarajan A, Aziz NA, Tan CE, Muhammad NA. The profile of headaches and migraine amongst medical students and its association to stress level, disability and self-management practices. *Malays Fam Physician*. 2022 May 25; 17(2):81-8. doi: 10.51866/oa1370.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Clinical Evaluation of Serological Diagnostic Assays for COVID-19 Antibody Detection

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ABSTRACT

Objective: This study was aimed to evaluate the laboratory performance of three different serological assays (Immunofluorescence Assay (IFA), Electrochemiluminescence Immunoassay (ECLIA) and Chemiluminescent Microparticle Immunoassay (CMIA) to see if they performed accurately according to the manufacturers' claims.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at Chughtai Institute of Pathology from 01st April to 30th May 2020.

Materials and Methods: Blood samples were collected from 75 adult male and female patients, 25 were pre pandemic samples and 50 were diagnosed cases of COVID-19 in whom sample was taken 21 days after they showed up symptoms. All cases were analyzed to detect the presence or absence of COVID-19 IgG antibodies using Immunofluorescence assay (IFA), electrochemiluminescence immunoassay (ECLIA) and Chemiluminescent Microparticle Immunoassay (CMIA). SPSS 23.0 and EP evaluator were used to assess sensitivity, specificity and Cohen's kappa.

Results: The study compares the effectiveness of three diagnostic methods (ECLIA, CMIA, and IFA) against PCR for detecting COVID-19 antibodies using Cohen's Kappa statistics. ECLIA showed the highest agreement with PCR (Kappa 0.748), followed by CMIA (Kappa 0.602), and IFA (Kappa 0.564), indicating that ECLIA is the most reliable method for detecting both positive and negative cases. The findings suggest variability in accuracy across these methods, with ECLIA being the most consistent.

Conclusion: Detection of anti-SARS-CoV-2 antibodies may act as a reliable diagnostic tool provided the assay is properly validated before use. Chemiluminescence immunoassay proves to be a better serological assay as compared to Electrochemiluminescence and Immunofluorescence assay.

Key Words*: Chemiluminescence, Electrochemiluminescence, Immunofluorescence, SARS-Cov-2, Serological Assay.*

Introduction

In Wuhan City, Hubei Province, Central China, several patients with pneumonia of unknown etiology surfaced at the start of December 2019. The pneumonia known as coronavirus disease 2019 (COVID-19) has been shown through genome sequencing to be caused by a novel coronavirus (CoV) called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), formerly known as 2019 novel coronavirus (2019-nCoV).[1] The four genera of Corona viruses are Alpha, Beta, Gamma, and Delta, and they are members of the "Corona Viridae" family. [2,3]Similar to SARS-CoV and MERS-CoV, the recently discovered SARS-CoV-2 virus is a member of the β-CoV B lineage.[3]

Once inside the epithelial cells, SARS-CoV-2 multiplies quickly and triggers a cytokine storm and immunological reaction that damages the pulmonary parenchyma. This hypercytokinemia results in multiple organ failure and acute respiratory distress syndrome due to its unchecked synthesis of proinflammatory cytokines.[4] Studies have revealed that cytokine storm syndrome occurred in severe cases of COVID-19, some of which deteriorated and died of multiple organ damage.[5]

SARS-CoV-2 outbreak and spread can only be controlled by rapid detection of the cases. Reverse transcriptase quantitative PCR (RT-qPCR) is a diagnostic tool based on nucleic acid sequencing

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with high sensitivity and specificity [6]. Apart from the diagnostic tests like RT-qPCR, serological tests have been in high discussion since the outbreak of this pandemic. A wide range of serological immunoassays with variable antibody specificities have been developed [7,8]. The COVID-19 virus has underscored the urgent need for reliable diagnostic antibody testing to accurately identify past infections and assess immunity levels within populations. Such testing is critical for guiding public health decisions, managing vaccination strategies, and understanding the virus's spread. Ensuring high accuracy in antibody tests helps prevent false results, thereby maintaining trust in public health measures. Accurate antibody testing is pivotal for monitoring and controlling the pandemic effectively. It is a major responsibility of clinical laboratories all around the world to validate these new methodologies before these techniques get introduced into routine clinical practice.[9]

In the given emergency of COVID-19, FDA issued relaxed regulatory guidelines to use SARS-CoV-2 serological assays to check the immune response of the population. Under these circumstances, it is now the duty of clinical laboratories to validate these assays rigorously to determine whether these assays perform accurately according to the package inserts. The serological assays being used around the world include rapid diagnostic tests (RDT), ELISA (Enzyme linked Immunosorbent assay), neutralization immunoassays and chemiluminescence. All these tests vary in the antigens they are designed to target e.g. Nucleocapsid protein (N Protein) or Spike protein (S Protein). This study aimed to detect the analytical performance of three different serological assays to detect COVID-19 IgG Antibody. The findings will help health care providers to identify a better serological assay for COVID-19 IgG antibody detection that is properly validated and solve many unanswered queries of the clinicians.

Materials and Methods

This cross-sectional study was conducted at Chughati Institute of Pathology from 01st April to 30th May 2020. Ethical approval was obtained by the Institutional Review Board under letter number CIP/IRB/1029. Blood samples were collected from 75 adult male and female patients. Of these, 25 were pre-pandemic samples and 50 were COVID-19 cases with confirmed diagnosis via RT-qPCR; the samples were obtained 21 days after the onset of symptoms. The pre-pandemic samples included specimens of healthy adult population collected in November 2019 and kept frozen at -80 ° Celsius. The healthy population was recruited according to WHO criteria (Constitution of the World Health Organization) after filling in the health questionnaire. These samples were collected as part of routine sample collection to establish a healthy sample pool for the laboratory's biobank. COVID-19 cases included in the study were admitted in high dependency corona units and hospital isolation wards and having mild to severe symptoms. COVID-19 patients with mechanical ventilation, asymptomatic cases, and those undergoing plasma infusion were not included in this research. In this study, we did not stratify the patients according to the severity of their symptoms. A volume of 3 ml blood was collected and centrifuged at 3000 RPM prior to analysis.

All samples were analyzed to detect the presence or absence of COVID-19 IgG antibodies using three different assays.

1. **Immunofluorescence Assay (IFA) Lifotronic FA 160**

   This is a rapid diagnostic test detecting the presence of antibody on nitrocellulose membrane using immunofluorescence as test principle. Sample is added on the sample pad which moves forward through capillary force towards detection line of enveloped antigen (recombinant nucleocapsid protein) on the test strip. The strip is then placed into the incubation chamber of the reader for 15 minutes. If antibody is present, it will combine with antigen and fluorescence marker to form immune complexes along with a control line that can also produce fluorescence. After incubation, the test strip is placed into the test chamber and the result is displayed on the screen and printed as well. The whole process takes 20 minutes.

2. **Elecsys Anti SARS-CoV-2 Assay- Roche Diagnostics**

   The electrochemiluminescence immunoassay (ECLIA) used in this study was for the qualitative detection of SARS-CoV-2-specific antibodies (IgG and IgM). The nucleocapsid (N) antigen recombinant protein is used in this assay to

measure the antibodies against SARS-CoV-2. The samples are classified as reactive (COI >1.00) or non-reactive (COI<1.00) based on a cut off index (COI) of 1.00.

3. **SARS-CoV-2 IgG assay- Abbott Diagnostics**
   This is a chemiluminescent microparticle immunoassay (CMIA) for qualitative detection of IgG antibodies against SARS-CoV-2. This technique measures IgG antibodies against SARS-CoV-2 using nucleocapsid (N) antigen recombinant protein coated microparticles. The samples are classified as reactive (COI >1.40) or non-reactive (COI<1.40) based on a cut off index (COI) of 1.40.

All samples were analyzed on these assays after quality check and calibration. RT-PCR was used as a reference method. SPSS 23.0 was used to calculate percentages and frequencies, Cohen Kappa, sensitivity and specificity and Cohen Kappa. Cohen's Kappa is a statistical measure used to assess the agreement between two raters or diagnostic tests, beyond what would be expected by chance. When applied to sensitivity and specificity analysis, Cohen's Kappa helps evaluate the sensitivity, which measures the proportion of actual positives that are correctly identified by the tests and the specificity, which measures the proportion of actual negatives that are correctly identified. Cohen's Kappa evaluates if the agreement on cases between two tests exceeds what would be expected by chance. Cohen's Kappa values range from -1 to 1, where: Kappa ≤ 0: Indicates no agreement or agreement worse than chance, 0.01–0.20: Slight agreement, 0.21–0.40: Fair agreement, 0.41–0.60: Moderate agreement, 0.61–0.80: Substantial agreement and 0.81–1.00: Almost perfect or perfect agreement. Higher Kappa values suggest better consistency between the two methods, while values near or below zero indicate that the agreement might be due to chance.

Results

The given results involved comparing three different diagnostic methods (ECLIA, CMIA, and IFA) against a reference standard (PCR) for detecting COVID-19 antibodies. The level of agreement between each method and PCR is assessed using Cohen's Kappa statistics, which helps determine how well these methods perform in identifying positive and negative cases relative to the PCR results. Our study showed that ECLIA and PCR both identified 25 negatives and 42 positives and ECLIA incorrectly identified 8 positive cases as negative. There is substantial agreement between ECLIA and PCR results, with a Kappa value of 0.748. This indicates that ECLIA is a reliable method for COVID-19 detection compared to PCR, with high consistency in detecting both positive and negative cases. CMIA and PCR both identified 25 negatives and 36 positives and CMIA incorrectly identified 14 positive cases as negative. There is moderate agreement between CMIA and PCR results, as indicated by a Kappa value of 0.602. While CMIA shows a good level of agreement, it is less consistent than ECLIA, especially in identifying positive cases. There is a higher rate of false negatives compared to ECLIA. IFA and PCR both identified 25 negatives and 33 positives. IFA incorrectly identified 17 positive cases as negative. The Kappa value of 0.564 indicates a moderate level of agreement between IFA and PCR results. IFA has the lowest agreement among the three methods, with a higher tendency to miss positive cases (false negatives). This suggests that IFA is less reliable than ECLIA and CMIA in accurately detecting COVID-19 cases when compared to PCR. These findings suggest that ECLIA is the most effective among the three methods for diagnosing COVID-19, based on the agreement with PCR results.
In this study, all three assays showed different negative and positive agreement along with Cohen's Kappa for the pre pandemic and post pandemic samples. Comparison of performance of all three assays is given in table I

Table I: Sensitivity And Specificity of Assays Used for Serological Testing (n=75)

Assay	Negative agreement (Specificity)	Positive agreement (Sensitivity)	Cohen's Kappa
IFA	59%	66%	0.564
ECLIA	100%	84%	0.748
CMIA	100%	72.0%	0.602

Discussion

In this work, we compared and clinically assessed three commercially available tests for the detection of SARS-CoV-2 antibodies. Among all the tests used for the qualitative assessment of Anti-SARS-CoV-2 antibodies, the ECLIA test from Roche Diagnostics had the best specificity, followed by the Abbott

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assay. IFA by Lifotronic demonstrated the lowest sensitivity and specificity and was linked to most false positive and false negative outcomes. The requirement for specialized equipment and skilled personnel to interpret results may also limit accessibility and consistency of results. Additionally, cross-reactivity with antibodies from other coronaviruses can cause false-positive results, while low antibody titers in early or mild infections may lead to false negatives.

Given these limitations, some labs opted to use Electrochemiluminescence Immunoassay (ECLIA) and Chemiluminescence Microparticle Immunoassay (CMIA) for COVID-19 antibody detection instead of Immunofluorescence Assay (IFA). ECLIA and CMIA offer higher throughput, automation capabilities, and improved sensitivity and specificity, leading to more consistent and faster results. These methods also minimize human error associated with manual interpretation in IFA and are less labor-intensive, making them ideal for large-scale testing in clinical settings.

A recent American study found that the Abbott assay using CMIA and ECLIA was more reliable than rapid tests after 14 days of symptom onset. Specifically, the study showed that the Abbott SARS-CoV-2 assay had a diagnostic sensitivity of 93.8% and a specificity of 99.4% after this period.[10] The variability in study results compared to manufacturers' claims can be attributed to several factors. Patients often present overlapping clinical scenarios and are under different treatment plans. Moreover, testing on hospitalized patients with immunodeficiencies and comorbidities can affect results. Some manufacturers also measure assay sensitivity from the time of RT-qPCR positivity rather than from the onset of symptoms, potentially leading to an overestimation of sensitivity.[10] In our study, serological assessments in COVID-19 patients were conducted 21 days post-symptom onset, a point at which the maximum serological response is typically observed.[11]

None of the pre-pandemic samples in our study showed seropositivity when analyzed using CMIA and ECLIA, whereas IFA showed considerable false positives, likely due to the assay's low specificity. Some studies have found false positive serological results in pre-pandemic confirmed cases of seasonal coronavirus, attributing this to the structural homology between seasonal coronaviruses and SARS-CoV-2, which can affect the specificity of assays like ELISA. In regions with low prevalence, such as Pakistan, where the current SARS-CoV-2 attack rate is 2.3 per 100,000 population, the necessity of high specificity becomes crucial to achieve a high positive predictive value. This is important for public health strategies and testing protocols because a low specificity can lead to an overestimation of infection rates, thereby affecting resource allocation and intervention strategies. Understanding the regional epidemiology helps inform the selection of assays with optimal specificity and sensitivity to ensure accurate diagnosis and effective public health response.[13] In this case, obtaining a high positive predictive value necessitates a serological test with good specificity.[14] According to the FDA, the performance of an assay depends on the population prevalence, and in low-prevalence populations, a single antibody test may not be sufficient to differentiate true positives from false positives. In clinical settings, especially among hospitalized patients with comorbidities, the immune response can be atypical, potentially leading to altered assay performance. These patients may have impaired immune responses due to their underlying conditions or treatments, which can affect the production of antibodies, thereby influencing both sensitivity and specificity of the tests. As a result, antibody tests may produce higher rates of false positives or false negatives in these environments, highlighting the need for confirmatory testing or using assays with high specificity to ensure accurate diagnosis. Understanding the impact of these clinical variables is crucial for interpreting test results and making informed public health decisions.[15]

Horber et al., assessed several SARS-CoV-2 serological tests for antibody detection and discovered that the assays had a good level of sensitivity and specificity at least 14 days after PCR positive. The investigators found the diagnostic sensitivity of Siemens to be highest compared to Roche and Euroimmun.[16] Clinical evaluation of different serological assays for SARS-CoV-2 reveals that chemiluminescence immunoassay (CLIA) show 100% specificity (sample collected 12 days post symptom onset), RDT show 90.3% clinical specificity

(sample collected 33 days post symptom onset) while the diagnostic sensitivity while using ELISA as assay of choice was 66.7% in the early phase of disease.[11,17,18] A comparison between Roche ECLIA and DiaSorin Liaison CMIA SARS-CoV-2 IgG assay is in accordance with our study demonstrated specificities of 100% and 98.9% with an overall agreement of 99% with RT-PCR.[19] Another recently published study compared the diagnostic sensitivities of Spike protein based serological assay and Nucleocapsid protein-based assay and found that later having high sensitivity (77.8%).[20]The assays used in our study were also Nucleocapsid protein based. An American study comparing the specificity of SARS-CoV-2 IgA and IgG assay (Euroimmun) found IgG assay to have higher specificity (97%) as compared to IgA assay (81%).[21] Our study is also in concordance with a recent evaluation of three commercial SARS-CoV-2 serological assays i.e. Abbott IgG, Roche total antibody and DiaSorin IgG. In this study, the nucleocapsid antibody test (Abbott and Roche) showed higher sensitivity as compared to Spike protein Antibody test (DiaSorin).[22]

The Infectious Diseases Society of America (IDSA) advises using serology to diagnosis patients who have a high suspicion of COVID-19 but who test negative for the virus by RT-PCR.[23] Using a variety of immunochromatographic tests, Demey et al. showed that antibodies against SARS-CoV-2 may be found approximately 10 days after the onset of symptoms where as Thevarajan recorded an increase in the antibody production from 7 to 20 days after beginning of the disease.[24,25] Many studies suggest that serological assays can act as reliable diagnostic tool for identification of SARS-CoV-2 infection as well as help to determine the immune status of the population since they have high sensitivity and specificity. Previously it was debated that serological assays cannot be used to diagnose SARS-CoV-2 infection, however, recently many studies postulate that antibody assays can be used to diagnose COVID-19.[26] Serological assays having high sensitivity and specificity can be used to screen asymptomatic cases, early diagnosis of the infection (with the help of IgM only), and monitoring response during treatment [27-29]. However, negative tests cannot be used to exclude the infection considering the fact that patients may have been recently exposed to the virus [30]. Another fact to be considered is assay showing cross reactivity to non-SARS-CoV-2 proteins. Risk assessment for healthcare personnel, epidemiological surveys, and vaccine research can all benefit from the use of high sensitivity serological testing. However, appropriate validation of the assays' diagnostic accuracy is necessary for all these surveys and investigations.

Conclusion

Besides RT-PCR, to confirm the presence of COVID-19 in the suspected cases, detection of anti-SARS-CoV-2 antibodies may act as a reliable diagnostic tool provided the assay is properly validated before use. Electrochemiluminescence immunoassay proves to be a better serological assay as compared to chemiluminescence and Immunofluorescence assay. Assays with higher diagnostic sensitivity and specificity can overcome the RT-PCR limitations helping to diagnose asymptomatic carriers and false negative RT-PCR cases.

Limitation

- Small sample size and single center study. Understanding the performance of these assays across diverse groups is essential for ensuring accuracy in diagnostic settings, guiding public health decisions and Informing vaccine deployment strategies.
- The study's sample collection at 21 days post-symptom onset may not account for the dynamic nature of antibody levels because antibody titers can vary over time and different individuals may experience peak antibody levels or declines at different rates.

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REFERENCES

1. Li H, Liu SM, Yu XH, Tang SL, Tang CK. Coronavirus disease 2019 (COVID-19): Status and future perspectives. Int J Antimicrob Agents. 2020 May;55(5):105951. doi: 10.1016/j.ijantimicag.2020.105951.
2. Banerjee A, Kulcsar K, Misra V, Frieman M, Mossman K. Bats and coronaviruses. Viruses. 2019;11 doi: 10.3390/v11010041. pii: E41.
3. Yang D, Leibowitz JL. The structure and functions of

 https://doi.org/10.57234/jiimc.march25.1785

coronavirus genomic 3′ and 5′ ends. *Virus Res*. 2015;206:120–133. doi: 10.1016/j.virusres.2015.02.025.
4. Villar J, Zhang H, Slutsky AS. Lung repair and regeneration in ARDS: role of PECAM1 and Wnt signaling. Chest. 2019;155:587–594. doi: 10.1016/j.chest.2018.10.022.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507–513. doi: 10.1016/S0140-6736(20)30211-7.
6. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill*. 2020;25 doi: 10.2807/1560-7917.ES.2020.25.3.2000045.
7. Vashist SK. In Vitro Diagnostic Assays for COVID-19: Recent Advances and Emerging Trends. *Diagnostics (Basel)* 2020;10:202.
8. Winter AK, Hegde ST. The important role of serology for COVID-19 control. [epub ahead of print] *Lancet Infect Dis* 2020 Apr 21 as doi: 10.1016/S1473-3099(20)30322-4.
9. Kirkcaldy RD, King BA, Brooks JT. COVID-19 and Postinfection Immunity: Limited Evidence, Many Remaining Questions. [epub ahead of print] *JAMA* 2020 May 11 doi: 10.1001/jama.2020.7869.
10. Tang M, Hock K, Logsdon N, Hayes J, Gronowski A, Anderson N, et al. Clinical performance of two SARS-CoV-2 serologic assays. *Clin Chem*. 2020;66(8):1055-62.
11. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis* 2020. doi: 10.1101/ 2020.03.02.20030189.
12. To KK-W, Tsang OT-Y, Leung W-S, Tam AR, Wu T-C, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020;20(5):565-74.
13. Abid K, Bari YA, Younas M, Tahir Javaid S, Imran A. Progress of COVID-19 epidemic in Pakistan. *Asia Pac J Public Health*. 2020;32(4):154-6. doi: 10.1177/1010539520927259.
14. Farnsworth CW, Anderson NW. SARS-CoV-2 serology: much hype, little data. *Clin Chem*. 2020;66(7):875-7. doi: 10.1093/clinchem/hvaa107.
15. EUA Authorized Serology Test Performance [Internet]. U.S. Food and Drug Administration. 2020 [cited 13 October 2020]. Available from: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance.
16. Hörber S, Soldo J, Relker L, Jürgens S, Guther J, Peter S et al. Evaluation of three fully automated SARS-CoV-2 antibody assays. *Clinical Chemistry and Laboratory Medicine (CCLM)*. 2020;0(0).
17. Infantino M, Grossi V, Lari B, Bambi R, Perri A, Manneschi M, et al. Diagnostic accuracy of an automated chemiluminescent immunoassay for anti-SARS-CoV-2 IgM and IgG antibodies: an Italian experience. *J Med Virol*. 2020.
18. Li, Z., Yi, Y., Luo, X., Xiong, N., Liu, Y., Li, S., et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J. Med. Virol.* 2020.
19. Merrill AE, Jackson JB, Ehlers A, Voss D, Krasowski MD. Head-to-Head Comparison of Two SARS-CoV-2 Serology Assays [published online ahead of print, 2020 Jul 27]. *J Appl Lab Med*. 2020;jfaa125. doi:10.1093/jalm/jfaa125.
20. Kohmer N, Westhaus S, Rühl C, Ciesek S, Rabenau H. Brief clinical evaluation of six high-throughput SARS-CoV-2 IgG antibody assays. *Journal of Clinical Virology*. 2020;129:104480.
21. Wheeler SE, Shurin GV, Keetch C, et al. Evaluation of SARS-CoV-2 prototype serologic test in hospitalized patients [published online ahead of print, 2020 Aug 26]. *Clin Biochem*. 2020;S0009-9120(20)30816-X. doi:10.1016/j.clinbiochem.2020.08.008.
22. Sarah E. Turbett, Melis Anahtar, Anand S. Dighe, Wilfredo Garcia Beltran, et al. Branda Journal of Clinical Microbiology Oct 2020, JCM.01892-20; DOI**:** 10.1128/JCM.01892-20.
23. Idsociety.org. 2020 [cited 13 October 2020]. Available from: https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-covid-19-antibody-testing-primer.pdf.
24. Demey B, Daher N, François C, Lanoix JP, Duverlie G, Castelain S, et al. Dynamic profile for the detection of anti-SARS-CoV-2 antibodies using four immuno-chromatographic assays. *J Infect*. 2020 Aug;81(2):e6-e10. doi: 10.1016/j.jinf.2020.04.033.
25. Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, van de Sandt CE, Jia X, Nicholson S, Catton M, Cowie B, Tong SYC, Lewin SR, Kedzierska K. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. *Nat Med*. 2020 Apr;26(4):453-455. doi: 10.1038/s41591-020-0819-2.
26. Xiang F, Wang X, He X, Peng Z, Yang B, Zhang J, Zhou Q, Ye H, Ma Y, Li H, Wei X, Cai P, Ma WL. Antibody Detection and Dynamic Characteristics in Patients with Coronavirus Disease 2019. *Clin Infect Dis*. 2020 Nov 5;71(8):1930-1934. doi: 10.1093/cid/ciaa461.
27. Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol*. 2020 Sep;92(9):1518-1524. doi: 10.1002/jmv.25727.
28. Wu X, Fu B, Chen L, Feng Y. Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China. *J Med Virol*. 2020 Oct;92(10):1795-1796. doi: 10.1002/jmv.25904.
29. Pan Y, Li X, Yang G, Fan J, Tang Y, Zhao J, et al. Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. *J Infect*. 2020 Jul;81(1):e28-e32. doi: 10.1016/j.jinf.2020.03.051.
30. Cheng MP, Papenburg J, Desjardins M, Kanjilal S, Quach C, Libman M, et al. Diagnostic Testing for Severe Acute Respiratory Syndrome-Related Coronavirus 2: A Narrative Review. *Ann Intern Med*. 2020 Jun 2;172(11):726-734. doi: 10.7326/M20-1301.

CONFLICT OF INTEREST

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ORIGINAL ARTICLE

Impact of Age and Ethnic Variability on Cardiovascular Risk in Chronic Kidney Disease Patients

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ABSTRACT

Objective: To investigate the effect of age and ethnicity on cardiovascular disease risk in patients with chronic kidney disease.

Study Design: Descriptive Cross-sectional.

Place and Duration of Study: This study was conducted at the Department of Nephrology, Jinnah Post Graduate Medical Centre and Cantonment board Clifton health care center, Karachi from 21st August 2023 to 21st February 2024.

Materials and Methods: One- forty male and female chronic kidney disease (CKD) patients aged 25–60 with diabetes and hypertension for at least five years were included. Patients on renal replacement therapy with coronary artery disease, liver disease, hormonal or steroidal medicine, pregnancy, or breastfeeding were excluded. Descriptive statistics employed mean for quantitative variables. The demographics and case history of patients were collected on a performa and grouped by ethnicity. BMI, Hb, creatinine, urea, lipid profile, and BNP were measured. Quantitative variables were shown. Data was analyzed using SPSS version 25.0. Statistical analysis included Pearson correlation test and One-way Anova to compare the biochemical parameters across the different groups.

Results: In CKD patients, age was positively linked with Hb% (P = 0.018), serum urea (P = 0.000), serum creatinine (P = 0.000), total cholesterol (P = 0.002), and LDL- Cholesterol (P = 0.024). Pathans had significantly higher total cholesterol levels (171.53± 39.75) with a P-value of 0.019. Sindhi had the highest HDL- cholesterol levels (mean 54.44 ±6.48) with a significant P-value < 0.001. Gilgiti had the highest BNP levels (307.37± 57.71) with a significant P-value< 0.0001.

Conclusion: The study found that age and ethnicity affect CKD-related CVD. Adding these traits to clinical practice should improve high-risk CKD screening and management. By closing demographic gaps and customizing treatments, clinicians can lower CVD risk and CKD consequences.

Key Words: *Chronic Kidney Disease, Cardiovascular Disease, Diabetes Mellitus Hypertension, Pathan.*

Introduction

Chronic kidney disease (CKD) is a major global health issue, with high incidences of cardiovascular disease, particularly among patients with complications like type 2 diabetes, obesity, hypertension, and atherosclerosis.[1] The rising prevalence of CKD, ranging from 11 to 13%, is widely documented globally, with 21 million people in Pakistan suffering from it.[2] Research indicates that older age significantly impacts cardiovascular risk and mortality in individuals with CKD, highlighting the complex interaction of age and cardiovascular events.

Patients with CKD who are older have a higher risk of cardiovascular disease (CVD) and death than those who are younger. Individuals over 75, for example, have a significantly higher risk of dying than individuals under 55 years.[3] In patients with CKD, aging is a major risk factor for cardiovascular disease (CVD). Traditional risk factors and comorbidities associated with CKD contribute to the greater prevalence of both atheromatous and non-atheromatous CVD in older adults.[4] The relationship between pulse pressure (PP) and negative outcomes changes with age; older patients are more impacted by kidney outcomes, whereas younger patients are at increased risk of atherosclerotic cardiovascular

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disease (ASCVD) events.[5]

Historically, various social, genetic, and biological factors have influenced the relationship between ethnicity and cardiovascular outcomes in CKD patients, with disparities evolving due to treatment options and healthcare access.

Studies show that Black individuals with CKD have a higher mortality rate than White patients, with a 34% mortality rate compared to 26% for White patients. Higher interleukin-6 (IL-6) levels are linked to a higher risk of death and cardiovascular disease (CVD), with a larger association shown in White patients.[6] cardiovascular disease (CVD) and chronic kidney disease (CKD) have historically been disproportionately prevalent in minority racial and ethnic groups.[7]

Research on the difficulties younger CKD patients encounter is lacking, which restricts our knowledge of age-related differences in cardiovascular outcomes as most existing research focuses on adults.[8] There is little data on the effects of age and ethnicity at every stage of the ESKD pathway, especially when it comes to end-of-life care. There are very few qualitative studies and few cross-country comparisons in the literature.[9]

Research on the effects of age and ethnicity on cardiovascular outcomes in individuals with CKD is crucial since it reveals notable differences in health outcomes. Numerous studies show that cardiovascular risks and death rates among patients with CKD are significantly influenced by both age and ethnicity, underscoring the necessity for focused therapies. According to certain research, these gaps might eventually be lessened by advancements in healthcare management and access, suggesting that future results could improve. By our study we can increase knowledge of the intricate relationships that exist between the risk of cardiovascular events, age, and ethnicity in CKD patients. We can help find ethnicities at high risk so that treatments can be focused on them. We can make informed judgments on healthcare policy and individualized treatment plans.

Materials and Methods

This descriptive cross-sectional study was conducted at Jinnah Post Graduate Medical Centre (JPMC) and, Cantonment board Clifton health care center, Phase 2 South circular avenue, Defense housing authority Karachi from August 21, 2023, to February 21, 2024, with Institutional Review Board approval (CBC/EL/PH-II/No.29). Patients were initially registered at CBC health care center and then followed in the JPMC after routine investigations. Hospitals were chosen using convenience sampling. Software open EPI version 3 determined sample size. Samples were drawn using a single proportion approach with 5% error and 95% confidence. The required sample size was 140. After informed permission, male and female CKD patients with diabetes mellitus and hypertension for more than 5 years and healthy persons aged 25-60 were enrolled in the study. Dialysis or kidney transplant patients with coronary artery disease, hepatopathologies, hormonal or steroidal treatment, pregnancy, or several co-existing illnesses were excluded from the study. The proforma comprising demographics, medical history, family history, and lifestyle issues was disseminated among the participants. Body mass index (BMI), baseline tests and research factors were recorded. Statistical product for services solution (SPSS) version 25.0 was utilized to analyze the data. The continuous variables were expressed as mean±SD. Pearson correlation test was employed to examine the differences between the age and biochemical parameters and one way ANOVA was applied for the comparison between different ethnic groups and biochemical parameters at a predetermined level of statistical significance of $p < 0.05$.

Results

A total of 140 subjects included in this study in which 101 (72.1%) male. Mean age was 56.69±10.53 with range of 38-78 years. Correlation of age (years) and different parameters were assessed. Positive correlation was observed among Hb% with significant P-value=0.018, Total cholesterol with significant P-value=0.002 and LDL with significant P-value=0.024. However negative correlation was observed among serum urea with significant P-value=0.000 and serum creatinine with significant P-value=0.000. (Table I)

Hb% was found with high mean value 11.71 ±2.14 among Pathan followed by Sindhi with mean 10.22± 2.64 with significant P-value 0.001.. Serum creatinine levels found higher value of mean 8.65 ±2.96 among Bengali followed by 5.88 ±3.3 in Sindhi

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Table I: Comparison of Age (years) with Different Study Parameters

	Variables	r-value (Correlation)	P-value
Age (years)	Hb%	.199*	0.018
	BMI	0.092	0.277
	Serum Urea	-.297**	0.000
	Serum Creatinine	-.518**	0.000
	Total Cholesterol	.257**	0.002
	Triglycerides	-0.002	0.984
	HDL	-0.162	0.055
	LDL	.190*	0.024
	BNP	0.036	0.669

***Pearson's Correlation was applied to see the significance**
***P-value < 0.05 considered statistically significant**
****Highly statistically significant P-value**

with highly significant value P< 0.001. Total cholesterol levels found higher value of mean 171.53± 39.75 among Pathan followed by 155.17± 23.2 in Sindhi with significant P-value= 0.019. HDL levels were observed highest in Sindhi with mean value 54.44 ±6.48 followed by Bengali with mean value 51.2± 2.86. The P-value <0.001 for this association was found significant. BNP levels were observed highest in Gilgiti with mean value 307.37± 57.71 followed by Pathan 277.88± 111.93 with significant P-value <0.0001. (Table II)

Discussion

Chronic kidney disease (CKD) constitutes a significant global health issue, substantially contributing to the burden and mortality associated with cardiovascular disease (CVD). This study examines the impact of age and ethnicity on cardiovascular outcomes in Pakistani patients with chronic kidney disease, highlighting demographic and clinical differences. The results indicate a favorable correlation between age and hemoglobin percentage (Hb%), total cholesterol (TC), and low-density lipoprotein (LDL). Hemoglobin levels seem to rise with age, perhaps as a result of erythropoiesis-stimulating agents (ESAs) or iron supplementation. This tendency corresponds with previous research that noted steady or elevated hemoglobin levels in older patients with chronic kidney disease (CKD).[10] A further study indicated that age had no impact on the factors across CKD stages.[11] A multicenter prospective study in China shown that age independently predicted the frequency of

Table II: Comparison of Ethnicity with Different Study Parameters

Parameters	Response	Bengali	Gilgiti	Pathan	Punjabi	Sindhi	Urdu
Hb%	Mean ±SD	8.92 ±2.01	9.7 ±1.27	11.71 ±2.14	10.68 ±1.74	10.22± 2.64	10.09± 1.86
	P-value	0.001*					
BMI	Mean ±SD	25.52 ±2.41	26.62± 2.08	25.17± 5.87	24.26 ±5.36	22.46± 4.89	23.37± 5.58
	P-value	0.398					
Serum Urea	Mean ±SD	121 ±20.08	146.62± 137.72	111.8 ±47.44	94.59 ±43.87	123.11 ±39.49	113.24 ±59.18
	P-value	0.406					
Serum Creatinine	Mean ±SD	8.65 ±2.96	3.66 ±3.09	4.84 ±2.54	3.73± 2.5	5.88 ±3.3	5.51 ±3.47
	P-value	0.001*					
Total Cholesterol (TC)	Mean ±SD	141.4 ±23.51	152.5± 2.12	171.53± 39.75	148.6 ±37.19	155.17± 23.2	148.84± 27.58
	P-value	0.019*					
Triglycerides (TG)	Mean ±SD	116 ±18.65	96.5 ±27.58	173.33± 72.49	152.12± 68.92	157.06 ±76.5	163.49± 51.1
	P-value	0.111					
HDL	Mean ±SD	51.2± 2.86	42± 0	47.03 ±6.61	42.72 ±8.72	54.44 ±6.48	42 ±8.68
	P-value	0.0000*					
LDL	Mean ±SD	111.8± 3.79	89± 4.24	119.78± 23.34	111.24 ±27.34	120.5± 23.33	111.84 ±25.62
	P-value	0.289					
BNP	Mean ±SD	135.81± 29.03	307.37± 57.71	277.88± 111.93	210.12± 123.54	122.18 ±47.48	290.86 ±116.92
	P-value	0.0000*					

***One way ANOVA test was applied to see the significance**
***P-value < 0.05 considered statistically significant**

cardiovascular disease in individuals with chronic kidney disease.[12] These data indicate that aging populations may preserve superior hematological profiles in the context of chronic kidney disease, maybe owing to specific therapeutic approaches. Additional research is required to comprehensively understand this link, especially in groups with varied genetic and environmental contexts. Renal parameters, including blood urea and creatinine, exhibit a substantial negative correlation with age, indicating an age-related loss in kidney function and an elevated risk of chronic kidney disease progression. This highlights the necessity of monitoring kidney parameters in elderly populations to customize therapies.[13] Elevated blood urea levels inversely correlate with the decrease of renal function associated with aging, indicating that age influences renal parameter dysregulation.[14]

In older CKD patients, increased TC and LDL levels signify substantial abnormalities in lipid metabolism linked to aging. Dyslipidemia, an established risk factor for atherosclerosis and cardiovascular disease, likely facilitates the relationship between chronic kidney disease and cardiovascular disease through processes including oxidative stress, inflammation, and endothelial dysfunction. In chronic kidney disease, elevated cholesterol and LDL levels correlate positively with age due to diminished lipid metabolism and heightened atherosclerotic risk in older individuals.[13] A separate study revealed that elevated total cholesterol levels significantly correlate with renal impairment, with aging serving as an exacerbating factor in these connections.[15] LDL-C levels significantly correspond with the decline in glomerular filtration rate (GFR) in elderly chronic kidney disease (CKD) populations, establishing LDL-C as a therapeutic target.[16] Consistent with our study findings, research identified a positive correlation between age and total blood cholesterol levels.[17] The oxidative alteration of LDL and its role in vascular injury offer a credible rationale for these observations. Elevated reactive oxygen species and compromised endothelial function are prevalent in chronic kidney disease and may contribute to the noted lipid abnormalities. This underscores the necessity for age-specific approaches in the management of dyslipidemia, especially for older patients with chronic kidney disease at increased cardiovascular risk.

Ethnicity is a significant factor influencing outcomes related to cardiovascular disease in chronic kidney disease. Differences in Hb%, serum creatinine, TC, HDL, and BNP across various ethnic groups illustrate the impact of genetic, environmental, and lifestyle influences. South Asians typically exhibit lower HDL levels and elevated triglycerides, which contribute to increased cardiovascular risks. In contrast, African Americans may present with favorable HDL levels but increased LDL cholesterol, thereby elevating their ASCVD risks. These patterns indicate variations in eating patterns, hereditary traits, and metabolic syndromes among different ethnic groups.[18] Research on Asian populations has shown a significant correlation between low estimated glomerular filtration rate (eGFR), albuminuria, and heightened cardiovascular disease (CVD) risk. The current study's findings align with existing research, emphasizing the influence of ethnicity on health outcomes in chronic kidney disease (CKD).[19] However, contrasting results from Hispanic CKD cohorts, where no significant racial or ethnic disparities in atherosclerotic or heart failure outcomes were observed, underscore the complex and context-dependent nature of these relationships.[20] BNP levels, indicative of cardiac strain, exhibit considerable variation among CKD patients of diverse ethnic backgrounds. Elevated BNP levels in specific ethnic groups, such as the Gilgiti in our study, may suggest variations in cardiac remodeling or stress responses. Ethnic disparities in BNP are associated with differences in blood pressure management and the occurrence of cardiovascular complications.[21]

The interaction of age and ethnicity in affecting CKD-related CVD outcomes highlights the importance of integrating these factors into standard risk evaluations. Identifying high-risk individuals using demographic variables can provide personalized therapies to reduce cardiovascular risks and enhance overall health outcomes. This method is especially pertinent for patients with chronic kidney disease, who are inherently susceptible to unfavorable cardiovascular outcomes.

This study, although having useful insights, has numerous drawbacks. The limited sample size for each ethnic group may constrain the generalizability

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of the findings, as results from communities may not be relevant to larger populations. Furthermore, socioeconomic position and healthcare access, which are known to significantly affect health outcomes, were not included in this study. The aforementioned issues may have led to the observed differences in biomarkers. Moreover, as a cross-sectional study, the research design prevents the establishment of causation, rendering it hard to ascertain whether the observed relationships are directly attributable to age or ethnicity. Longitudinal studies are essential to corroborate these findings and investigate the enduring impacts of age and ethnicity on CKD and CVD outcomes.

Subsequent study ought to rectify these limitations by incorporating larger, more heterogeneous cohorts and considering socioeconomic and healthcare access characteristics. Longitudinal studies are crucial for determining causality and revealing the reasons behind observed demographic differences. Moreover, research examining customized therapies according to age and ethnicity may yield significant insights for enhancing CKD management and mitigating cardiovascular risks. A deeper comprehension of these linkages might improve risk classification and guide tailored healthcare measures for CKD patients.

Conclusion

This study underscores the interconnected influence of age and ethnicity on CKD-related cardiovascular events. Incorporating these characteristics into clinical practice could markedly enhance early diagnosis and management options for high-risk CKD patients. By addressing demographic differences and customizing therapies, healthcare practitioners can improve outcomes and alleviate the burden of CKD and its related comorbidities predominantly cardiovascular risk.

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Conflict of Interest

There is no conflict of interest among the study authors.

REFERENCES

1. Nawaz S, Chinnadurai R, Al-Chalabi S, Evans P, Kalra PA, Syed AA, et al. Obesity and chronic kidney disease: a current review. *Obes Sci Pract*. 2023 Apr;9(2):61-74. doi: 10.1002/osp4.629.
2. Shaikh SU, Yasmeen G. β natriuretic peptide evaluation as a prognostic marker in chronic kidney disease associated complications. Biosci Res. 2022;19(1):198-203.
3. Raman M, Green D, Middleton RJ, Kalra PA. Comparing the impact of older age on outcome in chronic kidney disease of different etiologies: a prospective cohort study. *J Nephrol*. 2018;31(6):931–9. doi: 10.1007/s40620-018-0529-8.
4. Villain C, Metzger M, Combe C, Fouque D, Frimat L, Jacquelinet C, et al. Prevalence of atheromatous and non-atheromatous cardiovascular disease by age in chronic kidney disease. *Nephrol Dial Transplant*. 2020;35(5): 827–36. doi: 10.1093/ndt/gfy277.
5. Fischman CJ, Townsend RR, Cohen DL, Rahman M, Weir MR, Juraschek SP, et al. Pulse Pressure and Cardiovascular and Kidney Outcomes by Age in the Chronic Renal Insufficiency Cohort (CRIC). *Am J Hypertens*. 2024. doi: 10.1093/ajh/hpae136.
6. Barrows IR, Devalaraja M, Kakkar R, Chen J, Gupta J, Rosas SE, et al. Race, Interleukin-6, TMPRSS6 Genotype, and cardiovascular disease in Patients with Chronic Kidney Disease. *J Am Heart Assoc*. 2022;11(18):e025627. doi: 10.1161/JAHA.122.025627.
7. Nicholas SB, Norris KC. Race, Biomarkers, and cardiovascular disease in Patients with Chronic Kidney Disease. *J Am Heart Assoc*. 2022;11(18):e026998. doi: 10.1161/JAHA.122.026998.
8. Kula AJ, Prince DK, Limonte CP, Young BA, Bansal N. Rates of Cardiovascular Disease and CKD Progression in Young Adults with CKD across Racial and Ethnic Groups. *Kidney360*. 2022;3(5):834–42. doi: 10.34067/KID.0006712021.
9. Wilkinson E, Brettle A, Waqar M, Randhawa G. Inequalities and outcomes: end stage kidney disease in ethnic minorities. *BMC Nephrol*. 2019;20(1):234. doi: 10.1186/s12882-019-1410-2.
10. Raisinghani N, Kumar S, Acharya S, Gadegone A, Pai V. Does aging have an impact on hemoglobin? Study in elderly population at rural teaching hospital. *J Family Med Prim Care*. 2019 Oct;8(10):3345-9. doi: 10.4103/jfmpc.jfmpc_668_19.
11. Li JH, Luo JF, Jiang Y, Ma YJ, Ji YQ, Zhu GL, et al. red blood cell lifespan shortening in patients with early-stage chronic kidney disease. *Kidney Blood Press Res*. 2019 Nov;44(5):1158-65. doi: 10.1159/000502525.
12. Yuan J, Zou XR, Han SP, Cheng H, Wang L, Wang JW, et al. Prevalence and risk factors for cardiovascular disease among chronic kidney disease patients: results from the Chinese cohort study of chronic kidney disease (C-STRIDE). *BMC Nephrol*. 2017 Dec;18:1-2. doi: 10.1186/s12882-017-0441-9.

13. Miao L, Min Y, Qi B, Zhu CM, Chen JH, Deng GX, Wang Y, Li JF, Li RS. Causal effect between total cholesterol and HDL cholesterol as risk factors for chronic kidney disease: a Mendelian randomization study. *BMC Nephrol*. 2021;22:1-9.
14. He X, Zou R, Du X, Li K, Sha D. Association of remnant cholesterol with decreased kidney function or albuminuria: a population-based study in the US. *Lipids Health Dis*. 2024;23(1):2.
15. Theofilis P, Vordoni A, Koukoulaki M, Vlachopanos G, Kalaitzidis RG. Dyslipidemia in chronic kidney disease: contemporary concepts and future therapeutic perspectives. *Am J Nephrol*. 2021;52(9):693-701.
16. Lyu K, Liu S, Liu Y, You J, Wang X, Jiang M, et al. The effect of blood lipid profiles on chronic kidney disease in a prospective cohort: based on a regression discontinuity design. *Biomed Environ Sci*. 2024;37(10):1158-72.
17. Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, age, cardiovascular risk factors, and coronary heart disease: a prospective follow-up study of 14,786 middle-aged men and women in Finland. *Circulation*. 1999 Mar;99(9):1165-72. doi: 10.1161/01.cir.99.9.1165.
18. Palla AH, Fatimi AS, Virani SS, Fatima SS. Cardiovascular disease risk stratification in the Pakistani population with and without metabolic syndrome: A single centre cross-sectional study. *PLOS Glob Public Health*. 2023;3(9):e0002397.
19. Lim CC, Teo BW, Ong PG, Cheung CY, Lim SC, Chow KY, et al. chronic kidney disease, cardiovascular disease and mortality: a prospective cohort study in a multi-ethnic Asian population. *Eur J Prev Cardiol*. 2015 Aug;22(8):1018-26. doi: 10.1177/2047487314536873.
20. Lash JP, Ricardo AC, Roy J, Deo R, Fischer M, Flack J, et al. Race/ethnicity and cardiovascular outcomes in adults with CKD: findings from the CRIC (Chronic Renal Insufficiency Cohort) and Hispanic CRIC studies. *Am J Kidney Dis*. 2016 Oct;68(4):545-53. doi: 10.1053/j.ajkd.2016.03.429.
21. Shabana, Shahid SU, Sarwar S. The abnormal lipid profile in obesity and coronary heart disease (CHD) in Pakistani subjects. *Lipids Health Dis*. 2020;19:1-7.

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Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Perceived Barriers and Knowledge of Mammography Screening Among Saudi Women Attending Primary Health Centers

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ABSTRACT

Objective: To assess the knowledge and barriers of mammography screening among Saudi women attending primary health centers in Saudi Arabia.

Study Design: Descriptive cross-sectional.

Place and Duration of the Study: Conducted in the central region of the Kingdom of Saudi Arabia from 10th May 2024 to 31st October 2024.

Materials and Methods: The study was conducted among women attending the primary healthcare centers in the central region of Saudi Arabia. An Arabic questionnaire assessing sociodemographic, breast cancer awareness, and perceptions about mammographic screening was utilized. Data was analyzed in the Software Sciences (SPSS) version 26.

Results: Of the 349 Saudi women, 64.2% were married, and 61.3% were between 18 and 40 years old. Smoking behavior was identified as the most common breast cancer risk factor (75.1%), while fear of radiation was recognized as the most common personal barrier to mammographic screening (61.9%). Low levels of knowledge about cancer risk factors and mammographic screening were found in 51.9% of the women, whereas 9.5% were considered to have a high level of barrier toward MS. Increased knowledge and barrier scores were associated with being married, better education, and being an employee.

Conclusion: Saudi women have limited knowledge of the risks of breast cancer and have few perception barriers to mammogram screening too. Married women with better education and working status demonstrated a better understanding of the BC risk factors. Still, at the same time, they may exhibit high levels of barriers toward MS which needs to be focused on.

Key Words: *Breast Cancer, Mammography Screening, Knowledge, Saudi Women.*

Introduction

Breast cancer, which accounts for 30% of all new cancer cases worldwide, is the most frequent cancer among women, with an estimated 2.3 million new cases worldwide in 2020, according to the Global Cancer Statistics Report [1]. Therefore, it is the most common reported cancer (14.2%) in Saudi Arabia, and cancer-related fatalities among women have an annual incidence of 3.01% and a mortality rate of 0.93%.[2]

In the literature, well known strategies to detect breast cancer early, including regular physical exams, increased education about breast cancer, and routine mammography, have been promoted because there is compelling evidence linking early detection to a better prognosis and a decrease in breast cancer deaths.[3] Global recommendations for breast cancer screening vary; the US Preventative Services Task Force and the United Kingdom National Screening Committee both advise beginning mammography imaging screening at age fifty. However, as breast cancer is the most frequent cancer among Saudi women and a major cause of female fatalities, the suggested beginning age in Saudi Arabia is 40 years old.[4] Although mammography has been available in all regions of KSA since 2005, the Saudi Health Interview Survey 2015 showed a very low rate of breast cancer

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screening (BCS). Among the 10,735 participants, 1,135 were 50 years or older women, 89% of whom had never had a clinical breast examination and 92% hadn't had a mammogram in the past year. [9]

Mammography is a sophisticated established screening tool for lowering the death rate from breast cancer(BC), and is well used in developed countries than in underdeveloped ones, but it is crucial to recognize the psychological effects of women's worries about the results of the mammography.[5] As of right now, mammography stands as the gold standard for early BC identification and screening, and its use has been shown to lower treatment costs and minimize BC-related mortality.[6]

Improving screening rates in various demographics begins with raising awareness of the aspects related to mammography. In each nation and area, the cultural, social, and economic conditions are shaped in large part by knowledge, attitudes, and beliefs around breast cancer screening. Consequently, before developing and putting into action a plan to attain widespread coverage of breast cancer screening programs, it is essential to assess the obstacles and enablers of screening in various communities.[7]

Women should be informed about the importance and benefits of mammographic screening (MS) as an effective method for detecting breast cancer early. However, due to lack of awareness and knowledge about MS, many Saudi women were diagnosed with BC at an advanced stage.[8] Despite the availability of free breast cancer screenings to the general population in Saudi Arabia the rate of screening is low.[9] Factors that influence women's knowledge about MS, include their socio-demographic characteristics, awareness of BC risk factors, and having exposure of family members with BC.[10] MS has various barriers, which are categorized into three main groups: personal, health system, and economic barriers. According to Saudi Arabian cultural norms, women may not be allowed to use MS due to concerns about modesty, how they interact with men other than their husbands, and beliefs regarding the privacy of the body.[11]

Research conducted in the northern, western, and eastern regions of Saudi Arabia showed that a large number of women are still not sufficiently informed about the value, frequency, and advantages of mammograms. Low adherence to screening criteria is also influenced by individual factors such as cultural beliefs, misconceptions, and fear.[4,5,6,8] Therefore, this study aims to determine the knowledge gaps and perceived obstacles related to mammography screening among Saudi women who visit primary healthcare facilities in the central region of Saudi Arabia. It has shed light on how healthcare-related, financial, and personal barriers interact to influence screening uptake in this region. Furthermore, this study would assist in determining whether provider interventions and focused awareness campaigns can enhance screening adherence.

Materials and Methods

The study employs a cross-sectional, quantitative descriptive design to explore awareness, perceived barriers, and factors influencing mammography screening among Saudi women attending primary health centers (PHCs). Research approval was taken from the University's Deanship of Research: KFU-REC-2024-MAR- ETHICS2058. The data was collected by data collectors in primary health care centers through an online, self-administered questionnaire featuring structured questions to gather quantitative data on perceived barriers to mammography screening, levels of awareness, demographic information, and factors influencing screening decisions. The eligibility criteria included Saudi females, age 18 years and above, living in central region of Saudi Arabia. To ensure data is collected exclusively from PHCs, the designated data collectors in various PHCs distributed the survey link to the eligible females, guided them through the process, and ensured completeness. The minimum sample size of 385 was calculated using the Raosoft sample size calculator (Raosoft Inc., Seattle, WA, USA), based on a population estimate of approximately 32,175,224 according to the General Authority for Statistics in the Kingdom of Saudi Arabia, considering a 95% confidence interval, a 5% margin of error, and a 50% response distribution.

Questionnaire Criteria

The questionnaire comprised sections on sociodemographic features, knowledge evaluation of mammography screening, and risk factors for breast cancer. Additionally, had assessment of healthcare-related, financial, and personal barriers

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to mammography screening.

A pilot study was conducted beforehand to verify the feasibility and dependability of the original research. The overall Cronbach's alpha score for the questionnaire was 0.76, indicating strong item reliability and internal consistency.

The knowledge about BC risk factors and MS has been assessed using a 14-item questionnaire with "yes" coded with 1 and "no/I don't know" coded with 0 as the answer options. The total knowledge has been calculated by adding all 14 items. A possible score ranging from 0 to 14 points has been generated. The higher the score, the higher the knowledge about BC risk factors and MS. By using 50% and 75% as cutoff points to determine the level of knowledge, women were considered to have low knowledge if the total score was less than 50%, 50% to 75% were moderate and above 75% were considered as having high knowledge level.

Likewise, the barrier toward MS has been assessed using a 19-item questionnaire with "yes" coded with 1 and "no/I don't know" coded with 0 as the answer options. By summing up 19 items, we got scores ranging from 0 to 19 points. Similar criteria were applied following the knowledge representing the level of barrier: low barrier (<50% points), Average (50% to 75% points), and high (>75% points).

The data were presented by numbers and percentages for all categorical variables, while means and standard deviations were given to all continuous variables. The knowledge and barrier scores were compared with the socio-demographic characteristics of the women by using the Mann-Whitney Z-test. Normal tests have been performed using the Kolmogorov-Smirnov test. Based on the plot, both knowledge and barrier scores follow the non-normal distribution. Thus, a non-parametric test was applied. Further, the Spearman correlation coefficient has been conducted to determine the correlation between the knowledge and barrier scores. Statistical significance was set to $p<0.05$ level. All data analyses were performed using Statistical Packages for Software Sciences (SPSS) version 26 Armonk, New York, IBM Corporation.

Results

A total of three hundred and forty-nine Saudi women responded to our survey. Table 1 presents the socio-demographic characteristics of the women. 61.3% were between 18 and 40 years old. Most of the women lived in the Urban area (92.8%). With respect to marital status, 64.2% were married, and more than half (54.7%) had university or postgraduate degrees. Unemployed women constitute 67.3% of the total respondents, and those who earned less than 5,000 SAR per month constituted 60.5%. In addition, 17.5% had a family history of breast cancer.

Table I: Socio Demographic Characteristics of the Saudi Women (n=349)

Study variables	n (%)
Age group	
• 18 – 40 years	214 (61.3%)
• 41 – 50 years	103 (29.5%)
• 51 – 60 years	29 (08.3%)
• >60 years	03 (0.90%)
Residence	
• Urban	324 (92.8%)
• Rural	25 (07.2%)
Marital status	
• Single	108 (30.9%)
• Married	224 (64.2%)
• Divorced or widowed	17 (04.9%)
Educational level	
• Illiterate	04 (01.1%)
• Primary/Preparatory	67 (19.2%)
• Secondary/Diploma	87 (24.9%)
• University/Postgraduate	191 (54.7%)
Occupation	
• Employed	114 (32.7%)
• Unemployed	235 (67.3%)
Monthly income (SAR)	
• <5,000	211 (60.5%)
• 5,000 – 7,000	40 (11.5%)
• >7,000	98 (28.1%)
Family history of breast cancer	
• Yes	61 (17.5%)
• No	288 (82.5%)

Regarding the assessment of the knowledge of BC risk factors and MS (Table 2), the top 3 BC risk factors where women showed good knowledge were "smoking behavior" (75.1%), followed by "consuming unhealthy food" (66.8%) and "family history of BC" (65%). In contrast, women showed poor knowledge of other BC risk factors, such as "early menarche (19.5%), "first pregnancy after the age of 30 years" (22.9%), and "late menopause" (35.5%). Regarding knowledge about MS, the results showed gaps, particularly related to the frequency of doing MS (19.5%). The overall mean knowledge score was 6.52 (SD 3.56), with low, average, and high knowledge constituting 51.9%, 32.7%, and 15.5%, respectively.

Table II: Assessment of the knowledge regarding BC risk factors and MS (n=349)

Knowledge BC risk factors	n (%)
1. Smoking behavior	262 (75.1%)
2. Consuming unhealthy food	233 (66.8%)
3. Family history of BC	227 (65.0%)
4. Age of 35 years or older	199 (57.0%)
5. Overweight and obesity	171 (49.0%)
6. Non-lactating women	156 (44.7%)
7. Hormonal replacement therapy	150 (43.0%)
8. No exercise	145 (41.5%)
9. Late menopause	124 (35.5%)
10. First pregnancy after the age of 30 years	80 (22.9%)
11. Early menarche	68 (19.5%)
Knowledge of MS	
12. MS is the ideal method for detecting BC	204 (58.5%)
13. MS is recommended for over 40 years	189 (54.2%)
14. Frequency of doing MS	68 (19.5%)
Total knowledge score (mean ± SD)	**6.52 ± 3.56**
Levels of knowledge	
• Low	181 (51.9%)
• Average	114 (32.7%)
• High	54 (15.5%)

Regarding the assessment of the barriers to MS (Table 3), the top three personal barriers based on women's ratings were "fear of radiation" (61.9%), "fear of pain" (59.3%), and "fear of discovery of BC" (59%), while "MS is not safe" (28.1%) and "lack of time" (39.5%) were the personal barriers with the lowest ratings. Regarding economic barriers, most items showed poor ratings, with "MS is too costly" being the lowest (20.6%). Finally, regarding health system barriers, only two items showed good ratings: "fear of errors in diagnosis" (57.9%) and "I will not do MS except recommended by the doctor" (52.1%). The rest of the health system barrier items had ratings below 50%, most notably about "no female doctor/nurse" (23.8%), "not considering privacy during the examination" (26.6%), and "The site that provides is far" (28.9%). The overall mean barrier score was 7.93 (SD 5.11). Accordingly, low, average, and high barriers were found in 60.7%, 29.8%, and 9.5%, respectively.

Table III: Assessment of the barriers regarding MS (n=349)

Personal barrier	n (%)
1. Fear of radiation	216 (61.9%)
2. Fear of pain	207 (59.3%)
3. Fear of discovery of BC	206 (59.0%)
4. Lack of information about MS	197 (56.4%)
5. Fear of cancer treatment	190 (54.4%)
6. The embarrassment of breast examination	189 (54.2%)
7. Do not know where MS done	151 (43.3%)
8. Busy with no free time	138 (39.5%)
9. MS is not safe	71 (28.1%)
Economic barrier	
10. Transport problems	103 (29.5%)
11. Taking sick leave from work is difficult	98 (28.1%)
12. MS is too costly	72 (20.6%)
Health system barrier	
13. Fear of errors in diagnosis	202 (57.9%)
14. I will not do MS except if recommended by the doctor	182 (52.1%)
15. Too long time to get a medical appointment	158 (45.3%)
16. No adequate description of MS by the doctor	109 (31.2%)
17. The site that provides is far	101 (28.9%)
18. Not considering privacy during the examination	93 (26.6%)
19. No female doctor/nurse	83 (23.8%)
Total barrier score (mean ± SD)	**7.93 ± 5.11**
Level of barrier	
• Low	212 (60.7%)
• Average	104 (29.8%)
• High	33 (09.5%)

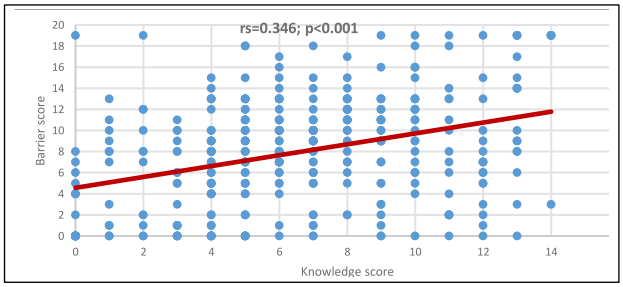

Figure 1: Correlation between knowledge and barrier score

Figure 1 depicts a positive significant correlation between knowledge and barrier scores (rs=0.346; p<0.001), suggesting that the increase in knowledge score correlates with the increase in barrier score.

Exploring the association between knowledge and barrier scores concerning the socio-demographic characteristics of the women found that higher knowledge scores were associated with being older (p=0.008), being married (p<0.001), being more educated (p<0.001), employed (p<0.001) and

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Table IV: Association between knowledge and barriers scores with the Socio-demographic characteristics of Saudi Women (n=349)

Factor	Knowledge Score (14) Mean ± SD	Barrier Score (19) Mean ± SD
Age group		
• ≤40 years	6.17 ± 3.65	7.64 ± 5.14
• >40 years	7.07 ± 3.36	8.38 ± 5.06
Z-test; p-value §	***2.663; 0.008 *****	***1.237; 0.216***
Residence		
• Urban	6.43 ± 3.53	7.82 ± 5.14
• Rural	7.72 ± 3.88	9.24 ± 4.70
Z-test; p-value §	***1.763; 0.078***	***1.241; 0.215***
Marital status		
• Unmarried	5.67 ± 3.55	7.05 ± 5.06
• Married	6.99 ± 3.49	8.42 ± 5.09
Z-test; p-value §	***3.488; <0.001 *****	***2.650; 0.008 *****
Educational level		
• Diploma or below	5.22 ± 3.48	7.20 ± 4.93
• University or higher	7.59 ± 3.27	8.52 ± 5.19
Z-test; p-value §	***6.361; <0.001 *****	***2.312; 0.021 *****
Occupation		
• Employed	7.67 ± 3.41	9.38 ± 5.18
• Unemployed	5.97 ± 3.51	7.22 ± 4.94
Z-test; p-value §	***4.428; <0.001 *****	***3.637; <0.001 *****
Monthly income (SAR)		
• <5,000	6.09 ± 3.49	7.65 ± 5.17
• ≥5,000	7.18 ± 3.58	8.35 ± 5.01
Z-test; p-value §	***2.912; 0.004 *****	***1.388; 0.165***
Family history of breast cancer		
• Yes	6.95 ± 3.05	8.13 ± 4.77
• No	6.43 ± 3.66	7.88 ± 5.19
Z-test; p-value §	***1.186; 0.236***	***0.377; 0.706***

§ P-value has been calculated using Mann Whitney Z-test.
** Significant at p<0.05 level.

increasing monthly income (p=0.004). Regarding barrier scores, higher barrier scores were associated with being married (p=0.008), having better education (p=0.021), and being an employee (p<0.001). No significant differences were observed between the knowledge and barrier scores with residence and family history of BC (Table IV).

Discussion

Breast cancer is one of the most prevalent cancers globally, and early detection through mammograms is crucial in improving survival rates. However, the effectiveness of MS can be influenced by both knowledge about BC risk factors and barriers to screening. Evaluating these factors can help outline interventions to improve awareness and partaking in BC screening programs.

The findings of this study showed gaps in the knowledge of BC risk factors and screening. According to the given criteria, more than half of the women (51.9%) were below the threshold of satisfactory ratings (mean score: 6.52 out of 14 points). Several studies documented an unfavorable knowledge about BC risk factors, symptoms, and MS.[2,6,10] In contrast, studies conducted by Hamshari et al.[12] and Bawazir et al.[13] documented an adequate understanding of women regarding BC and MS, while in a study by Amkongo et al. an average knowledge about BC risk factors and MS were detected among women attending two health facilities in Windhoek, Namibia.[11] The differences in knowledge levels are mainly attributed to study methodologies, regional settings, and the research focus.

Among BC risk factors, lack of understanding was seen in the early menarche, first pregnancy after the age of 30 years, and late menopause, while the knowledge of MS had a poor rating on the frequency of doing MS with only 19.5%. Consistent with our results, Abdel-Salam et al. also found low ratings on the following BC risk factors such as early menarche (14.9%), late pregnancy (>30 years old) (18%) and late menopause (18.7%). Regarding MS, approximately half of the women correctly recognized mammograms as the ideal modality for detecting BC.[3] In contrast, Bakarman et al. reported that the most common BC risk factors recognized by the women were having a close relative with BC (49.5%) and previous history of BC (44.9%).[5] In our study, smoking behavior, followed by consuming unhealthy food and a family history of BC, were the most recognized risk factors for BC, which did not coincide with previous reports.

Data from this study suggest that increasing age, being married, having higher education, being an employee, and increasing monthly income are the factors associated with increased knowledge. Corroborating these reports, studies done in the Jouf region found that age, healthcare workers category, education, and residence location were the influential knowledge factors.[2,3] However, conflicting reports enunciated in Yemen revealed that lower educational levels, unemployed, and women who

never performed self-breast examinations were associated with limited knowledge of BC risk factors.[13] Growing evidence shows that age, education, and marital status are key contributors to knowledge about BC. The most common reason for this effect was that older women had more exposure to health-related information about BC, while women with better education may possess better health literacy than women who were less educated. Similarly, married women may have better social support from their partner than unmarried women.

Although participating women in this study were considered to have poor knowledge, the barriers toward MS yielded favorable results. Only 9.5% were deemed to have high levels of barriers; the rest were low to average levels (90.5%), and the overall mean barrier score was 7.93 out of 19 points. Limited studies have been done across publications stratifying barrier scores into levels. Hence, further investigations are necessary to confirm this result.

Assessing the details of the barrier toward MS, we noted "fear of radiation," "fear of pain," "fear of discovery of BC," "lack of information about MS," "fear of cancer treatment," and "embarrassment" were the most prominent personal barriers being identified by the women. "Transport problems" and "being on leave from work" are rated as the top 2 most common economic barriers, whereas "fear of errors in diagnosis" and "non-adherence to MS, except if advised by doctors," have been recognized as the most common health system barriers. Across the literature, there was ample evidence that the barriers related to MS were mostly likely associated with stigma, including "fear of radiation exposure," "fear of BC discovery," "fear of BC diagnosis," and "fear of pain".[2-5,8,13,14] Other prominent barriers to MS reported by the publication include the absence of symptoms [11,14], the lack of knowledge about the method and its importance [15,16], race/ethnicity, and low socioeconomic and educational levels.[17] Addressing these barriers is critical to early detection and management to reduce mortality associated with BC.

The analysis of confounding variables with barriers to screening suggested that higher barrier levels were associated with being married, having a university or higher degree, and being an employee. However, this study finds no differences between the barrier scores to age, residence, monthly income, and family history of BC ($p>0.5$). The most compelling reason for these effects was that married women may have to balance work and family, and MS adherence will be of less priority, while the lack of perception of older women regarding MS could be attributed to the fear of detecting BC. On the other hand, employees may have been associated with high barriers to MS due to a lack of employer support and limited access to healthcare. These factors must be addressed to improve adherence to MS. The factors influencing barriers identified in this study are almost following the study of Abdel-Aziz et al. This reflected low utilization of BC screening had positive associations with a woman's age, better education, increased family income, using hormonal contraception, and previous history of BC.[8]

We further detected a positive significant correlation between knowledge and barrier scores, indicating that whenever the knowledge of women increases, the barrier toward MS will also likely increase. This positive association could be due to complex reasons, such as women's fear of BC and increased awareness about the risks, cultural or social beliefs, and deep-rooted misinformation or knowledge. Contradicting these reports, studies done in the Jouf region documented an inverse correlation between knowledge and barrier scores, suggesting that the increase in knowledge correlates with the decrease in barriers.[2,6]

Conclusion

Despite a lack of knowledge regarding BC risk factors and MS, Saudi women's general perception of the barriers to MS achieved better ratings. Younger women who were unmarried and had a lower monthly income were more likely to exhibit a poor understanding of the BC risk factors; however, participants who had better education and were currently working could demonstrate high barriers toward mammogram screening which is alarming and needs to improve Saudi women's knowledge of the basic facts of BC.

Study Limitations

The generalizability of the findings is subject to mild study limitations as cross-sectional research unable to determine cause and effect and cannot be used to measure behavior over time.

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Recommendation

Health education among women visiting primary health centers could bridge knowledge gaps and eliminate barriers. Addressing these obstacles through targeted outreach, policy changes, and healthcare system improvements can enhance early detection rates and decrease breast cancer mortality.

REFERENCES

1. Omari M, Amaadour L, Zarrouq B, Al-Sheikh YA, El Asri A, Kriya S, et al. Evaluation of psychological distress is essential for patients with locally advanced breast cancer prior to neoadjuvant chemotherapy: Baseline findings from Cohort Study. *BMC women's health*. 2023; 23(445):1-10 doi: 10.1186/s12905-023-02571-1.
2. Alenezi AM, Thirunavukkarasu A, Wani FA, Alenezi H, Alanazi MF, Alruwaili AS, et al. Female Healthcare Workers' knowledge, attitude towards breast cancer, and perceived barriers towards mammogram screening: A multicenter study in North Saudi Arabia. *Curr Oncol*. 2022;29(6):4300-4314. doi: 10.3390/curroncol29060344.
3. Abdel-Salam DM, Mohamed RA, Alyousef HY, Almasoud WA, Alanzi MB, Mubarak AZ, et al. Perceived Barriers and Awareness of Mammography Screening Among Saudi Women Attending Primary Health Centers. *Risk Manag Healthc Policy*. 2020;13:2553-2561. doi: 10.2147/RMHP.S277375.
4. AlAbdulKader A, Gari D, Al Yousif G, Alghamdi A, AlKaltham S, AlDamigh F, et al. Perceived barriers and facilitators to breast cancer screening among women in Saudi Arabia. *Breast cancer (Dove Medical Press)*.2023;15:505-513. doi: 10.2147/BCTT.S406029.
5. Bakarman M, Kalthoum D, Wahby Salem I, Alshuaibi RO, Almohammadi TA, Beser RA, et al. Barriers to using breast cancer screening methods among adult females in Jeddah, Saudi Arabia: A cross-sectional study. *Cureus*. 2023;15(7): e41739. doi: 10.7759/cureus.41739 .
6. Alanazi MF, Thirunavukkarasu A, Alrowily M, Alaqel N, Alaqel A, Alruwaili M, et al. A cross-sectional evaluation of knowledge about breast cancer and perceived barriers to the uptake of mammogram screening among northern Saudi women: A population-based study. *Breast cancer (Dove Medical Press)*.2023;15(1):451–460. doi: 10.2147/BCTT.S414635.
7. Momenimovahed Z, Tiznobaik A, Taheri S, Hassanipour S, Salehiniya H. A review of barriers and facilitators to mammography in Asian women. *E cancer medical science*. 2020; 14(1s):e1146. doi: 10.3332/ecancer.2020.1146.
8. Abdel-Aziz SB, Amin TT, Al-Gadeeb MB, Alhassar AI, Al-Ramadan A, Al-Helal M, et al. Perceived barriers to breast cancer screening among Saudi women at primary care setting. *J Prev Med Hyg*. 2018;59(1): E20-E29. doi: 10.15167/2421-4248/jpmh2018.59.1.689.
9. Moridi A, Mahmoodi S, Rahmati N, Fathi M, Naeiji Z. Comparison of Awareness Level about Breast Cancer Risk Factors, Presentations, and Screening Rules and Tools: A Cross-sectional Study on General Female Population. *Journal of Obstetrics, Gynecology and Cancer Research*. 2021;6(4):188-94. doi: 10.30699/jogcr.6.4.188.
10. Prusty RK, Begum S, Patil A, Naik DD, Pimple S, Mishra G. Knowledge of symptoms and risk factors of breast cancer among women: a community-based study in a low socioeconomic area of Mumbai, India. *BMC women's health*. 2020;20(1):1-2. doi: 10.1186/s12905-020-00967-x.
11. Amkongo M, Karera A, Kalondo L, Nakweenda M, Namene M, Shilumba M, Izaacs LA. A correlational study on the awareness of breast cancer screening methods and risk factors among women attending two health facilities in Windhoek, Namibia. *PAMJ-One Health*. 2023;12(4). doi; 10.11604/pamj-oh.2023.12.4.39770.
12. Hamshari S, Nazzal Z, Altell M, Nanaa I, Jbara R, Sabri R. Mammogram uptake and barriers among Palestinian women attending primary health care in North Palestine. *European Journal of General Practice*. 2021;27(1):264-270. doi: 10.1080/13814788.2021.1985996.
13. Bawazir A, Bashateh N, Jradi H, Breik AB. Breast cancer screening awareness and practices among women attending primary health care centers in the Ghail Bawazir District of Yemen. *Clinical breast cancer*. 2019 Feb 1;19(1): e20-29. doi: 10.1016/j.clbc.2018.09.005.
14. Jones T, Wisdom-Chambers K, Freeman K, Edwards K. Barriers to mammography screening among black women at a community health center in South Florida, USA. *Medical research archives*. 2023 ;11(4). doi: 10.18103/mra.v11i4.3814.
15. Joho AA, Mdoe MB, Masoi TJ, Yahaya JJ. Perceived barriers and factors influencing uptake of breast cancer screening among women: a population-based cross-sectional study. *Scientific Reports*. 2024 ;14(1):12291. doi: 10. 1038/s 41598-024-62218-5.
16. van den Broek-Altenburg EM, Leslie AA, Benson JS, DeStigter KK. Disparities in Mammography Screening: Analyzing Barriers to Access Using Individual Patient Perspectives and the Health Belief Model. *Cancer Control*. 2024; 31:10732748241248367. doi: 10.1177/107327 48241248367.
17. Ponce-Chazarri L, Ponce-Blandón JA, Immordino P, Giordano A, Morales F. Barriers to breast cancer-screening adherence in vulnerable populations. *Cancers*. 2023 Jan 18;15(3):604. doi: 10.3390/cancers15030604.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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ORIGINAL ARTICLE

Prevalence and Interrelationship of Polypharmacy, Potentially Inappropriate Prescribing, and Drug-drug Interactions, in a Tertiary Care Hospital, in Lahore, Pakistan: A Cross-Sectional Study

Waqar Ahmed Siddiqui[1], Aamina Quddus Qureshi[2], NosheenIftikhar[3], Shabir Ahmed[4], Hadiya Nadeem[5], Ayesha Saeed[6]

ABSTRACT

Objective: To determine the prevalence and interrelationship of drug-drug interactions (DDIs) potentially inappropriate prescribing (PIPs) and polypharmacy in admitted patients.

Study Design: Cross-sectional study.

Place and Duration of the Study: Conducted at the Medical Inpatient Department of Combined Military Hospital (CMH), Lahore from 15th January 2024 to 18th May 2024.

Materials and Methods: A total of 180 patients aged 65 years and above, taking at least two medications were included. Patients with critical illnesses or psychiatric disorders were excluded. Prescriptions were analyzed for DDIs using Medscape's "drug interaction checker" and PIPs were evaluated using the STOPP/START criteria (version 3). Descriptive statistics, including frequencies and percentages, were used to assess the prevalence and association of polypharmacy, DDIs, and PIPs.

Results: Among all prescriptions analyzed, 37.1% included at least one drug identified by the STOPP criteria. DDIs were present in 72.1% of prescriptions, of which 19.7% were minor, 47.5% were significant, and 4.9% were major. Polypharmacy was observed in 67.2% of cases.

Conclusion: Polypharmacy was common among geriatric patients. A moderate proportion of prescriptions exhibited DDIs, out of them the majority classified as significant. Thus, emphasizing the importance of managing complex medication regimens to avoid adverse effects. These findings underline the necessity for vigilant medication review, deep pharmacological knowledge and management to enhance patient safety.

Key Words: *Drug-drug Interactions (DDIs), Polypharmacy, Potentially Inappropriate Prescribing (PIPs) Prescriptions, Screening Tool of Older Persons' Prescriptions (STOPP) Criteria.*

Introduction

The clinicians and medical practitioners try to inculcate and build upon the knowledge to stay up to date, with pharmacological advancements taking place and new drugs being approved and introduced into the market and thus modify their prescriptions. However, this poses a concern about the use of different medications in prescriptions without a complete medical review.[1] The people who mostly fall victim to such prescriptions are usually the ones suffering from multiple comorbidities requiring multiple medications, especially the geriatric population which comprises of almost 6% of the total population in Pakistan.[2] Multiple drugs also have different effects on the older population as compared to the younger.

Polypharmacy is the practice of writing more than 5 medications on a single prescription.[3] It is mostly prevalent in the Asian community with research showing polypharmacy being practiced in at least 30% of the geriatric community.[4,5] This can be attributed to ease of access to drugs unlike in the other parts of the world practicing controlled medication. Polypharmacy also leads to multiple other problems including drug-drug interactions (DDIs) in the medication prescribed and potentially inappropriate prescribing (PIPs).[6,7] PIP is the over or under-prescribing of medications which may cause

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significant harm whereas DDIs are alteration in the efficacy and the toxicity of one drug due to the presence of another simultaneously administered drug.[8,9] Polypharmacy, DDIs and PIMs, also referred to as "the iatrogenic triad", are responsible for many adverse drug reactions (ADRs) in older patients.[10] This issue leads to numerous hospital admissions, contributing to significant morbidity and mortality while imposing financial strain. [13]

The physiological manifestation of drugs in geriatric population needs to be studied and require the prescription written to be tailored to the individual. Prior research has shown that elderly patients experience a high prevalence of iatrogenic effects, with polypharmacy affecting 5-78% of individuals, DDIs impacting 13-58%, and PIP affecting 2.9-38.5%.[10] While studies in Pakistan have examined these factors individually, few have investigated them concurrently thus posing a need to evaluate the frequency of this triad practice.[11,12] This study was conducted to underscore the need for establishment of standard protocols to minimize iatrogenic risks in this vulnerable group. The aim of this study was to address the knowledge gap by evaluating the prevalence and interconnections of polypharmacy, potentially inappropriate prescribing (PIP), and drug-drug interactions (DDIs) in older patients to help develop better therapeutic strategies.

Materials and Methods

A cross-sectional study, conducted in the medical inpatient department of CMH, Lahore. The ethical approval was obtained from Ethical Review Board of CMH, Medical College Lahore (Ref: 750/ERC/CMH/LMC, dated 24-05-2023). Using Cochran's formula at a 95% confidence interval, a sample size of 174 patients was calculated. Systematic random sampling was employed, enrolling patients aged 65 years and above who were prescribed at least two medications and who provided informed consent. The patients excluded were the ones who had one drug in their prescription or with critical illnesses or psychiatric disorders. Demographic data, medical history (including over-the-counter drug use and substance abuse), and laboratory parameters (e.g., liver and renal function tests) were recorded. Each prescription was categorized using the International Classification of Diseases (ICD) coding.[14]

Polypharmacy was defined as the concurrent use of five or more chronic medications. The Anatomical Therapeutic Chemical (ATC) classification system was used to categorize medications. [15,16] Potentially inappropriate prescriptions (PIPs) were evaluated using the Screening Tool of Older Persons' Prescriptions (STOPP) criteria, version 3. Each prescription was assessed for drug relevance, dosage, and duration.[17,18] Drug-drug interactions (DDIs) were identified using the Medscape Drug Interaction Checker®, with interactions classified as minor, significant, or major. [19] The findings were verified by pharmacology experts.

Data were initially compiled in Microsoft Excel and subsequently analyzed using SPSS version 24. Descriptive statistics, including frequencies and percentages, were calculated. The Chi-Square Goodness-of-Fit test was applied to assess data distribution, with statistical significance set at $p < 0.05$.

Results

Of the 180 samples analysed it was found that 67.2% of the prescriptions were falling under the category of polypharmacy. On further analysis it was found that 52.2% of the prescriptions were written for two or more chronic diseases while the rest 47.8% were written for acute diseases or one chronic disease (Fig 1).

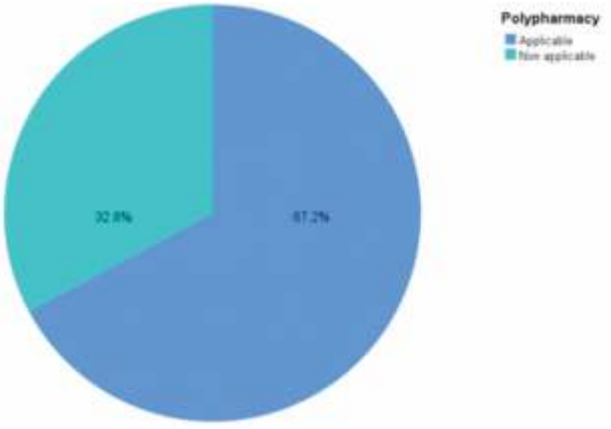

Figure 1: The Frequency of Polypharmacy in Geriatric Patients

After statistical analysis of PIPs, it was found that 37.1% of the prescriptions were found to have medications that were following the STOPP criteria. On further analysis of these medications, it was found that 90.5% of the prescriptions had one PIP and 9.5% had more than one (Fig 2).

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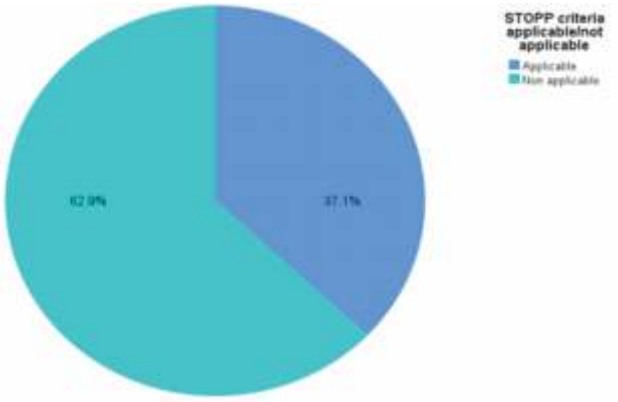

Figure 2: The Frequency of Medications Falling in Potentially Inappropriate Prescription (PIPs)

After analysis of DDIs of the drugs written in the prescriptions by an expert pharmacologist, it was found that 72.1% of the prescriptions had some level of DDI as specified by the Medscape interaction checker®. It was found that 47.5% came under the significant (moderate) category whereas 19.7% fell in the minor category as shown in Fig 1.3 as well as Table I. The prescriptions that fell in the major category were 4.9% (Fig 3).

Table I: The Frequency of DDIs by Categories (Based on Medscape Interaction Checker)

		Frequency (N)	Percent (%)	Valid Percent	Cumulative Percent
Valid	None	51	27.4	27.9	27.9
	Minor	36	19.4	19.7	47.5
	Significant	87	46.8	47.5	95.1
	Major	9	4.8	4.9	100.0
	Total	183	98.4	100.0	
Missing	System	3	1.6		
Total		186	100.0		

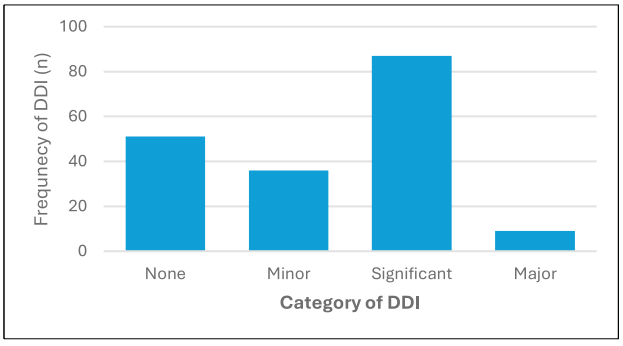

Figure 3: The categories of drug-drug interactions (DDIs) based on Medscape Interaction Checker®.

Discussion

This study highlights significant prescribing patterns among geriatric patients in Pakistan, with polypharmacy identified in 67.2% of prescriptions. This prevalence is consistent with international findings from several European nations, such as Sweden and Italy, but exceeds rates reported in North America.[15] Polypharmacy was notably linked to the presence of multiple chronic diseases, such as hypertension, diabetes, and cardiovascular disorders, a trend similarly observed in other studies from the region and globally.[20]

The prevalence of potentially inappropriate prescribing (PIP) using STOPP criteria was 37.1%, aligning with previous research conducted in similar populations.[21] Large proportions (90.5%) of PIPs were associated with single medication, commonly anticoagulants like clopidogrel and heparin. These results suggest a potential need to adapt PIP screening tools to account for regional disease patterns, such as the higher incidence of atherosclerotic cardiovascular diseases among South Asian populations.[22]

A concerning finding was the high prevalence of drug-drug interactions (DDIs) in 72.1% of prescriptions, with 47.5% categorized as significant and 4.9% as major. This suggests a possible knowledge gap among prescribers regarding common DDIs, particularly in cardiovascular pharmacotherapy. Aspirin and other antiplatelet agents were commonly involved in significant or major interactions, increasing the risk of bleeding, as reported in prior literature.

These findings underscore the importance of routine medication reviews and the integration of reliable DDI screening tools, such as Medscape Drug Interaction Checker®, in clinical workflows.[23] However, as the pharmacokinetics and pharmacodynamics in geriatric populations differ from younger adults, there is a need for age-specific and region-specific DDI screening systems.

The data reflects an ongoing challenge in balancing the necessity of polypharmacy for multimorbidity management with the risks of inappropriate prescribing and harmful drug interactions. While polypharmacy itself is not inherently harmful, inappropriate combinations and unnecessary medications elevate the risk of adverse drug reactions (ADRs) and hospitalizations.[24]

Limitations of this study include its single-center design, which may limit generalizability. Furthermore, reliance on one DDI screening tool may

not capture all potential interactions. Future multicenter studies incorporating multiple interaction-checking platforms and exploring clinical outcomes related to ADRs would provide more comprehensive insights. The study identifies a critical need for clinician training on rational prescribing practices in older adults and the implementation of standard operating procedures to mitigate iatrogenic risks in this vulnerable population.

Conclusion

Polypharmacy, potentially inappropriate prescribing, and drug-drug interactions are highly prevalent among geriatric inpatients, with significant clinical implications. A substantial proportion of prescriptions demonstrated clinically relevant DDIs, particularly within cardiovascular therapies.

These findings emphasize the urgent need for routine medication reviews, tailored prescribing strategies, and the use of reliable drug interaction screening tools to enhance patient safety in older adults. Additionally, there is a need to develop region-specific prescribing guidelines and improve clinician education to minimize iatrogenic risks in this vulnerable population.

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REFERENCES

1. Bachewar N, Choudhari SR, Dudhgaonkar SJ. Assessment of prescription patterns using WHO drug prescribing indicators in medicine wards of a tertiary care teaching hospital: a retrospective observational study. *Int J Basic Clin Pharmacol*. 2018;6(8):2070-2077. doi:10.18203/2310-2003.ijbcp20173298.
2. Usmani BA, Lakhdir MPA, Sameen S, Batool S, Odland ML, Goodman-Palmer D, et al. Exploring the priorities of ageing populations in Pakistan, comparing views of older people in Karachi City and Thatta. *PLoS One.* 2024;19(7):e0304474. doi:10.1371/journal.pone.0304474.
3. Alsuwaidan A, Almedlej N, Alsabti S, Daftardar O, Al Deaji F, Al Amri A, et al. A comprehensive overview of polypharmacy in elderly patients in Saudi Arabia. *Geriatrics* (Basel). 2019;4(2):36. doi:10.3390/geriatrics4020036.
4. Lee H, Baek YH, Kim JH, Liao TC, Lau WCY, Man KKC, et al. Trends of polypharmacy among older people in Asia, Australia and the United Kingdom: a multinational population-based study. *Age Ageing.* 2023;52(2):afad014. doi:10.1093/ageing/afad014.
5. Bhagavathula AS, Vidyasagar K, Chhabra M, Rashid M, Sharma R, Bandari DK, et al. Prevalence of polypharmacy, hyperpolypharmacy and potentially inappropriate medication use in older adults in India: a systematic review and meta-analysis. *Front Pharmacol.* 2021;12:685518. doi:10.3389/fphar.2021.685518.
6. Shetty V, Chowta MN, Chowta KN, Shenoy A, Kamath A, Kamath P. Evaluation of potential drug-drug interactions with medications prescribed to geriatric patients in a tertiary care hospital. *J Aging Res*. 2018;2018:5728957. doi:10.1155/2018/5728957.
7. Tian F, Chen Z, Zeng Y, Feng Q, Chen X. Prevalence of use of potentially inappropriate medications among older adults worldwide: a systematic review and meta-analysis. *JAMA Netw Open.* 2023;6(8):e2326910. doi:10.1001/jamanetworkopen.2023.26910.
8. Liew TM, Lee CS, Goh SKL, Chang ZY. Potentially inappropriate prescribing among older persons: a meta-analysis of observational studies. *Ann Fam Med*. 2019;17(3):257-266. doi:10.1370/afm.2373.
9. Baclet N, Calafiore M, Fregnac C, Gavazzi G, Forestier E, Roubaud-Baudron C, et al. Explicit definitions of potentially inappropriate prescriptions of antibiotics in hospitalized older patients. *Infect Dis Now*. 2022;52(4):214-222. doi:10.1016/j.idnow.2022.02.004.
10. Novaes PH, da Cruz DT, Lucchetti ALG, Leite ICG, Lucchetti G. The "iatrogenic triad": polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults. *Int J Clin Pharm.* 2017;39(4):818-825. doi:10.1007/s11096-017-0470-2.
11. Humza AU, Akbar MA, Bilal Awan MA, Yousuf JB, Khan K, Ammar A. Prevalence and comparative analysis of potential drug-drug interactions among hospitalized patients at a tertiary care cardiac institute in Pakistan: Findings from a single centre. *Pak J Pharm Sci*. 2024 Sep;37(5):961-968. doi:10.36721/PJPS.2024.37.5.REG.961-968.1.
12. Saqlain M, Ali H, Kamran S, Munir MU, Jahan S, Mazhar F. Potentially inappropriate medications are used and its association with health-related quality of life among elderly cardiac patients. *Qual Life Res.* 2020 Oct;29:2715-24. doi:10.1007/s11136-020-02530-5.
13. Watanabe JH, McInnis T, Hirsch JD. Cost of prescription drug-related morbidity and mortality. *Ann Pharmacother*. 2018;52(9):829-837. doi:10.1177/1060028018765159.
14. Tanno LK, Calderon MA, Demoly P; Joint Allergy Academies. New allergic and hypersensitivity conditions section in the international classification of diseases-11. *Allergy Asthma Immunol Res.* 2016;8(4):383-388. doi:10.4168/aair.2016.8.4.383.
15. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr.* 2017;17(1):230. doi:10.1186/s12877-017-0621-2.
16. Zhou JP, Chen L, Guo ZH. iATC-NRAKEL: an efficient multi-label classifier for recognizing anatomical therapeutic chemical classes of drugs. *Bioinformatics*. 2019;36(5):1391-1396. doi:10.1093/bioinformatics/btz757.
17. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age*

Ageing. 2015;44(2):213-218. doi:10.1093/ageing/afu145.
18. Lavan AH, Gallagher P, Parsons C, O'Mahony D. STOPP Frail (Screening Tool of older persons prescriptions in frail adults with limited life expectancy): consensus validation. *Age Ageing*. 2017;46(4):600-607. doi:10.1093/ageing/afx005.
19. Sancar M, Kaşık A, Okuyan B, Batuhan S, İzzettin FV. Determination of potential drug-drug interactions by using various software programs at community pharmacy settings. *Turk J Pharm Sci*. 2019;16(1):14-19. doi:10.4274/tjps.30932.
20. Arabyat RM, Alazzam OM, Al-Azzam SI, Nusair MB. Association between Charlson comorbidity index and polypharmacy: a retrospective database study from Jordan. *Int J Pharm Pract.* 2021;29(6):580-586. doi:10.1093/ijpp/riab067.
21. Hudhra K, García-Caballos M, Jucja B, Casado-Fernández E, Espigares-Rodriguez E, Bueno-Cavanillas A. Frequency of potentially inappropriate prescriptions in older people at discharge according to Beers and STOPP criteria. *Int J Clin Pharm.* 2014;36(3):596-603. doi:10.1007/s11096-014-9943-8.
22. Volgman AS, Palaniappan LS, Aggarwal NT, Gupta M, Khandelwal A, Krishnan AV, et al. Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American Heart Association. *Circulation.* 2018;138(1):e1-e34. doi: 10.1161/CIR.0000000000000580.
23. Suthar J, Tandel A, Patel V. Evaluation of drug-drug interactions in hospitalized geriatric patients at tertiary care hospital. *Indian Drugs.* 2021;58(3):12008. doi:10.53879/id.58.03.12008.
24. Cadogan CA, Ryan C, Hughes CM. Appropriate polypharmacy and medicine safety: when many is not too many. *Drug Saf.* 2016;39(2):109-116. doi:10.1007/s40264-015-0378-5.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

A Comparative Study of Microdebrider Versus Cold Steel Instruments in Nasal Polypectomy: Recurrence Rates and Post Operative Synechiae Formation

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ABSTRACT

Objective: To evaluate and compare the effectiveness of microdebrider and cold steel instruments in nasal polypectomy, focusing on the recurrence of polyps and the formation of post-operative synechiae.

Study Design: Comparative observational study.

Place and Duration of Study: ENT department, Fauji Foundation Hospital Rawalpindi, from 1st July 2022 to 30th June 2023.

Materials and Methods: After the approval of the Hospital Ethical Committee, 96 patients from both genders between 10-60 years of age, presenting with nasal polyps, and fulfilling the selection criteria, were selected by non-probability consecutive technique. By lottery method two equal groups from these patients were formed, Group A & Group B. Patients in Group A underwent microdebrider assisted polypectomy while patients in Group B underwent surgery with cold steel instruments. After taking a detailed history and conducting a thorough ENT and general physical examination, nasal endoscopy was performed on all patients. CT scan PNS, both axial and coronal views were done. Post-operative follow ups of these patients were carried out in the 1st week, 3rd month and 6th month and all the patients were examined endoscopically. The data was expressed as frequency & percentage and analyzed using SPSS version 25.0.

Results: The mean age of the patients was 39.22 (±5.67) years. There were 36.5% females and 63.5% males. Recurrence of nasal polyps was observed in 54.2% patients. Postoperative synechiae formation was observed in 30.2% of patients. Recurrence was found to be statistically lower among patients in Group A, i.e., 41.7% vs 66.7% in Group B. (p=0.007). Postoperative synechiae formation was also found statistically lower among patients in Group A, i.e., 18.75% vs 41.7% in Group B. (p= 0.007).

Conclusion: The results indicated that the microdebrider was more effective than cold steel instruments in reducing the recurrence of nasal polyps and minimizing post-operative synechia formation in patients undergoing nasal polypectomy.

Key Words: *Cold Steel Instruments, Microdebrider, Recurrence, Synechiae Formation.*

Introduction

Nasal polyps are non-neoplastic masses of Sino nasal mucosa occurring because of recurrent or persistent inflammation of sinonasal mucosa.[1] It is the underlying chronic disease of the nasal mucosa that manifests as Nasal polyps and prevail in 1-4 % of the population.[2] Males are relatively affected more. About 25%-30% of patients with Chronic Rhinosinusitis (CRS) develop Nasal Polyposis.[3]

Patients present with nasal blockage, nasal discharge, postnasal drip, hyposmia, as well as a feeling of facial pressure persisting for a duration of over 12 weeks.[4] The quality of life of the patients having nasal polyps, due to these symptoms, is badly affected.[5] Nasal polyps may affect physical and emotional wellbeing and may even lead to sleep disturbances.[6] These patients may suffer from asthma along with these symptoms (Samter's triad) and may be sensitive to aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs).[7] These appear as unilateral or bilateral, single or multiple, mobile, smooth, grey, grape like masses originating from the middle meatus or spheno-ethmoid recess.[8]

Although diagnosis is clinical, imaging helps in assessing the disease and its potential complications as well as help in management planning. The initial

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management is medical, including topical intranasal steroid sprays/ local nasal drops or oral steroid therapy or both along with the use of antibiotics and antihistamines.[9] Surgery is the main option for the people who do not respond to medical treatment, or they have recurrence. Around 30-50% of people may require surgery, either by cold steel instruments or by microdebrider.[10] Conventional nasal polypectomy has almost been replaced by Endoscopic Nasal Polypectomy.

Surgery for Sino nasal polyposis is challenging due to higher chances of bleeding, obscuring the operating field, thus decreasing the chances of complete removal. Microdebrider or shaver is a powered instrument that gives better outcome by making dissection quicker and precise, ensuring clear visual field, thus leading to fast healing.[11]

Despite microdebrider's precision in removal of diseased mucosa, a controversy prevails regarding its superiority over endoscopic assisted conventional cold steel polypectomy. Moreover, a lot of work has not been done in Pakistan on this topic, as concept of use of microdebrider in FESS Nasal Polypectomy has not gained the popularity it deserves. Hence, we carried out this study with the aim to compare the use of microdebrider and cold steel instruments to see the frequency of recurrence and post-operative synechiae formation, in order to play our part in resolving this controversy.

Materials and Methods

A comparative observational study was undertaken from 1st July 2022 to 30th June 2023 at the ENT department, Fauji Foundation Hospital Rawalpindi. After approval of the Hospital Ethical Committee, vide their letter number 824/RC/FFH/RWP dated 5 January 2022, the sample size was calculated by the WHO calculator keeping the power of test equal to 80% and level of significance equal to 5%. Hence, 96 patients from both genders between 10-60 years of age, presenting with nasal polyps, and fulfilling the selection criteria, were selected by non-probability consecutive technique.

Informed consent of the study subjects was obtained. By lottery method two equal groups from these patients were formed, Group A & Group B. Patients in Group A underwent microdebrider assisted polypectomy while patients in Group B underwent surgery with cold steel instruments.

Proper history was taken, including history of atopy, aspirin sensitivity, asthma etc. Complete ENT and Head and neck and the general examination were carried out. Nasal endoscopy was performed on all the patients. CT scan PNS was carried out on all the patients with both axial and coronal views. The patients who had unilateral or congenital disease underwent surgery previously, or were immunocompromised, or had underlying malignancy or fungal etiology, were excluded from the study.

Post-operative follow ups of these patients were carried out in the 1st week, 3rd month and 6th month. All the patients were examined endoscopically to see any recurrence of nasal polyps and any synechiae formation.

The data was expressed as frequency & percentage and analyzed using SPSS version 25.0. The same software was used for analysis and the Chi-square test was applied between 2 groups to see recurrence and post-operative synechiae formation.

Results

A total of 96 patients were selected with the mean age of 39.22 (±5.67) years. Among them 55 (57.3%) patients were aged ≤40 years of age, while 41 (42.7%) patients were older than 40 years of age. (Figure 1)

Regarding gender distribution, 35 (36.5%) patients were females, and 61 (63.5%) patients were males. (Figure 1)

Recurrence of nasal polyps was observed in 52 (54.1%) patients, while postoperative synechiae formation occurred in 29 (30.2%) patients.

The recurrence was found significantly lower in Group A with 20 (41.7%) patients affected compared to 32 (66.7%) in Group B. (p= 0.007). (Table I).

Similarly postoperative synechiae formation was

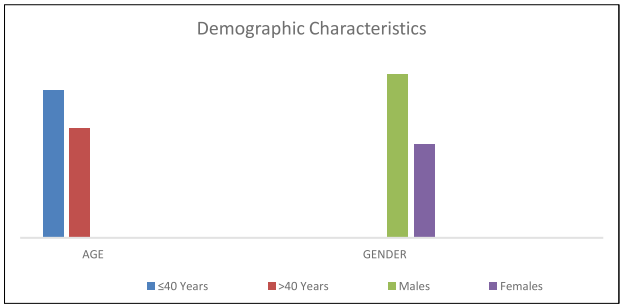

Figure 1: Demographic Characteristics of Study Participants (n=96)

significantly lower in Group A, occurring in 9 (18.75%) patients compared to 20 (41.7%) patients in Group B (p= 0.007). (Table II).

Table I: Recurrence of Polyps (n=96)

Group	Recurrence		Total	p-value
	Yes	No		
A (Microdebrider)	20 (41.7%)	28 (58.3%)	48 (100%)	0.007
B (Cold Steel Instruments)	32 (66.7%)	16 (33.3%)	48 (100%)	
Total	52 (54.2%)	44 (45.8%)	96 (100%)	

Table II: Postoperative Synechiae formation (n=96)

Group	Postoperative Synechiae Formation		Total	p-value
	Yes	No		
A (Microdebrider)	09 (18.75%)	39 (81.25%)	48 (100%)	0.007
B (Cold Steel Instruments)	20 (41.7%)	28 (58.3%)	48 (100%)	
Total	29 (30.2%)	67 (69.8%)	96 (100%)	

Discussion

Incidence of Nasal Polyps is usually found among people of ages between 40 to 60 years. Though the disease is more prevalent among males, but the disease is more severe among females.[4]

In the recent past, shavers or microdebriders emerged as a far better surgical tool than the conventional cold steel Nasal Polypectomy, due to less bleeding,less damage to the surrounding tissues, early healing and less crust and synechiae formation.[12] These are much more precise in removing the pathology, hence leading to lesser complications.[13]

However surprisingly, many of the recent studies do not consider that microdebriders give better results than the conventional instruments in attaining postoperative healing. In contrast, our study has shown that recurrence was found significantly lower among patients who underwent microdebrider assisted polypectomy than those who underwent conventional cold steel instruments polypectomy. Similarly, postoperative synechiae formation was also found significantly lower with microdebrider as compared to cold steel instruments. Our results do not differ from many of the studies. According to a study by Bellad, Manjunath & Ravi (2018), patients who underwent nasal polypectomy by microdebrider had lower recurrence rates and post-operative synechiae formation.[9] Observations of this study are like those of our study. Another study also showed that patients who underwent polypectomy by microdebrider had lower recurrence rates and post-operative synechiae formation as compared to cold steel instruments.[14] One local study also showed a little higher polyp recurrence rates in cold steel instruments as compared to microdebrider group while post-operative synechiae formation was 3.6% in microdebrider group as compared to 16.4% in cold steel group.[15]

But a study by Kaipuzha et al (2019) though showed better healing in microdebrider assisted polypectomies, but did not find any significant difference between the two instruments.[2] Another study was also of the same observations, though microdebrider assisted surgery was found relatively blood less.[16] Yet another study showed no significant difference between microdebrider assisted polypectomy with conventional nasal polypectomy regarding post-operative outcomes like scarring or recurrence.[17] Similarly another comparative study by Acharya et al (2023) also did not find any significant difference in the outcome either by microdebrider or the conventional nasal polypectomy.[18]

In contrast, a review study deduced that microdebrider assisted polypectomy resulted in more severe complications than the procedures carried out by conventional surgical instruments.[19]

Hopkins et al concluded that other factors like patient factors and disease characteristics were more important in causing complications rather than the surgical modality.[20] Another retrospective study concluded that complication rates of FESS were not high even in patients with severe nasal polyposis.[21]

However, it is a fact to be noted that microdebrider is quite expensive as compared to cold steel instruments surgery.[22] But it must be compared with the extra cost caused by revision procedures in the recurrent cases who underwent conventional nasal polypectomies.

The findings of the study have limitations like certain important effect modifiers that were not studied in the current study. Moreover, this study was carried out in only one hospital on a limited number of patients hence its findings cannot be generalized. In future, such studies at a more comprehensive level may be carried out to draw a more meaningful conclusion.

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Conclusion

The results indicated that the microdebrider was more effective than cold steel instruments in reducing the recurrence of nasal polyps and minimizing post-operative synechia formation in patients undergoing nasal polypectomy.

REFERENCES

1. Mgbe RB, Adekayne AG, Francis PM, Offiong ME. Management of nasal polyps in Calabar, South-South Nigeria. *Calabar J Health Sci*, 2023; 7 (1); 20-24. doi: 10.25259/ CJHS_38_2021.
2. Kaipuzha RR, Venkataramanujam NC, Karthikeyan P, Pulimoottil DT. Comparison of microdebrider-assisted endoscopic sinus surgery and conventional endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps. *Romanian J Rhinol*. 2019; 9 (34): 91–95. DOI: 10.2478/rjr-2019-0011
3. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology*. 2012 Mar; 50 (1): 1-12. DOI: 10.4193/ Rhino12.000
4. Stevens WW, Schleimer RP, Kern RC. Chronic Rhinosinusitis with Nasal Polyps. *J Allergy Clin Immunol Pract*. 2016 Jul; 4 (4): 565–572. doi: 10.1016/j.jaip.2016.04.012.
5. Ta NH. Will we ever cure nasal polyps? *Ann R Coll Surg Engl*. 2019 Jan; 101 (1): 35-39. doi: 10.1308/rcsann.2018.0149.
6. Bachert C, Bhattacharyya N, Desrosiers M, Khan AH. Burden of Disease in Chronic Rhinosinusitis with Nasal Polyps. J *Asthma Allergy*. 2021; 14:127–134. doi: 10.2147/JAA. S290424.
7. Krouse HJ, Krouse JH. Samter's Triad to Aspirin-Exacerbated Respiratory Disease: Historical Perspective and Current Clinical Practice. *ORL Head Neck Nurs*. 2015; 33 (4):14-8.
8. Meng, L., Qu, X., Tao, P. et al. Quercetin Alleviates the Progression of Chronic Rhinosinusitis Without Nasal Polyps by Inhibiting Nasal Mucosal Inflammation and Epithelial Apoptosis. *Mol Biotechnol* (2024). doi.org/10.1007/s 12033-024-01269-5
9. Morse JC, Miller C, Senior B. Management of Chronic Rhinosinusitis with Nasal Polyposis in the Era of Biologics. J *Asthma Allergy*. 2021; 14: 873–882. doi: 10.2147/ JAA.S258438.
10. Lageju N, Pradhan B, Thapa N. Endoscopic Sinus Surgery for Sinonasal Polyposis: Microdebrider or Conventional Instruments. *J Nepal Med Assoc*. 2017; 56 (208): 447–450. PMID: 29453478.
11. Bellad SA, Manjunath N, Ravi S. Comparison between microdebrider assisted surgery and the conventional methods in the surgical treatment of nasal polyps. *Int J Otorhinolaryngol Head Neck Surg*. 2018; 5(1):154. doi: 10.18203/issn.2454-5929.ijohns20185305
12. Ramakrishnan V, Kingdom T. Surgical Instruments in Revision Endoscopic Sinus Surgery. In: *Revision Sinus Surgery. Springer, Berlin, Heidelberg*. 2008. doi: 10.1007/978-3-540-78931-4_8.
13. Saafan ME, Ragab SM, Albirmawy OA, Elsherif HS. Powered versus conventional endoscopic sinus surgery instruments in management of sinonasal polyposis. *Eur Arch Otorhinolaryngol*. 2013; 270: 149– 155. DOI 10.1007/ s00405-012-1969-8
14. Varman K, Borlingegowda V, Hussain S M, Vijayashree MS, Killera S. Conventional versus Microdebrider Assisted Endoscopic Sinus Surgery for Sinonasal Polyposis -A Comparative Study. *Research in Otolaryngology*, 2017; 6 (1):10–15. doi: 10.5923/ j.otolaryn.20170601.03.
15. Aziz T, Ashfaq AH, Mahmood K, Malik AA, Bashir F. Comparison of frequency of synechiae formation in patients of sinonasal polyposis undergoing endoscopic sinus surgery with and without using microdebrider. *Rawal Med J*. 2017; 42 (3): 363–365.
16. Singh R, Hazarika P, Nayak DR, Balkrishnan R, Gangwar N, Hazarika M. A comparison of micro debriders assisted endoscopic sinus surgery and conventional endoscopic sinus surgery for nasal polypi. I*ndian J Otolaryngol Head Neck Surg*. 2013; 65 (3):193– 196. doi: 10.1007/s12070-011-0332-5.
17. Sharma B, Pokharel A, Bhandari C, Upadhayay HP. Comparitive study between conventional polypectomy with microdebrider assisted endoscopic sinus surgery. *IJSIRT*, 2023; 1 (2): 41-48. doi: 10.3126/ijsirt.v1i2.61401.
18. Acharya S, Mallick G, Prusty N, Kar S, Agasty S. Comparative Study of Microdebrider And Conventional Instruments In Endoscopic Sinus Surgery For Sinonasal Polyposis. *JCTCP*, 2022; 29 (4): 611-615.doi: 10.53555/jptcp.v29i04.2913.
19. McMains KC. Safety in endoscopic surgery. Curr Opin *Otolaryngol Head Neck Surg* 2008; 16 (3): 247-251. doi: 10.1097/MOO.0b013e3282fdccad.
20. Hopkins C, Browne JP, Slack R, Lund VJ, Topham J, Reeves BC, et al. Complications of surgery for nasal polyposis and chronic rhinosinusitis: the results of a national audit in England and Wales. *Laryngoscope*. 2006; 116 (8): 1494–1499. doi: 10.1097/01 .mlg.0000230399.24306.50.
21. Ecevit MC, Sutay S, Erdag TK. The microdébrider and its complications in endoscopic surgery for nasal polyposis. *J. Otolaryngol*. Head Neck Surg. 2008; 37(2):160–164.
22. Bernstein JM, Lebowitz RA, Jacobs JB. Initial report on postoperative healing after endoscopic sinus surgery with the microdebrider. *Otolaryngol Head Neck Surg.* 1998; 118 (6): 800–803. doi: 10.1016/S0194-5998(98)70272-4.

CONFLICT OF INTEREST

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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ORIGINAL ARTICLE

The Difference of Gingival Inflammation, Oral Hygiene, and Periodontal Treatment Needs Between Metabolic Syndrome and Nonmetabolic Syndrome in Periodontitis Patients

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ABSTRACT

Introduction: This research aimed to determine the difference of gingival index, papillary bleeding index, oral hygiene, and periodontal treatment needs between periodontitis patients with and without MetS.

Study Design: Analytic observational study using cross-sectional research design

Place and Duration of Study: Dental and Oral Hospital Universitas Sumatera Utara, Medan, Indonesia from November 2023 to January 2024.

Materials and Methods: This study involved ninety participants who were diagnosed with periodontitis. The determination of MetS patients and nonmetabolic syndrome (NMetS) patients was performed by examining blood pressure, blood glucose levels, body weight, height, and abdominal circumference. Oral examination was performed by measuring gingival index (GI), papillary bleeding index (PBI), oral hygiene index (OHI), and community periodontal index of treatment needs (CPITN). The data was analyzed using descriptive and parametric statistical tests with $p<0.050$ was considered significant.

Results: There was no significant difference in gingival inflammation as evaluated by GI ($p=0.592$) and PBI ($p=0.216$) between MetS patients and NmetS patients. There was a significant difference in oral hygiene examination as evaluated by OHI ($p= 0.005$) between MetS patients and NmetS patients. There was a significant difference in the examination of treatment needs as measured by the CPITN ($p=0.023$) between MetS patients and NmetS patients.

Conclusions: The gingival inflammation in periodontitis patients with MetS is more severe than the NMetS patients. The oral hygiene in periodontitis patients with MetS is worse than the NMetS patients. The patients with MetS have higher periodontal treatment needs than NMetS patients.

Key Words: *Gingival Inflammation, Metabolic Syndrome, Oral Hygiene, Periodontal Treatment, Periodontitis.*

Introduction

A complex inflammatory condition known as periodontitis develops when the human immune system interacts intricately with bacterial plaque. It can be identified by the degeneration of periodontal tissues, such as the periodontal ligament, gingiva, and alveolar bone, which results in the formation of periodontal pockets around the teeth that harbor numerous pathogenic bacteria that exacerbate the inflammatory process and contribute to further tissue destruction.[1] The worldwide prevalence of periodontal disease as stated by The World Health Organization (WHO) ranges from 20 to 50 percent.[2]

The factors that are interconnected to periodontitis other than bacteria are the presence of systemic diseases. One of the non-infectious conditions linked to periodontitis is metabolic syndrome.[3] Metabolic syndrome (MetS) is defined by elevated blood pressure, blood glucose, and abdominal circumference, as per the Adult Treatment Panel III (ATP III) criteria of the National Cholesterol Education Programme (NCEP).[4] In 2020, the anticipated global prevalence of MetS is 4.8% for adolescents and 2.8% for children, which translates to about 35.5 million adolescents and 25.8 million children.[5] Numerous studies on MetS have been carried out. In Indonesia, 21.66% of the population has MetS according to a study by Herningtyas et al.[6]

The condition that links MetS and periodontitis is oxidative stress. Metabolic syndrome stimulates

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adipose tissue in the body to produce proinflammatory cytokines that cause oxidative stress.[7] Oxidative stress disrupts the equilibrium between the synthesis of reactive oxidative stress (ROS) and antioxidants in the cell, so that the antioxidant defense system cannot neutralize the increased ROS production. Decreased levels of antioxidants impair the body's ability to defend itself against pathogenic bacteria in oral cavity, which can cause periodontitis.[8]

There are several parameters of periodontal disease. Gingival index measurement is done by visually assessing the condition of the gingiva. A commonly used scale is the Löe and Silness Gingival Index.[9] Papillary bleeding index (PBI) measurement is used to evaluate bleeding between the papillae in patients with periodontitis. It gives an idea of the health of the gingival papillae and the presence of inflammation.[10] Another parameter of periodontal disease is oral hygiene. An individual's level of oral hygiene can be calculated using the Oral Hygiene Index (OHI), which measures the amount of plaque and calculus that has accumulated on the teeth surface.[11] The Community Periodontal Index of Treatment Needs (CPITN) is often used to describe changes in periodontal tissues. In this index, gum bleeding, the presence of calculus, and periodontal pocket depth are taken as references for the diagnosis of periodontitis.[12]

There is a pressing need for new research to provide deeper insights into how MetS may influence periodontal health. The updated knowledge on this field is crucial for enhancing both clinical practice and public health guidelines, ensuring that healthcare providers are equipped with the most current information regarding these interconnected health concerns. This research aimed to determine the difference of gingival index, papillary bleeding index, oral hygiene, and periodontal treatment needs between periodontitis patients with and without MetS.

Materials and Methods

This was an analytical observational study, utilizing a cross-sectional approach carried out on 90 patients who visited the dental and oral hospital of Universitas Sumatera Utara, Medan, Indonesia from November 2023 to January 2024. The patients were selected by purposive sampling method. A total of 50 patients were grouped as MetS patients and 40 patients were grouped as NMetS patients. The inclusion criteria were: periodontitis patients suffering from MetS, periodontitis patients without MetS, aged ≥17 years, has ≥ 20 teeth, had not received periodontal treatment for a minimum of 6 months, and were prepared to take part in this investigation. This study excluded the patients who were using anticoagulant medications and patients with systemic illnesses other than MetS. Informed consent is signed by patients prior to participating in the study. Demographic data was obtained through a questionnaire. Data obtained from patients included: age, gender, education, and employment status. This research project has been approved on December 15, 2023 by the Health Research Ethics Committee, Universitas Sumatera Utara (No: 1203/KEPK/USU/2023).

The presence of MetS was confirmed by assessing blood glucose levels, blood pressure, weight, height, and abdominal circumference. Blood glucose level assessments were performed using a glucometer to determine the presence of hyperglicemia in the patients. Hypertension in the patients was evaluated through blood pressure tests using a digital sphygmomanometer. The patient's Body Mass Index (BMI) was measured by dividing the patient's body weight (kilograms) by the square of their height (meters). A tape measure positioned parallel to the floor and encircling the midpoint of the body was used to measure the abdomen's circumference. The number at the point where the measuring tape intersects is the measurement of the abdominal circumference. Patients who have been examined were divided into two groups: MetS patients and NmetS patients.

Every participant had a comprehensive oral and periodontal assessment at the Dental and Oral Hospital, Universitas Sumatera Utara. The periodontal examination comprised several assessments. The evaluation of gingival inflammation was conducted using the gingival index (GI) and the papillary bleeding index (PBI). Gingival index was evaluated by gingival palpation. Papillary bleeding index was assessed by applying slight pressure with a periodontal probe to the oral and buccal gingival sulcus. The GI and PBI score was calculated based on the extent of bleeding in the

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gingiva. The oral hygiene index (OHI) was used to assess patient's oral hygiene. Oral hygiene index was determined by adding the debris score and calculus score, which were evaluated according to the extent of the tooth surface covered by debris and calculus. The assessment of treatment needs was conducted using the community periodontal index of treatment needs (CPITN). The CPITN score was determined based on the gum bleeding, the presence of calculus, and the depth of the pockets.

Version 22 of the Statistical Package for Social Sciences (SPSS) software was utilised for data analysis. The data was calculated using mean ± SD descriptive test. Statistical tests using Saphiro-Wilk test showed that the data was not normally distributed, so the data was considered non-parametric, thus the Mann-Whitney test was performed. Mann-Whitney statistical test was used to compare the GI, PBI, OHI, and CPITN between periodontitis patients with MetS and without MetS. A p-value of less than 0.05 was considered statistically significant.

Results

The data in Table 1 shows the demographic data of the research patients. The majority of patients suffering from MetS come from the age range of 46-55 years, while the majority of patients without MetS come from the age range of 17-25 years. Based on gender, 27 out of 50 (54%) patients with MetS were male, while 23 out of 40 (57,5%) patients without MetS were female. Both groups of study participants had high school degrees as their primary educational attainment level. Thirty (60%) patients suffering from MetS is employed, while 23 (42,5%) patients without MetS is unemployed, as determined by their employment status.

The data in Table 2 shows that the mean of blood glucose levels (MetS: 180.86 mg/dL; NMetS: 89.38 mg/dL), blood pressure (MetS: 153.40/91.96 mmHg; NMetS: 119.13/78.60 mmHg), height (MetS: 1,61 m; NMetS: 1,60 m), weight (MetS: 77,91 kg; NMetS: 58.83 kg), BMI (MetS: 29.85 kg/m^2; NMetS: 22.92 kg/m^2), and abdominal circumference (MetS: 100,79 cm; NMetS: 81.55 cm) in MetS patients were higher than NmetS patients.

The comparison of periodontal assessment results in periodontitis MetS patients and NMetS patients is shown in table 3. The patients with and without MetS differ significantly in terms of OHI (p=0.005) and CPITN (p=0.023), while the GI (p=0.592) and PBI (p=0.216) showed no significant difference between MetS and NMetS patients.

Table I: Demographic Characteristic of The Research Patients

Demographic characteristic	Mets (n=50)		No MetS (n=40)	
	n	%	n	%
Age (years)				
17-25	4	8	13	32.5
26-35	6	12	3	7.5
36-45	9	18	11	27.5
46-55	19	38	9	22.5
56-65	10	20	1	2.5
>65	2	4	3	7.5
Gender				
Female	23	46	23	57.5
Male	27	54	17	42.5
Education				
Elementary school	1	2	2	5
Middle school	1	2	3	7.5
High school	27	54	25	62.5
Bachelor	21	42	10	25
Employment Status				
Employed	30	60	17	42.5
Unemployed	20	40	23	57.5

Table II: Blood Glucose, Blood Preasure, Body Mass Index and Abdominal Circumference in Patients with MetS and No MetS

Variables	MetS	No. MetS
	Mean±SD	Mean±SD
Blood glucose level (mg/dL)	180.86±76.54	89.38±11.37
Systolic blood pressure (mmHg)	153.40±13.38	119.13±12.19
Diastolic blood pressure (mmHg)	91.96±5.35	78.60±10.43
Height (m)	1.61±0.09	1.60±0.06
Weight (kg)	77.91±11.56	58.83±8.88
BMI (kg/m^2)	29.85±3.99	22.92±2.72
Abdominal circumference (cm)	100.79±7.94	81.55±9.92

Table III: Periodontal Assessment Results of The Research Patients

Variables	Mets	No MetS	p
	Mean±SD	Mean±SD	
Gingival Index	1.19±0.37	1.15±0.39	0.592
Papillary Bleeding Index	1.47±0.57	1.31±0.44	0.216
Oral Hygiene Index	3.01±1.36	2.22±0.81	0.005*
Community Periodontal Index of Treatment Needs	3.54 ± 0.50	3.30 ± 0.46	0.023*

Mann-Whitney test; * Significant p<0.050

Discussion

This research was an analytical observational study, utilizing a cross-sectional approach to examine people ranging from late adolescents (17-25 years old) to eldery (>65 years old). The World Health Organization classifies age as young (25-44), middle age (44-60), elderly (60-75), senile (75-90), and long-livers (>90).[13] In this study, we classify age according to the Indonesian Ministry of Health. The selection of patients with this age range considers the time of third molar tooth eruption, which is between 17-25 years of age. The majority of the patients with MetS in this study came from the age range of 46-55 years. The study conducted by Campos et al. similarly demonstrated comparable findings, indicating that the majority of MetS patients were in the age range of 45-55 years.[14] As individuals grow older, the body's metabolism naturally declines, causing a reduction in the body's capacity to efficiently metabolize sugar and fat, which leads to a steady accumulation of body fat and a reduction in muscle mass. This shift in body composition can potentially contribute to insulin resistance and dyslipidemia development, which are the primary components of MetS.[15]

This study found that the patients suffering from MetS were more common in males than females. This difference may occur because of varying metabolic regulation in male and female patients due to differences in muscle mass, adiposity, and hormones. Male patients tend to have more visceral fat in their abdominal regions or upper bodies, whereas female patients typically exhibit a greater quantity of adipose tissue in their lower extremities.[16] Visceral fat tissue actively produces adipokines and inflammatory mediators associated with insulin resistance. The socioeconomic status of the patients in this study is seen in terms of education level and employment status. Patients with MetS had the majority of education for 10-12 years and are currently employed. Patients with an employment and a high level of education are at risk of obesity and MetS which is much higher compared to those who have a lower level of education and are unemployed. This is due to lifestyle changes that often involve the consumption of high-calorie foods and decreased physical activity.[17]

The data in table 2 shows that the results of the MetS component examination in each patients show differences, where patients with MetS have higher scores than patients without MetS. According to the criteria of NCEP ATP III,[4] which describes the normal threshold scores of MetS components, most MetS patients examined in this study exceeded normal scores, while patients without MetS were in the normal range of values.

The data in table 3 shows an insignificant difference in GI scores between individuals who have MetS and those who have not (p=0.592). However, patients with MetS still have higher scores than patients without MetS. Metabolic syndrome is characterized by chronic low-grade inflammation, which can extend to the periodontium and exacerbate gingival inflammation. Inflammatory mediators associated with MetS, such as Tumour necrosis factor-alpha (TNF-α), C-reactive protein, and interleukin-6 (IL-6), can enhance the inflammatory response in periodontitis, leading to increased gingival and papillary bleeding.[18] The findings in this study also showed that the PBI score of patients with MetS (PBI=1.47±0.57) was slightly higher than the PBI score of patients without MetS (PBI=1.31±0.44). This discovery aligns with the findings of the study conducted by Pietropaoli et al., which states that the number of patients with MetS who experience generalized gingival bleeding is more than patients who do not suffer from MetS. They also found that the serum CRP levels rose as the number of MetS constituents grew.[19]

Some studies show that hyperglycemia, which is one of the MetS components, was connected to elevated levels of serum CRP. C-reactive protein can induce the expression and activity of matrix metalloproteinases (MMPs) in the periodontium. Matrix metalloproteinases degrade extracellular matrix components, including collagen and elastin, leading to tissue breakdown and destruction. Increased MMP activity in the gingival tissues can weaken the structural integrity of the periodontium, making the gingiva more susceptible to bleeding upon mechanical stimulation.[20]

The data presented in table 3 indicates that patients with MetS have a high OHI score, with a mean of 3.01 ± 1.36, while patients without MetS have a moderate OHI score, with a mean of 2.22 ± 0.81. These scores are determined by the presence of debris and calculus. According to a study conducted by Jaramillo

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et al., the development of glucose intolerance in individuals with MetS strongly correlates with the presence of microorganisms that contribute to the formation of debris and calculus.[21] Insulin resistance leads to decreased cell sensitivity to insulin, which causes an increase in insulin levels, resulting in hyperglycemia. Hyperglycemia creates an advantageous environment for oral bacteria to flourish due to their utilization of glucose as the primary energy source, leading to increased oral bacterial proliferation. Increased bacterial proliferation leads to the formation of dental plaque, which is a biofilm consisting of bacteria, saliva proteins, and food debris.[22] Progressive bacterial colonization will eventually result in mineralization, resulting in the formation of calculus, which causes the increase in OHI score.

The large difference in OHI examination could be attributed to factors related to long-term habits because the accumulation of debris in the oral cavity takes some time to develop into dental calculus. Over the course of a person's life, dental calculus can accumulate on the supragingival and/or subgingival tooth surfaces. Its creation may be influenced by variables like age, food, systemic health, dental treatment frequency, and oral hygiene practices.[23] Gingival inflammation, which consists of papillary bleeding and gingival enlargement can occur spontaneously, resulting in a minimal difference in GI and PBI scores between the MetS and NmetS patients.

This study revealed that individuals with MetS had a higher CPITN score (CPITN=3.54 ± 0.50) compared to individuals without MetS (CPITN = 3.30 ± 0.46). Increased ROS in patients with MetS syndrome are susceptible to the emergence of chronic inflammatory mediators that will cause alveolar bone destruction, deep pocket formation, and higher attachment loss. Damage to the periodontium and worsening of periodontal disease can result from oxidative stress, which can be caused by an imbalance of ROS formation and antioxidants in saliva and gingival sulcus fluid. The imbalance of ROS formation and antioxidants will lead to collagen degradation and loss of attachment to periodontal tissues, resulting in higher CPITN scores.[24,25] The limitation of this study is the absence of laboratory tests, such as hemoglobin A1c (HbA1c), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels as parameters determining MetS. Future studies are expected to conduct laboratory tests to determine whether patients can be categorized as MetS or NMetS ptients.

Conclusions

The gingival inflammation in periodontitis patients with MetS is more severe than the NMetS patients. The oral hygiene in periodontitis patients with MetS is worse than the NMetS patients. The patients with MetS have higher periodontal treatment needs than NMetS patients.

Acknowledgments

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Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication. of this article.

REFERENCES

1. Könönen E, Gursoy M, Gursoy U. Periodontitis: A Multifaceted Disease of Tooth-Supporting Tissues. *J Clin Med*. 2019;8(8):1135. doi:10.3390/jcm8081135.
2. Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. *Int J Health Sci (Qassim)*. 2017;11(2):72-80.
3. Nibali L, Tatarakis N, Needleman I, et al. Association Between Metabolic Syndrome and Periodontitis: A Systematic Review and Meta-analysis. *J Clin Endocrinol Metab*. 2013;98(3):913-920. doi:10.1210/jc.2012-3552.
4. Huang PL. A comprehensive definition for metabolic syndrome. *Dis Model Mech*. 2009;2(5-6):231-237. doi:10.1242/dmm.001180.
5. Noubiap JJ, Nansseu JR, Lontchi-Yimagou E, et al. Global, regional, and country estimates of metabolic syndrome burden in children and adolescents in 2020: a systematic review and modelling analysis. *Lancet Child Adolesc Health*. 2022;6(3):158-170. doi:10.1016/S2352-4642(21)00374-6.
6. Herningtyas EH, Ng TS. Prevalence and distribution of metabolic syndrome and its components among provinces and ethnic groups in Indonesia. *BMC Public Health*. 2019;19(1):377. doi:10.1186/s12889-019-6711-7.
7. Oktay S, Ozoner O, Emekli Alturfan E, Noyan U. Determination of Oxidative Stress Parameters and Tissue Factor Activity in the Saliva of Patients with Periodontitis. *European Journal of Biology*. 2019;78(2):63-68. doi:10.26650/EurJBiol.2019.0002.
8. Khan SN, Kumar S, Iqbal S, Joy MT, Ramaprabha G. Oxidative stress, antioxidants, and periodontitis: How are they linked. *International Journal of Oral Care and Research*. 2018;6(2):107-112.

9. Löe H. The Gingival Index, the Plaque Index and the Retention Index Systems. *J Periodontol*. 1967;38(6):610-616. doi:10.1902/jop.1967.38.6.610.
10. Engelberger T, Hefti A, Kallenberger A, Rateitschak K -H. Correlations among Papilla Bleeding Index, other clinical indices and historically determined inflammation of gingival papilla. *J Clin Periodontol*. 1983;10(6):579-589. doi:10.1111/j.1600-051X.1983.tb01296.x.
11. Greene JG, Vermillion JR. The Simplified Oral Hygiene Index. *J. Am. Dent. Assoc.* 1964;68(1):7-13. doi: 10.14219/jada.archive.1964.0034.
12. Bansal M, Mittal N, Singh T. Assessment of the prevalence of periodontal diseases and treatment needs: A hospital-based study. *J Indian Soc Periodontol*. 2015;19(2):211. doi:10.4103/0972-124X.145810.
13. Dyussenbayev A. Age Periods Of Human Life. *Adv Soc Sci Res J*. 2017;4(6). doi:10.14738/assrj.46.2924.
14. Campos JR, Costa FO, Cota LOM. Association between periodontitis and metabolic syndrome: A case-control study. *J Periodontol*. 2020;91(6):784-791. doi:10.1002/JPER.19-0298.
15. Mohamed SM, Shalaby MA, El-Shiekh RA, El-Banna HA, Emam SR, Bakr AF. Metabolic syndrome: risk factors, diagnosis, pathogenesis, and management with natural approaches. *Food Chemistry Advances*. 2023;3:100335. doi:10.1016/j.focha.2023.100335.
16. Nauli AM, Matin S. Why Do Men Accumulate Abdominal Visceral Fat? *Front Physiol*. 2019;10. doi:10.3389/fphys.2019.01486.
17. Silvestri E, Giacco A. Diet, Exercise, and the Metabolic Syndrome: Enrollment of the Mitochondrial Machinery. *Nutrients*. 2022;14(21):4519. doi:10.3390/nu14214519.
18. Rodrigues WF, Miguel CB, Lazo-Chica JE, et al. Interleukin-6, tumor necrosis factor-α, C-reactive protein, and hematological parameters in experimental periodontal disease after β-adrenergic blockade. *J Indian Soc Periodontol*. 2019;23(6):511-516. doi:10.4103/jisp.jisp_77_19.
19. Pietropaoli D, Altamura S, Ortu E, et al. Association between metabolic syndrome components and gingival bleeding is women-specific: a nested cross-sectional study. *J Transl Med*. 2023;21(1):252. doi:10.1186/s12967-023-04072-z.
20. Radzki D, Negri A, Kusiak A, Obuchowski M. Matrix Metalloproteinases in the Periodontium—Vital in Tissue Turnover and Unfortunate in Periodontitis. *Int J Mol Sci*. 2024;25(5):2763. doi:10.3390/ijms25052763.
21. Jaramillo A, Contreras A, Lafaurie GI, et al. Association of metabolic syndrome and chronic periodontitis in Colombians. *Clin Oral Investig*. 2017;21(5):1537-1544. doi:10.1007/s00784-016-1942-9.
22. Valm AM. The Structure of Dental Plaque Microbial Communities in the Transition from Health to Dental Caries and Periodontal Disease. *J Mol Biol*. 2019;431(16):2957-2969. doi:10.1016/j.jmb.2019.05.016.
23. Forshaw R. Dental calculus - oral health, forensic studies and archaeology: a review. *Br Dent J*. 2022;233(11):961-967. doi:10.1038/s41415-022-5266-7
24. Wulandari P, Siburian AB, Ivanka AW, Ananda A. The relationship between oxidative stress and periodontium destruction. *Bali Medical Journal*. 2024;13(3):87.
25. Arreguin-Cano JA, Ayerdi-Nájera B, Tacuba-Saavedra A, et al. MMP-2 salivary activity in type 2 diabetes mellitus patients. *Diabetol Metab Syndr*. 2019;11(1):113. doi:10.1186/s13098-019-0510-2.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Effect of Phototherapy on Serum Calcium Level in Neonatal Jaundice

Hina Sohail[1], Alia Halim[2], Sahira Aaraj[3], Nazia Mushtaq[4]

ABSTRACT

Objective: The aim of this study was to determine the effect of phototherapy induced hypocalcemia in icteric newborns and to compare it between preterm and term neonates.

Study Design: Quasi experimental study.

Place and Duration of Study: Pakistan Air Force (PAF) hospital Islamabad, from 1st July 2021 to 31st January 2022.

Materials and Methods: A total of 62, full term and late preterm neonates, requiring phototherapy for indirect hyper-bilirubinemia were included. The serum calcium levels were checked, pre and post phototherapy or 48 hours after start of phototherapy whichever came earlier. The data of patients, regarding gender, gestational age, chronological age and mode of delivery was recorded. The data was analysed in SPSS version 22. The frequency and percentages were calculated for qualitative variables i.e gender and mode of delivery. The mean and standard deviation were calculated for quantitative variables i.e age, gestational age, duration of phototherapy, pre and post phototherapy serum calcium levels. The paired sample t test was applied to compare pre and post phototherapy serum calcium levels. The *p*-value < 0.05 was considered statistically significant.

Results: There were 39 (62.90%) males and 23 (37. 10%) females, with mean age of 4.52 ± 1.25 days. The mode of delivery was cesarean section in 41 (66.13%) cases while 21 (33.87%) were delivered as vaginal delivery. The mean gestational age was 38.11 ± 1.49 weeks. The mean duration of phototherapy was 3.17 ± 0.55 hrs. The mean value of pre and post therapy serum calcium level was 9.59 ± 0.52 mg/dl and 9.07 ± 0.44 mg/dl respectively (*p* value = 0.0001). The post phototherapy calcium levels did not have any significant association with gestational age, gender and chronological age of the newborns i.e. the *p* value was 0.174, 0.269, 0.134 respectively.

Conclusions: Phototherapy resulted in a significant reduction in serum calcium levels after 48 hours; however, none of the neonates developed hypocalcemia.

Key Words: *Calcium, Neonatal Jaundice,Phototherapy.*

Introduction

Neonatal jaundice is a significant contributor to morbidity and the primary cause for hospitalization within the initial week of life. The global occurrence of severe neonatal jaundice varies across regions, ranging from 3.34% in Africa to 2.58% in South-East Asian regions.[1] About 60% of term and 80% of preterm infants develop jaundice in the first seven days of their lives.[2] Majority of these cases are of physiologic jaundice. Various factors contribute towards physiologic jaundice including increased neonatal erythrocyte destruction, slow bilirubin elimination through hepatocytes and underdeveloped liver conjugating enzymes. In full term infants, physiologic jaundice tends to self resolve within a week while in preterm neonates, it is more severe and takes a longer time to resolve.[3]

Pathological hyperbilirubinemia always has some serious underlying pathology. It can be caused by genetic or familial factors, immune or non-immune hemolytic anemia, congenital infections, birth trauma or prematurity.[4]

In either scenario, it is imperative to maintain the total bilirubin (TB) concentration below the specified

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threshold as per AAP hour-specific phototherapy nomograms, to prevent the grave ramifications of kernicterus.[5] Various treatment modalities including phototherapy, exchange transfusion or immunoglobulins can be used, depending upon the cause.[3] Phototherapy is required in 5-10% of term neonates for preventing a steep rise of bilirubin to harmful level.[2]

The adverse effects associated with phototherapy include diarrhea, temperature instability, rashes, retinal damage, increased fragility of red blood cells, bronze baby syndrome, dehydration, and thrombocytopenia.[6] A less acknowledged side effect of phototherapy is its potential association with neonatal hypocalcemia.[7]

Calcium is an important micronutrient involved in normal homeostasis, neuromuscular excitability, proper membrane and cellular enzymatic activity. Hypocalcemia can lead to disturbance of all these functions leading to seizures in neonates.[8]

A decrease in serum calcium is observed in infants receiving phototherapy.[8,9] Blue light of phototherapy increases vitamin D breakdown in the skin, enhances urinary excretion of calcium and stimulates multiple hormonal and enzymatic pathways that result in transient drop of serum calcium.[9]

Neonatal hypocalcemia is defined as serum calcium level <8mg/dl in full-term infants and < 7mg/dl in preterm.[8] Early-onset hypocalcemia can be seen within 48-72 hours of life, in preterm and very low birth weight infants (VLBW), babies experiencing hypoxic ischemic encephalopathy (HIE), infant of diabetic mother (IDM) and intrauterine growth retardation (IUGR) babies.[8] Late-onset hypocalcemia is caused by excessive phosphate intake, low serum magnesium levels, hypoparathyroidism, and vitamin D deficiency.[10]

In 80% of neonates ,serum calcium level decreases after phototherapy.[9,10] Research conducted in Egypt reveals that calcium level, pre and post phototherapy was 9.63±0.79 and 9.04±0.78 respectively. Neonates (26%) developed hypocalcemia following phototherapy.[9] The effect of phototherapy on serum calcium level in neonates is not well perceived in Pakistan. This makes it imperative to assess and quantify phototherapy induced decrease in serum calcium level, in order to avoid life threatening complications of hypocalcemia in neonates. Current study aimed to determine the magnitude of decline in serum calcium level after 48 hours of therapy and to find the effect of gestation , chronological age of neonate or gender on this decline .

Materials and Methods

This Quasi experimental study was carried out in NICU of PAF hospital, Islamabad from 1st July 2021 to 31st January 2022, after approval from the hospital ethical committee (ERC#12).The sample size was calculated as 62, using world health organization (WHO) calculator.The confidence level was taken as 95%, precision of 1%, population mean was 0.43 and SD was 0.04 .[11] After taking informed written consent, full term and late preterm neonates of gestational age (34 0/7 - 41 6/7) having indirect hyper-bilirubinemia and requiring phototherapy according to American Academy of Pediatrics (AAP) guidelines, were enrolled in study.[5] Neonates <34 weeks of gestation, neonates with cardiopulmonary compromise, those having hypocalcemia or any maternal risk factor like gestational diabetes (GDM) and pregnancy induced hypertension (PIH) were excluded. The data was collected on a self-designed proforma. Under aseptic measures, 3ml blood was drawn from a peripheral vein of neonate by duty staff/duty resident and sent to labortary for serum bilirubin and serum calcium levelsS.

Serum calcium levels were repeated after discontinuation of phototherapy or 48 hours after start of phototherapy whichever came earlier. The labortary investigations were free for the study participants. Neonatal hypocalcemia was defined as total serum calcium concentration < 8 mg/dL (< 2 mmol/L) in term infants or < 7 mg/dL (< 1.75 mmol/L) in preterm infants.[11] The data was entered and analysed in statistical package for social sciences version (SPSS) 22. The qualitative variables like gender, mode of delivery were calculated in terms of frequency or percentage. The quantitative variables like age, gestational age, duration of phototherapy, pre phototherapy serum calcium levels, post phototherapy serum calcium levels were calculated as mean and standard deviation. The effect modifiers such as age, gender, and gestational age were accounted for by applying stratification techniques. A post stratification paired t-test was conducted to assess the significance of the findings. In order to

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compare the pre and post therapy serum calcium, t-test was appplied. A *p* value of < 0.05 was considered statistically significant.

Results

There were 62 neonates in total. The mean age was 4.52 ± 1.25 days. Males were 39 (62.90%) and 23 (37.10%) were females. The male to female ratio was 1.7:1. The mean gestational age was 38.11 ± 1.49 weeks (Table 1). The mean duration of phototherapy was 3.17 ± 0.55 hrs. The delivery via caesarean section was seen in 41 (66.13%) patients and 21 (33.87%) were delivered by vaginal delivery. The mean pre-therapy serum calcium levels were 9.59 ± 0.52 mg/dl and post-therapy levels were 9.07 ± 0.44 mg/dl (*p* value 0.0001) (Table 2). Stratification of post-therapy calcium levels with respect to age groups, gestational age and gender is shown in Table 3.

Table I: Demographics of Study Population

Characteristics		Number (n=62)	Percentage (%)	Mean
Age (in days)	0-3 4-7	15 47	24.19 75.81	4.52 ± 1.25 days
Gender	male female	39 23	62.90 37.10	
Gestational Age (weeks)	34-36 37-41	7 55	11.29 88.71	38.11 ± 1.49 weeks

Table II: Effect of Phototherapy on Serum Calcium Level

Serum Calcium level (mg/dl)	Mean±SD (mg/dl)	*P* value
Pre therapy	9.59 ± 0.52	<0.001*
Post therapy	9.07 ± 0.44	

*The *p* value ≤ 0.05 was considered statistically significant

Table III: Stratification of Post Therapy Serum Calcium Level with Various Parameters

Post therapy Ca level (mg/dl)		Mean±SD (mg/dl)	*P* Value
Age in days	0-3	9.22 ± 0.33	0.134
	4-7	9.02 ± 0.46	
Gestational age (weeks)	34-36	8.86 ± 0.62	0.174
	37-41	9.09 ± 0.41	
Gender	Male	9.02 ± 0.45	0.269
	Female	9.14 ± 0.40	

*The *p* value ≤ 0.05 was considered statistically significant

Discussion

The initial proposition of an association between hypocalcemia in a neonate and phototherapy was made by Romagnoli *et al*.,[12] Phototherapy has inhibitory effect on pineal gland, reducing melatonin levels. Melatonin is known to influence calcium metabolism, and its reduction can lead to decreased calcium absorption and increased risk of hypocalcemia.[13]

Our study found a total of 22 neonates (35.4%) to exhibit a decrease in serum calcium level after 48 hours of phototherapy.This percentage is quiet high as compared to Rajesh *et al*.,[14] who documented a decline in serum calcium in 26% of full-term neonates.The difference is due to the fact that we have included both full and pre term neonates while Rajesh *et al*.,[14] have included only full term neonates. Preterm babies are already at risk of hypocalcemia due to their immature metabolisms.[9] Amna *et al*.,[15]reported a comparable value of 40% babies showing low serum calcium with phototherapy. They have checked the levels at 24 hours of therapy yet they have reported the similar value like ours. According to literature, early onset hypocalcemia can be seen anytime between day 1 to 3 of phototherapy, although low calcium is seen mostly after 48 hours of phototherapy. [16] Our study reinforces the same association with a significant decrease (*p* value <0.001) in serum calcium level of neonates after 48 hours of phototherapy.

As per our results, decrease in serum calcium level after 48 hours of phototherapy, was significant (*p* < 0.001). Rajesh *et al*.,[14] have reported comparable finding with a *p* value of <0.01. Literature reports a significant reduction in calcium level following phototherapy (9.14±0.78mg/dl to 8.53±0.77mg/dl) *p* value 0.001.[7] In a recent research conducted in Pakistan , the average serum calcium level of neonates before and after phototherapy was measured as 9.28 mg/dl ± 0.23 and 8.54 mg/dl ± 0.68 respectively.[15] Others report that duration of phototherapy does not affect the magnitude of hypocalcemia in term neonates.[16] In another research encompassing term neonates in Faisalabad, it was determined that the decrease in pre and post phototherapy serum calcium levels was statistically significant (*p* <0.005).[17]

In our study, we did not find any case of phototherapy induced hypocalcemia. (Mean post phototherapy calcium 9.07 ± 0.44). The neonates have compensatory mechanisms that can prevent a major decline in serum calcium. Once serum calcium

level falls below 6 mmol/L, hypocalcemia becomes symptomatic in the form of agitation, apnea, lethargy, stridor, irritability and seizures.[18] While the decrease in calcium level is significant, it often does not lead to symptomatic hypocalcemia. One study noted that although there was a decrease in calcium levels, none of the neonates developed symptomatic hypocalcemia.[19] However, some studies reported a small percentage of neonates developing asymptomatic hypocalcemia.[20,21] Muhammad *et al*.,[20] have reported symptomatic hypocalcemia of 1.2% in their research with restlessness as only clinical finding. Feeding pattern, concommittent illnesses and birth weight of babies can affect the serum calcium levels in neonates.[15] Subash *et al.*, [22] reported that there is a reduction in the serum calcium with increased duration of phototherapy, however, it does not fall to the level where treatment is required. Similar findings are reported by other researchers.[23,24] The reason for symptomatic hypocalcemia could be associated sepsis but as our study excluded septic neonates so, this could be the reason that we have not observed hypocalcemia.

The gender did not have any significant effect on serum calcium level in our study (*p* value 0.269). We had 39 (62.90%) male and 23 (37.10%) female infants. In a study by Khan *et al.*, [1] there were (n=77 ,62.6%) males and (n= 46,37.4%) females. Similar findings are reported by others. Gender does not significantly influence the outcome of hypocalcemia or other complications associated with phototherapy in neonates. According to literature, the primary factors affecting phototherapy outcomes are related to other clinical characteristics rather than gender.[24]

Most of our patients were term neonates of > 4 days old with the mean age of 4.52 ± 1.25 days. The possible reason is that physiologic jaundice starts at 2nd day of life (DOL) and reaches its peak at around 5th DOL. So phototherapy is mostly required during first week of life. Although literature describes a physiologic decline in neonatal serum calcium level within same time period which returns to normal by the tenth DOL but this is almost never symptomatic.[10] Chandra *et al.,*[22] also report majority of neonates in the age group of 1-5 days (n =156; 77.6%), with the mean age of 4.50± 3.39 days, in their study. Similar demographics are reported by Amna *et al.*, [15] with mean age of 7.0 ±2.62 days. Literature has reported an increased risk of phototherapy induced hypocalcemia with decreasing gestational age. [25] We did not find a significant relationship between the two (*p value* = 0.172) .This might be because we had less number of preterm babies in our cohort (n =7,11.29%) . Others also report that there is no association of birth weight and serum bilirubin levels with decrease in serum calcium level [24,] which was not scope of our study.

The main strength of our study was that it reports phototherapy induced decrese in calcium levels. Our study was subject to few constraints. The comprehensive prenatal profile of mothers, such as weight, toxemias of pregnancy, and serum calcium levels, was not documented. Additionally, crucial data such as the feeding history of neonates, their birth weight, and Ballard scoring could have been included. These variables hold the potential to act as confounding factors and should be taken into account in future investigations with a larger sampe size. It is imperative that future research incorporates the aforementioned information into its analysis.

Conclusion

Phototherapy resulted in a significant reduction in serum calcium levels after 48 hours; however, none of the neonates developed hypocalcemia.

REFERENCES

1. Panneerselvam K, Mani S, Vasudevan N, S P, Krishnamoorthy N, Rk P et al. Effect of Light- Emitting Diode Phototherapy on Serum Calcium Levels in Neonates with Jaundice. Cureus. 2022 Apr 7;14(4): e23938. doi: 10.7759/cureus.23938.
2. Zhou S, Wu X, Ma A, Zhang M and Liu Y. Analysis of therapeutic effect of intermittent and continuous phototherapy on neonatal hemolytic jaundice. Exp Ther Med. 2019 ;17(5):4007-4012. doi: 10.3892/etm. 2019.7432.
3. Ayalew T, Molla A, Kefale B, Alene TD, Abebe GK, Ngusie HS et al. Factors associated with neonatal jaundice among neonates admitted at referral hospitals in northeast Ethiopia: a facility-based unmatched case-control study. BMC Pregnancy Childbirth. 2024 Feb 21;24(1):150. doi: 10.1186/s12884-024-06352-y.
4. Bajwan D, Thakur N, Bhardwaj R and Chaorsiya A . Neonatal Jaundice: An Overview. *Int. J. of Adv. Res.* 2024 ; 110-113 . doi:10.21474/ijar01/18855.
5. Kemper AR, Newman TB, Slaughter JL, Maisels MJ, Watcho JF, Downs SM et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant

https://doi.org/10.57234/jiimc.march25.1972

35 or More Weeks of Gestation. American Academy Of Pediatrics. Clinical Practice Guideline. Pediatrics 2022;150 (3): doi:10.1542/peds.2022-058859.
6. Wang J, Guo G, Li A, Cai WQ and Wang X. Challenges of phototherapy for neonatal hyperbilirubinemia (Review). Exp Ther Med. 2021; 21(3): 231.
7. Goyal M, Sharma R and Dabi DR. Phototherapy induced hypocalcemia in neonates: A case–control prospective study. Indian J Child Health. 2018; 5(3): 208-212.
8. ThomasT, Smith J, White P and Adhikari S . Transient Neonatal Hypocalcemia: Presentation and Outcomes. Pediatrics.2012; 129: e1461 - e1467. doi:10.1542/peds. 2011-2659.
9. Gaafar MM, Rasheed EM, Abdel Halim SM, Abdullah MM and El Gendi M. Effect of Phototherapy on serum Level of Calcium and Magnesium in Term and Preterm Neonates with Hyperbilirubinemia. Egyptian J Hosp Med. 2020; 80(1): 743-7.
10. Vuralli D. Clinical Approach to Hypocalcemia in Newborn Period and Infancy: Who Should Be Treated? Hindawi Int J Pediatr. 2019;(3):1-7. doi:10.1155/2019/4318075.
11. Abram SA. Section editor, Garcia-prates JA Tehrani N. Neonatal hypocalcemia Jun 2024. Up to date. Updated on Sep 19; 2022. Cited on July 2024.
12. Romagnoli C, Polidore G and Cataldi L. Phototherapy induced hypocalcaemia. J Pediatr., 1979;94(5):815-16.
13. Shahriarpanah S, Haji Ebrahim Tehrani F, Davati A, Ansari I. Effect of Phototherapy on Serum Level of Calcium, Magnesium and Vitamin D in Infants with Hyperbilirubinemia. Iran J Pathol. 2018;13(3):357-362.
14. Rajesh KC and Kanodia P. Phototherapy Induced Hypocalcaemia in Neonates with Jaundice. Journal of Nepalgunj Medical college, 2020; 18 (2) :1-3.
15. Khan A, Farhat A, Anwar H, Shamim S, Rehman M U and Khan I. Phototherapy Induced Hypocalcemia in Neonates with Unconjugated Hyperbilirubinemia. J Bahria Uni Med Dental Coll. 2021; 11(1) 4–8. doi:10.51985/GUBK9588.
16. Basnet S, Gauchan E, Bhatta M, Thapa R. Phototherapy induced hypocalcemia in neonatal hyperbilirubinemia and correlation of hypocalcemia with the duration of phototherapy. Int J Contemp Pediatr. 2022;9(4):324-328. doi:10.18203/2349-3291.ijcp20220756.
17. Javaid S, Sultana S, Omer MT, Murtaza A, Ahsan Ul Haq M. Effect of Phototherapy on Serum Calcium Levels in Neonates in A Tertiary Care Hospital. Ann Punjab Med Coll .2021; 15(3) 185-187. doi:10.29054/apmc/2021.1251.
18. Shoris I, Gover A, Toropine A, Iofe A, Zoabi-Safadi R, Tsuprun S et al. Light on Phototherapy-Complications and Strategies for Shortening Its Duration, A Review of the Literature. Children (Basel). 2023;10(10):1699. doi: 10.3390/children 10101699.
19. Pereira R, Avasthi B, Saste S, Bavdekar S . Prevalence of hypocalcemia in term newborns requiring phototherapy. Int. J. Contemp. Pediatr. 2023; 10(6):793-797 . doi:10. 18203/2349-3291.ijcp20231480.
20. Padippura MY, Mammen DS, Parameswaran J and Vadakedom S. Hypocalcaemia due to phototherapy in term neonates with neonatal hyperbilirubinemia. *J. Evolution Med. Dent. Sci. 2018;7(48):6007*-6011. doi:10.14260/ jemds/*2018*/1155.
21. Shrestha S, Budhathoki S, Sanjel S, Sindan N, Kayastha N, Shrestha A. Effect of phototherapy on serum calcium level in neonatal hyperbilirubinemia. JKAHS. [Internet]. 2021 Aug.31 [cited 2024Dec.6];4(2).
22. Jha CB, Rimal HS and Subedi RB. Phototherapy induced hypocalcemia in icteric newborns attending Birat medical College teaching hospital ,Morang,Nepal. JCMC [Internet]. 2022 Aug. 28 [cited 2024 Nov. 13];12(2):10-3. Available from: https://www.nepjol.info/index.php/JCMC/ article/view/47858.
23. Rozario CI, Pillai PS and Ranamol T. Effect of phototherapy on serum calcium level in term newborns. Int J Contemp Pediatr. 2017;4(6):1975-9.
24. Kumar G. A Study to Evaluate Phototherapy Induced Hypocalcemia and Its Correlation Of With the Duration of Phototherapy in Neonatal Hyperbilirubinemia. IJTPR .2023; 13(10); 395-399.
25. Refaee SAH. 821 Risk factors for short-term side effects of phototherapy in neonatal jaundice. Arch Dis Child. 2021;106 (1):A124-A125. doi:10.1136/archdischild-2021-rcpch.216.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Comparison of Topical Treatments and Chemical Cauterization for Recurrent Anterior Epistaxis in Pediatric Patients

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ABSTRACT

Objective: To compare the effectiveness of topical treatment methods versus chemical cauterization in managing recurrent anterior epistaxis in pediatric patients.

Study Design: Comparative cross sectional study design

Place and Duration of Study: ENT Department of Imran Idrees Teaching Hospital, Sialkot, from 15th June 2023 to 30th December 2023.

Materials and Methods: Eighty individuals, aged 5 to 18 years, with recurrent anterior epistaxis (≥4 episodes in the past month) were enrolled in the study and randomly assigned to two groups using a lottery method. Patients with coagulation disorders, chronic nasal conditions, autoimmune diseases, use of anticoagulant medications, or significant nasal structural abnormalities were excluded. Group A (n=40) underwent 75% silver nitrate chemical cautery of the anterior nasal septum, while Group B (n=40) received a week-long topical treatment consisting of 0.05% xylometazoline and a local oil-based antibacterial ointment. All patients were monitored for one month after treatment, with follow-up visits scheduled for two and four weeks. Data were analyzed using SPSS version 23, with quantitative variables expressed as mean ± standard deviation and qualitative variables as frequencies and percentages. The chi-square test was used to compare treatment efficacy with statistical significance set at $p < 0.05$.

Results: The average age of study participants was 14.24 ± 2.620 years. There were 43 (40%) men and 48 (60%) women patients. The therapy was effective in 75% of Group A and in 65% of Group B.

Conclusion: Although chemical cauterization resulted in a higher number of successful cases, there was no statistically significant difference between chemical cauterization and local antiseptic ointment at the 30-day post-treatment mark. Consequently, local antiseptic ointment can be considered a viable alternative when cauterization is not feasible.

Key Words: *Cauterization , Efficacy, Epistaxis, Topical Treatment.*

Introduction

Epistaxis, commonly known as nosebleeds, is one of the most frequently encountered emergencies in otolaryngology and has been recognized in medical literature for centuries.[1,2] It affects individuals of all ages, with a prevalence ranging from 10% to 60%. While most cases are mild and self-limiting, approximately 7% to 14% require medical intervention due to significant blood loss, recurrent episodes, or underlying medical conditions.[3] Epistaxis is classified as anterior or posterior, with anterior epistaxis being the most common type, accounting for nearly 80% of cases. It originates from Kiesselbach's plexus in the anterior nasal septum and is frequently seen in children and young adults.[4] Posterior epistaxis, which arises from branches of the sphenopalatine artery, is more severe and occurs more often in older adults.[5] Various local and systemic factors contribute to epistaxis, including nasal trauma, allergic rhinitis, infections, digital manipulation, hypertension, and anticoagulant use.[6] Several treatment modalities have been developed to manage recurrent anterior epistaxis effectively. Chemical cauterization using silver nitrate is widely practiced due to its ability to induce localized tissue coagulation, sealing bleeding vessels and reducing

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recurrence.[7] Another approach involves topical agents, such as vasoconstrictors and antiseptic ointments, which help control bleeding by constricting blood vessels and promoting mucosal healing. Both chemical cauterization and topical treatments have shown effectiveness, but there is no consensus on which method provides superior long-term outcomes. Some studies suggest that chemical cautery offers a more definitive resolution by directly targeting the bleeding site, while others argue that topical treatments provide a less invasive and equally effective alternative with fewer complications.[8,9]

Despite the availability of these treatments, there remains a lack of comparative studies evaluating their efficacy, particularly in pediatric patients. Most existing research on recurrent epistaxis has been conducted in Western populations, where healthcare settings and patient demographics differ significantly from those in developing countries.[10] This limits the generalizability of findings to resource-limited environments, such as Pakistan, where access to specialized interventions may be restricted. Furthermore, while individual studies have examined the effects of chemical cautery and topical therapy separately, few have directly compared their effectiveness in a controlled clinical setting. This gap in knowledge makes it challenging for clinicians to make evidence-based treatment decisions, particularly for pediatric patients who may have different healing responses and treatment tolerances than adults.

To address this gap, this study was conducted to compare the efficacy of 75% silver nitrate chemical cautery with a combination of 0.05% xylometazoline and an oil-based antiseptic ointment in managing recurrent anterior epistaxis in pediatric patients. By assessing treatment success rates and recurrence over a defined follow-up period, the study aimed to provide empirical evidence to guide clinical decision-making and contribute to the development of evidence-based treatment protocols. The objective of this study was to assess and compare the effectiveness of chemical cautery and topical therapy in managing recurrent anterior epistaxis in pediatric patients.

Materials and Methods

This comparative interventional study was conducted at Imran Idrees Teaching Hospital, Sialkot, from June 2023 to December 2023. Ethical approval was obtained from the hospital's Ethical Review Committee (Ref: 2023/IITH/RA/0014). Written informed consent was obtained from the parents or guardians of all participants before enrollment in the study. To maintain anonymity and confidentiality, each participant was assigned a unique identification code, and all personal data were kept anonymous throughout the study. Patients aged 5 to 18 years with recurrent anterior epistaxis, defined as at least four episodes of nasal bleeding in the previous month, were included in the study. Patients with specific comorbidities that could influence epistaxis severity or treatment outcomes were excluded. These included coagulation disorders, chronic nasal conditions (e.g., chronic rhinosinusitis, nasal vestibulitis), use of anticoagulant medications (e.g., warfarin, aspirin), autoimmune disorders and significant nasal structural abnormalities (e.g., severe septal deviation, nasal polyps). Patients who met the inclusion criteria were randomly assigned to two groups using a lottery method. Group A patients received 75% silver nitrate chemical cautery of the anterior nasal septum, while Group B patients were treated with a one-week course of topical therapy consisting of 0.05% xylometazoline and a local oil-based antiseptic ointment. The procedures were performed by experienced ENT specialists with a minimum of five years of clinical expertise in managing epistaxis, ensuring standardized and skillful application of both treatment modalities. Initially, a vasoconstrictor spray was applied, followed by the ointment, which was administered to the septum as far as possible using the little finger. All patients were provided with a local antibiotic ointment for one-week post-procedure. Follow-up assessments were conducted two and four weeks after treatment under the supervision of senior ENT faculty members.

Data were collected through structured clinical assessments and follow-up evaluations conducted by trained ENT residents under the supervision of senior faculty members. Each patient's demographic details, medical history, and treatment response were recorded on a standardized data collection form. Follow-up assessments were conducted at two- and four-week post-treatment, during which

patients were evaluated for symptom resolution and recurrence of epistaxis. Data was entered and analyzed using SPSS version 23. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. The chi-square test was used to compare the efficacy of treatments, with a p-value of <0.05 considered statistically significant.

Results

The mean age of the patients was 14.24±2.62 years, with a range from 5 to 18 years. There was no significant difference in the mean age between the two groups, with Group A having a mean age of 14.20±2.77 years and Group B having a mean age of 14.28±2.50 years. The study included a total of 80 patients, comprising 32 males (40%) and 48 females (60%), with no significant gender distribution differences between the groups, as shown in Table I and Table ll provides a summary of the treatment efficacy in both groups. In Group A, 30 patients (75.0%) found the treatment effective, while 10 patients (25.0%) did not. In Group B, 26 patients (65.0%) reported effective outcomes, while 14 patients (35.0%) did not. Overall, 56 patients (70.0%) experienced effective treatment outcomes, with no significant difference between the groups (P = 0.329).

Table I: Demographic Data of Study Subjects (n= 80)

Group	Group A (n=40)	Group B (n=40)	Total	P Value
Male	17 (42.5%)	15 (37.5%)	32 (40.0%)	0.648
Female	23 (57.5%)	25 (62.5%)	48 (60.0%)	
Age (years)	14.20±2.77	14.28±2.50	14.24±2.62	0.778

Table II: Efficacy Among the Subjects

Efficacy	Group A	Group B	Total	P Value
Effective	30 (75.0%)	26 (65.0%)	56 (70.0%)	0.329
Not Effective	10 (25.0%)	14 (35.0%)	24 (30.0%)	

Discussion

This study aimed to evaluate the efficacy of two treatment modalities chemical cauterization and topical therapy in managing recurrent anterior epistaxis, as no prior research in Pakistan has compared these approaches.

The findings of this study align with previous research on the management of recurrent anterior epistaxis, further supporting the efficacy of both chemical cauterization and topical therapy. Several studies have demonstrated comparable success rates between these two treatment approaches. For instance, Özmen and Özmen found that while chemical cauterization had a slightly higher initial success rate, long-term recurrence rates were similar to those of topical treatment, reinforcing the idea that both methods offer effective symptom control.[7] Similarly, a study by Chaitanya et al. comparing different concentrations of silver nitrate for cautery reported that while cauterization provided immediate hemostasis, the long-term benefits of antiseptic ointments and nasal decongestants were comparable.[12] Additionally, research by Vis and van den Berge highlighted that non-invasive treatments, such as antiseptic ointments, can be effective alternatives to nasal packing or cauterization, particularly in patients with mild to moderate epistaxis.[10] These parallels with existing literature strengthen the credibility of our findings and emphasize the need for individualized treatment selection based on patient preferences, tolerability, and clinical presentation.

The study found that chemical cauterization was effective in 75% of cases, while topical treatment achieved a 65% success rate. Although the cautery group showed a higher success rate, the difference between the two groups was not statistically significant. These findings are consistent with previous research by Robertson and Kubba, who reported superior long-term outcomes with antiseptic nasal cream alone compared to cautery combined with antiseptic treatment.[16] Similarly, a study by Qureshi and Burton concluded that various treatment modalities, including antiseptic creams and chemical cautery, did not demonstrate significant differences in efficacy.[17]

These results contribute to the existing body of evidence by reinforcing that both treatment approaches are effective, with chemical cauterization showing a slight advantage. However, the lack of a statistically significant difference suggests that topical therapy remains a viable alternative, offering a less invasive option for patients. This flexibility is particularly valuable for individuals in whom cauterization is impractical due to discomfort, medical contraindications, or

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resource limitations.[13,14,15]

Further research with larger, multicenter trials is necessary to validate these findings and examine additional factors affecting treatment outcomes, such as epistaxis severity, recurrence rates, and patient adherence. Long-term follow-up studies would help assess the durability of treatment effects and compare cost-effectiveness. Additionally, evaluating patient preferences and quality of life after treatment could provide further insights into optimizing management strategies for recurrent anterior epistaxis.

The study has certain limitations. The relatively small sample size of 80 patients may restrict the generalizability of the findings. Additionally, as research was conducted at a single hospital in Sialkot, the results may not be applicable to other populations. The one-month follow-up period may be insufficient to assess long-term recurrence rates, and the study focused solely on specific treatment protocols, potentially overlooking other therapeutic options. Despite measures to reduce bias, observer bias could still have influenced the outcomes. Addressing these limitations in future studies would enhance the robustness of findings and provide clearer guidance for clinical practice.

Conclusion

Although there were more patients who improved with chemical cauterization in our research, there was no significant difference between local antiseptic ointment and chemical cauterization on the 30th day of therapy. So, if cauterization is not an option, local antiseptic ointment might be utilized as an alternative.

Conflict of Interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Alqarni ZM, Alajmi TA, Alhumaidi HH, AlharethAlhussain YM, Alzahrani HS. Prevalence, causes, treatment, and outcome of epistaxis. Age [Internet]. 2019 [cited 2024 Feb 5];60:30. doi: 10.24911/IJMDC.51-1546952315
2. Bequignon E, Vérillaud B, Robard L, Michel J, Escabasse VP, Crampette L, et al. Guidelines of the French Society of Otorhinolaryngology (SFORL). First-line treatment of epistaxis in adults. Eur Ann Otorhinolaryngol Head Neck Dis [Internet]. 2017 [cited 2024 Feb 5];134(3):185-9. doi: 10.1016/j.anorl.2016.09.008
3. Alkhalifah KM, Alhumaidan NI, Alotaibi TA, Almnjwami RFM, Alzelfawi LA, Almughamsi RH, et al. A systematic review and meta-analysis of the awareness of and attitudes toward epistaxis. Cureus [Internet]. 2023 [cited 2024 Feb 5];15(10). doi: 10.7759/cureus.46590
4. Gouripur K, Patil MN, Malashetti S. Study of risk factors and treatment methods in patients presenting with epistaxis to a tertiary care hospital in North Karnataka [Internet]. 2023 [cited 2024 Feb 5].
5. Tunkel DE, Anne S, Payne SC, Ishman SL, Rosenfeld RM, Abramson PJ, et al. Clinical practice guideline: nosebleed (epistaxis). Otolaryngol Head Neck Surg [Internet]. 2020 [cited 2024 Feb 5];162. doi: 10.1177/0194599819890327
6. Helmy MR, Ahmed HE-S, AbdelWahab AA. Local sclerotherapy with lauromacrogol versus chemical cautery with chromic acid in treatment of idiopathic recurrent anterior epistaxis. Egypt J Neck Surg Otorhinolaryngol [Internet]. 2020 [cited 2024 Feb 5];6(3):12-8. doi: 10.21608/EJNSO.2021.139667
7. Özmen S, Özmen ÖA. Is local ointment or cauterization more effective in childhood recurrent epistaxis? Int J Pediatr Otorhinolaryngol [Internet]. 2012 [cited 2024 Feb 5];76(6):783-6. doi: 10.1016/j.ijporl.2012.02.040
8. Misra A, Basu A, Mandal PK, Mahapatra NC. Management of pediatric epistaxis in different age groups in a tertiary care centre. Int J Contemp Pediatr [Internet]. 2016 [cited 2024 Feb 5];3(4):1206-9. doi: 10.18203/2349-3291.ijcp20162418
9. Andreeff R. Epistaxis. JAAPA [Internet]. 2016 [cited 2024 Feb 5];29(1):46-7. doi: 10.1097/01.JAA.0000473373.47749.5f
10. Mylonas S, Skoulakis C, Nikolaidis V, Hajiioannou J. Epistaxis treatment options: literature review. Indian J Otolaryngol Head Neck Surg [Internet]. 2023 Sep [cited 2024 Feb 5];75(3):2235-44 doi: 10.1007/s12070-023-03824-z.
11. Ahmed AE, Abo El-Magd EA, Hasan GM, El-Asheer OM. A comparative study of propranolol versus silver nitrate cautery in the treatment of recurrent primary epistaxis in children. Adolesc Health Med Ther [Internet]. 2015 Sep 30 [cited 2024 Feb 5]:165-70. doi: 10.2147/AHMT.S84806
12. Chaitanya V, Manampuram MT, Sreelakshmi PS, Sreedevi NT. Comparative study of topical application of injection tranexamic acid and anterior nasal packing in the management of epistaxis. Indian J Otolaryngol Head Neck Surg [Internet]. 2024 Apr 5 [cited 2024 Feb 5]:1-5 doi: 10.1007/s12070-023-03345-9.
13. Shahsavarinia K, Faridaalaee G, Ahranjani RE, Balafar M, Milanchian N, Hajebrahimi S, et al. What is the best management for geriatric epistaxis? A comprehensive systematic review and meta-analysis. Int J Drug Res Clin [Internet]. 2023 Jul 7 [cited 2024 Feb 5];1(1):e11. doi: 10.34172/ijdrc.2023.e11.
14. EL-Baz HM, Mohammed KA, Said HS. Risk factors of epistaxis in primary school children in Dakahlia Governorate, Egypt. Egypt J Hosp Med [Internet]. 2021 Oct 1 [cited 2024 Feb 5];85(2):4035-41. doi: 10.21608/EJHM.2021.207085
15. Li T, Li F, Cha X, Wang S, Yan J, Wang T, et al. systematic

review and meta-analysis of the effects of topical tranexamic acid versus topical vasoconstrictors on the management of epistaxis. Curr Pharm Des [Internet]. 2023 May 1 [cited 2024 Feb 5];29(19):1497-503 doi: 10.2174/1381612829666 230214093136.
16. Robertson S, Kubba H. Long-term effectiveness of antiseptic cream for recurrent epistaxis in childhood: five-year follow-up of a randomized, controlled trial. J Laryngol Otol [Internet]. 2008 [cited 2024 Feb 5];122(10):1084-7. doi: 10.1017/S0022215107001600
17. Chiang CY, Lin JS, Tsai TY, Tu YK, Tsai MJ. Comparative effectiveness of various noninvasive local treatments in patients with epistaxis: A systematic review and network meta-analysis. Acad Emerg Med [Internet]. 2023 Oct [cited 2024 Feb 5];30(10):1047-58.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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The data that support the findings of this study are available from the corresponding author upon request.

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- There is clear evidence that the findings are unreliable, either as a result of major error (e.g., miscalculation or experimental error), or as a result of fabrication (e.g., of data) or falsification (e.g., image manipulation)
- It constitutes plagiarism.
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- It contains material or data without authorization to use.
- Copyright has been infringed or there is some other serious legal issue.
- It reports unethical research
- It has been published solely on the basis of a compromised or manipulated peer review process.
- The author(s) failed to disclose a major competing interest that, in the view of the editor, would have unduly affected interpretations of the work or recommendations by editors and peer reviewers.

At times the article may occasionally be retracted for correction of errors in submission or publication and will be replaced with the corrected one.

Retraction Process

JIIMC adopts the following retraction process to ensure best practice of retraction:

1. An article requiring potential retraction will be brought to the attention of JIIMC editor.
2. Managing Editor will follow the step-by-step guidelines according to the COPE flowcharts and will seek the response from the author of the article as well.
3. JIIMC Publication & Research Integrity Committee will evaluate the evidence of misconduct and response of the authors. Based on the findings, the committee will recommend a final decision whether to retract the publication or otherwise.
4. The final decision is then communicated to the author and, if necessary, any other relevant bodies(PMC, HEC), or the author's institution as deemed appropriate.
5. The retraction-note titled "**Retraction: [article title]"** will be published in the paginated part of a subsequent issue of the journal and listed in the contents list.

6. The text of the retraction should explain why the article is being retracted.
7. The statement of retraction and the original article must be clearly linked in the electronic database so that the retraction will always be apparent to anyone who comes across the original article.
8. The relevant changes in the online version will be reflected through **Crossmark** icon.

INSTRUCTIONS FOR AUTHORS

The material submitted for publication should be sent completely to the Journal of Islamic International Medical College, Pakistan. Research work that has already been reported in a published paper or is described in a paper sent or accepted elsewhere for publication should not be submitted. Duplicate submission of the same research work to another journal should be avoided as this falls into the category of publication misconduct. A complete report following publication of a preliminary report, usually in the form of an abstract, or a paper that has been presented at a scientific meeting, if not published in a full proceeding, may be submitted. Manuscripts are submitted online on the following link:

https://journals.riphah.edu.pk/index.php/jiimc. All authors are supposed to provide their contact details such as institution, cell numbers and e-mail addresses on the title page. It is mandatory to submit online, a duly filled-in copyright, authorship and undertaking proforma along with the manuscript. *(https://jiimc.riphah.edu.pk/downloads/)*. The sequence/ order of the names of authors submitted at the time of initial submission of manuscript shall not be changed at any stage. It is mandatory to submit the institutional ethical review board/committee approval/exemption for all research articles, at the time of online submission of articles. Dissertation/ thesis approval letter from relevant authority is also acceptable.

PROCESSING AND PUBLICATION CHARGES

Original Article/ Review Article

- Processing Charges (Revised with effect from 01 February 2024) = PKR 3,000/-
- Publication Charges (Revised with effect from 01 February 2024) = PKR 12,000/-

Case Report

- Processing Charges (Revised with effect from 01 February 2024) = PKR 3,000/-
- Publication Charges (Revised with effect from 01 February 2024) = PKR 9,000/-

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MANAGING EDITOR JIIMC

Westridge-III, Pakistan Railway Hospital
Islamic International Medical College, Rawalpindi
Pakistan
Tel: +92515481828 – Ext 220

MATERIAL FOR PUBLICATION

The material submitted for publication may be in the form of an original research (Randomized controlled trial – RCT, Meta-analysis of RCT, Quasi experimental study, Case Control study, Cohort study, Observational Study with statistical support, etc.), a Review Article, a Case Report, Recent Advances, New Techniques, Debates, Book/CDs Review on Clinical/Medical Education, Adverse Drug Reports or a Letter to the Editor. Survey Articles and Studies more than five years old at the time of submission are not accepted for publication in JIIMC. Non-English articles are not accepted for publication in JIIMC.

ORIGINAL ARTICLES should report original research of relevance to clinical medicine and may appear either as papers or as short communications. The original paper should be of about 2000-2500 words excluding abstract and references. The abstract should be structured of about 250 words. Three to 10 keywords should be mentioned at the end of the abstract as per MeSH (Medical Subject Headings). There should be no more than four tables or illustrations. The data should be supported with 20 to 25 locals as well as international references. More than 50% of the references should be from the last five years.

SHORT COMMUNICATIONS should be about 1000 words, with a non-structured abstract, two tables or illustrations and 5 references.

CLINICAL CASE REPORT should be of academic value and provide relevance of the disease being reported as rare or unusual. The word count of the case report should not be more than 800 words with 3- 5 key words. The abstract should be non-structured of about 150 words (case specific) with a maximum of 5 references. It should not include more than 2 figures and one table.

REVIEW ARTICLE should consist of structured overview of relatively narrow topic providing background and recent development with reference of original literature. An author can write a review article only if he/she has written a minimum of three original research articles and some case reports on the same topic. Review articles should be of 2500 to 3000 words with a non-structured abstract of 150 words and minimum 3 key words.

LETTERS TO THE EDITOR should normally not exceed 400 words, have no more than 05 references and be signed by all the authors-maximum 3 are allowed. Preference is given to those that take up points made in contributions published recently in a journal. Letters may be published with a response from the author of the article being discussed. Discussions beyond the initial letter and response will not be entertained for publication.

OBITUARIES should be of about 250 words.

EDITORIALS are written by invitation.

DISSERTATION/THESIS BASED ARTICLE An article based on dissertation/thesis submitted as part of the requirement for a postgraduate degree (M. Phil, FCPS, MS) can be sent for publication after it has been approved by the institution's ethical review board/committee and the college/university evaluation committee/board. The data should not be more than five years old. Thesis/dissertation-based articles will be assessed by proper review process. Once accepted for publication, disclosure will be made that 'it is a Dissertation based article.'

RANDOMIZED CONTROLLED TRIALS

- When reporting the results of a randomized trial, JIIMC requires a completed CONSORT 2010 checklist and flow diagram as a condition of submission.
  - o CONSORT 2010 checklist
  - o CONSORT 2010 flow diagram
- Templates for these can be readily accessible here or on the CONSORT website, which also describes several CONSORT checklist extensions for different designs and types of data beyond two group parallel trials
- Authors should ensure that your article, at minimum, reports content addressed by each item of the checklist. Meeting these basic reporting requirements will greatly improve the value of your trial report and may enhance its chances for eventual publication.
- As per recommendation of ICMJE, Journal of Islamic International Medical College requires registration of clinical trials in a public trials registry as a prerequisite for publication of all clinical trials.
- **Clinical Trials:** Clinical Trials submitted for publication must be registered in public registry, e.g., http://clinicaltrial.gov/ , must provide registration proof & all RCTs must be based on CONSORT statement. Unregistered trials will not be published.

  A clinical trial is any research study that prospectively assigns human participants or groups to one or more health-related interventions to assess their effects on health outcomes. These interventions can include drugs, surgical procedures, devices, behavioral treatments, dietary changes, and modifications in care processes. Health outcomes encompass any biomedical or health-related measures collected from patients or participants, including pharmacokinetic data and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

GENERAL ARCHIVAL INSTRUCTIONS

The manuscript should be typed in MS Word. Each manuscript should include a title page (containing email address, cell numbers, institution, and postal address of the corresponding author), abstract, key words, text, acknowledgements (if any), references, tables (each table, complete with title and footnotes) and legends for illustrations and photographs. Each component should begin on a new page. Sub-headings should not be used in any section of the script except in the abstract.

TEXT ORGANIZATION

All manuscripts except Short Communication and Letter to the Editor should be divided into the following sections.

ABSTRACT

Abstracts of original article should be in structured with following sub-headings:

- Objective
- Study Design

- Place & Duration of Study
- Materials & Methods
- Results
- Conclusion

Four elements should be addressed: "why did you start?", "what did you do?", "what did you find?" and "what does it mean? “.” Why did you start?" is addressed in the objective. "What did you do?" constitutes the methodology and could include design, setting, patients or other participants, interventions, and outcome measures. "What did you find?" is the 'results', and "what does it mean?" would constitute the conclusions. Please label each section clearly with the appropriate sub-headings. Structured abstract for an original article, should not be more than 250 words. At least 3 key words should be written at the end of the abstract. Review articles, case reports and others require a short, unstructured abstract. Commentaries do not require an abstract.

INTRODUCTION

Write this section with references as per following instructions:

1. Give background information about the subject matter and the issues your study intends to address. Only strictly pertinent references should be cited, and the subject should not be extensively reviewed.
2. Describe what is known (in the literature) and what is not clear about the subject with reference to relevant literature thus identifying the literature gap.
3. You write the rationale (justification) of your study.
4. Finally, you mention the objective of your study

MATERIALS AND METHODS

Methodology is written in past tense.

Follow this sequence **without headings:**

- Study design
- Place and Duration of Study
- Sample size
- Sampling technique
- Mention about permission of the ethical review board and other ethical issues addressed.
- Inclusion and Exclusion Criteria
- Data collection procedure-
- Type of data: parametric or nonparametric
- Data analysis: including Statistical Software used, and statistical test applied for the calculation of p value and to determine the statistical significance. Exact p-values and 95% confidence interval (CI) limits must be mentioned instead of only stating greater or less than level of significance. All percentages must be accompanied with actual numbers.

RESULTS

These should be presented in logical sequence in the text, tables, and illustrations. All the data in the tables or illustrations should not be repeated in the text; only important observations should be emphasized or summarized. No opinion should be given in this portion of the text.

DISCUSSION

This section should include the author's comments on the results. Write in present tense, active voice except for results, which are written in past tense. It should be written in following sequence:

- First, very briefly summarize, Interpret and discuss main results and don't merely repeat the results.
- Discuss key studies relevant to your study.
- Compare your work with other's work.
- Describe limitations of your study.
- Suggest future work if necessary.

CONCLUSION

Conclusion should be provided under a separate heading. It should be in congruence with the objective. No recommendations are needed under this heading.

REFERENCES

References must be written in Roman Number and in the Vancouver Style only. References should be numbered in the order in which they are superscripted in the text. At the end of the article, the full list of references should give the names and initials of all authors (unless there are more than six when only the first six should be given followed by et al). The author's names are followed by the title of the article; title of the journal abbreviated according to the style of the Index Medicus (see “List of Journals Indexed”, printed yearly in the January issue of Index Medicus); year, volume, and page number, e.g., Hall, RR. The healing of tissues by C02 laser. Br J. Surg: 1970; 58:222-225. References to books should give the names of editors, place of publication, publisher, and year. The author must verify the references against the original documents before the

article. References to papers accepted but not yet published should be designated as “in press” or “forthcoming”; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication.

TABLES AND ILLUSTRATIONS

Tables and illustrations should be merged within the text of the paper, maximum number of tables and illustrations should not exceed four, and legends to illustrations should be typed on the same sheet. Tables should be simple and should supplement rather than duplicate information in the text; tables repeating information will be omitted. Each table should have a title and be typed in double space without horizontal and vertical lines on an 8 ½” x 11’ paper. Tables should be numbered consecutively with Roman numerals in the order they are mentioned in the text. Page number should be in the upper right corner. If abbreviations are used, they should be explained in footnotes and when they first appear in text. When graphs, scattergrams, or histograms are submitted, the numerical data on which they are based should be supplied. All graphs should be made with MS Excel and be sent as a separate Excel file even if merged in the manuscript. For scanned photographs the highest resolution should be used.

S.I.UNITS

System International (SI) Unit measurements should be used. All drugs must be mentioned in their generic form. The commercial name may however be mentioned within brackets, if necessary.

PHOTOGRAPHS AND FIGURES

Figures and Photographs should only be included when data cannot be expressed in any other form. Figures and photographs must be cited in the text in consecutive order. Legends must be typed on the same paper. Legends for photomicrographs should indicate the magnifications, internal scale, and method of staining. Figures should be numbered in Arabic numbers.

OBLIGATORY FILES

Obligatory supporting documents for all types of Manuscripts except the letter to editor, without which JIIMC will not accept the manuscript for initial processing.

- Cover Letter
- JIIMC Checklist
- JIIMC Conflict of Interest Performa
- JIIMC CopyRight and Undertaking Agreement
- IRC Certificate
- Bank draft as initial processing fee (Original bank draft send in JIIMC office)

Template of these files is available in the download section.

CONFLICT OF INTEREST

Any funding source for the research work must be informed at the time of submitting the manuscript for publication in JIIMC. Any associations that might be construed as a conflict of interest (stock ownership, consultancies, etc.) shall be disclosed accordingly. Examples of financial conflicts include employment, consultancies, stock ownership, honoraria, paid expert testimony, patents or patent applications, and travel grants, all within 3 years of beginning the work submitted. If there are no conflicts of interest, authors should state that. All authors are required to provide a signed statement of their conflicts of interest as part of the author's declaration.

FINANCIAL DISCLOSURE & ROLE OF THE FUNDING SOURCE

- Author is supposed to declare the funding source as acknowledgement at the end of the manuscript.
- Author will describe the role of the study sponsor (s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.
- If there is no Methodology section, the role of the funding source should be stated as an acknowledgment.
- The corresponding author should confirm that he/she had full access to all the data in the study and had final responsibility for the decision to submit for publication.
- JIIMC publishes FINANCIAL DISCLOSURE & ROLE OF THE FUNDING SOURCE statement for each article.

AUTHORSHIP CRITERIA

All those designated as authors should meet all four criteria for authorship as stated in *ICMJE recommendations (http://www.icmje.org/icmje-recommendations.pdf).* According to ICMJE recommendations authorship is based on the

following four criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; and
2. Have been involved in drafting the work or revising it critically for important intellectual content; and
3. Have given final approval of the version to be published; and
4. Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. We strongly discourage gift or ghost authorship. Mere supervision, collection of data, statistical analysis and language correction do not grant authorship rights. To avoid any dispute regarding authorship authors are advised to consult COPE guidelines to avoid authorship problems.

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CORRIGENDUM

In the article titled **"Maxillary Sinus and Nasal Cavity Anatomical Variants Evaluation in Adult Karachi Population, A CBCT Based Analysis"** published in the June 2024 edition of the Journal of Islamic International Medical College(JIIMC) VOL. 19, no. 2, there is a correction to be made in the authorship.

The name of the Fourth author is corrected as follows:

From: Tabina Urooj to Tabinda Urooj

The corrected authorship should now read as follows:

Lubna Faisal, Rizwan Ajmal, Zia ul Islam, **Tabinda Urooj**, Saima Athar, Fatima Rehman

Sincerely,

JIIMC

CORRIGENDUM

In the article titled **"A Morphological and Biochemical Study of Ethanolic Fruit Extract of Berberis Vulgaris Against Gentamicin Induced Renal Damage in Albino Rats"** published in the June 2023 edition of the Journal of Islamic International Medical College(JIIMC) VOL. 18, no. 2, there is a correction to be made in the authorship.

The name of the Second author is corrected as follows:

From: Tabina Urooj to Tabinda Urooj

The corrected authorship should now read as follows:

Lubna Faisal, Tabinda Urooj, Zia ul Islam, Fatima Rehman, Sadia Abdul Qayyum, Aaqiba Rasheed

Sincerely,

JIIMC