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AIMS & SCOPE

HMDJ is the journal of HITEC Institute of Medical Sciences (HITEC-IMS), Taxila. It is an open access, peer-reviewed, bi-annual journal that aims to keep the medical & dental health professionals updated with the latest information relevant to their fields.

HMDJ welcomes scholarly work from medical, dental and allied subjects (basic & clinical), community health issues and medical education. It publishes original research, review articles, case reports, editorials, letters to editor, short communication, book reviews, recent advances, new techniques, debates, adverse drug reports, current practices, and conference reports. All publications of HMDJ are peer reviewed by subject specialists from Pakistan and abroad.

OBJECTIVES

1. To publish original, peer reviewed clinical and basic sciences articles.
2. To promote research culture in HITEC-IMS and beyond, by inculcating the habit of medical writing in doctors.
3. To assist physicians to stay informed about the developments in their own & related fields.
4. To support knowledge & experience sharing among the health professionals for the benefit of the patients.
5. To attain top-notch ethical medical journalism by delivering credible and reader-friendly publications.

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EDITOR'S CUTTING EDGE

EMBRACING THE FUTURE: THE TRANSFORMATIVE ROLE OF ARTIFICIAL INTELLIGENCE IN MEDICAL SCIENCES

Hamid Shafiq[1], Muhammad Moeed Azwar Bhatti[2]

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INTRODUCTION

By 2030, Artificial intelligence (AI) will power over half of global diagnostic and therapeutic decisions. In Radiology, Dermatology, and Pathology and even in primary health care, AI algorithms are showing potential to perform as good as, or even better than human clinicians in various tasks of speed, accuracy, and consistency. While the High Income Countries (HICs) are progressively incorporating these tools in clinical care and medical education, a number of low and middle Income Countries (LMICs), Pakistan included, have failed to develop the required infrastructure and framework to embrace, regularize, and harness the advantages of these state-of-the-art interventions [1].

CAPSULE SUMMARY

Artificial Intelligence (AI) is transforming diagnostics, clinical care, and medical education worldwide. However, low- and middle-income countries like Pakistan lag due to infrastructural, ethical, and educational gaps. This editorial calls for curriculum reform, policy development, and responsible adoption to harness AI's potential. Embracing AI is vital not only for advancing healthcare but also as a professional responsibility to shape its equitable future.

As a physician in Pakistan, I view this as both an opportunity and a danger. The advantage is AI's never-before-seen ability to improve patient care, reduce medical errors and provide additional access to underserved populations. The danger of such inaction is that we neither prepare our systems, nor train our healthcare workers, and we will not ethically engage with AI, and if we do not take such steps then we will fall behind in a field that some would consider to be at the very centre of modern Medicine.

AI can no longer be considered as a futuristic embellishment to Medicine when it needs to be fully integrated within clinical reasoning, patient management and education. Its thoughtful embedding within healthcare systems, especially in the low-resource settings, is not just nice to have, but is critical.

The Current and Emerging Roles of AI in Medicine

Artificial intelligence is already transforming several aspects of healthcare. Machine learning methods that leverage thousands of radiographic or histopathological images are now used in clinical diagnostic tools to help identify early-stage malignancies with extraordinary accuracy. These networks are being used to forecast cardiovascular events, stratify cancer prognoses, and screen for diabetic retinopathy in primary care centers—often more effectively than the conventional techniques [2].

Beyond diagnostics, AI-guided decision support systems are enhancing the capacity of clinicians to treat complex patients. In the intensive care units (ICUs) predictive analytics software, monitors live data to catch early signs of decline or sepsis or ventilator-associated events. In the operating room, AI-enabled robotic systems would provide even more precise and assistive control in real time, limiting variability and maximizing benefits [3].

Medical education is quietly undergoing revolution. AI-fueled virtual reality is allowing students to immerse themselves in simulations, and natural language processing tools generate adaptive learning platforms that adapt to an individual student's pace and knowledge gaps. AI-powered digital tutors and diagnostic reasoning simulators have the power to simulate a clinic environment that traditional classroom instructions never could [4].

These developments are not born in labs or ivory towers. AI applications are becoming more accessible through open-source resources, cloud-based solutions, and in some cases,

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smartphones, reducing barriers to entry even in low-resource regions.

And yet, even as AI progresses at a rapid pace, perhaps the most significant challenge is not about the potential of AI, but about the understanding, ability and willingness of health systems to deploy and shape these technologies responsibly.

Challenges to Implementation – Ethical, Infrastructural, and Educational Gaps

Although AI holds potential, the transformation of modern medical practice in Pakistan and other developing countries is coupled with many challenges. The primary cause is infrastructural constraints. Access to digital infrastructure, such as high-speed internet, computing power and secure data storage, remains variable in healthcare institutions, particularly in rural and underserved regions. Without such building blocks, the most sophisticated AI tools are out of reach.

As pressing is the shortage of human capital prepared to interact with AI. Core medical curricula in Pakistan and similar settings lack content on data science, medical informatics, and algorithmic decision-making. This leaves the medical graduates unequipped to be critical consumers of AI-based tools in the clinics, let alone be able to contribute (or adapt) to their development for local needs [5].

Ethical issues also come into play with adoption. Algorithmic bias, in which AI systems mirror the biases contained within the data with which they were trained can result in differences in care. For example, Western-trained models may have limited performance or misclassify diseases in South Asians. There are even bigger concerns around data privacy, transparency and consent. Without strong regulations, there is an actual possibility of abuse or harm in the process [6].

Another undertheorized challenge is, trust. Both doctors and patients might think twice before trusting "black box" systems whose internal logic remains opaque. Here the significance of explainable artificial intelligence (XAI) comes into play. Systems that provide interpretations of their outputs not only results, but reasons will be critical for acceptance in clinical settings.

Addressing these challenges require a pro-active and strategic response, not just from the technologists and policy advisors, but from the medical community as well.

A Roadmap for Responsible Integration – From Curriculum Reform to Policy Action

If AI is to be implemented adequately and ethically in medical science, we need a careful, concerted path forward through education, clinical implementation, policy development and interdisciplinary collaboration.

First, medical education curricula need to change. AI literacy must be incorporated into undergraduate and postgraduate education, not in terms of optional electives, but as central to clinical education. Modules in medical data-analysis, algorithmic reasoning and digital ethics could prepare the doctors of the future to be more critical users of AI tools. Organizations such as HITEC IMS and similar others in the vicinity have a relevant role to play in this paradigm shift by collaborating with computer science (CS) departments, training faculty members, and providing resources for interdisciplinary research [7].

Second, national and institutional health policies need to enable the development and utilization of AI that targets local health challenges. Government–private partnerships can also help to develop and field test AI tools for regionally specific burdens, for example tuberculosis, maternal mortality, cardiovascular diseases, while keeping in place validation and monitoring mechanisms. There needs to be some kind of a central regulator that has the authority to approve and view is AI's clinical use, as well as set data protection standards and ethical guidelines.

Third, training should not be limited to the clinicians but should also cover hospital administrators, IT staff and biomedical engineers. Training, credentialing and grant mechanisms will generate local expertise and reduce reliance on inbound technology import. Certainly, patient engagement cannot be forgotten. Establishing trust involves clear communication about the role of AI in diagnosis and treatment, as well as strong consent processes.

Finally, Pakistan and other LMICs should not be defined solely as consumers of AI technologies that are created elsewhere. We have a wealth of clinical data, a growing tech sector and an abundance of high-quality academic institutions, making our country well-positioned to contribute to global AI research, provided the necessary infrastructure, incentives, and vision are in place.

CONCLUSION

For countries like Pakistan, the potential impact of AI is game-changing. It could provide a way to transcend the longstanding obstacles in healthcare delivery, from workforce deficiencies to diagnostic delays. Taking advantage of this moment require more than enthusiasm, it needs preparation, leadership and accountability.

As conferences are more than knowledge-sharing platforms, they are the blueprint for the future. It demonstrated that when clinicians, educators, and technologists converge with purpose, even institutions in resource-constrained settings can become hubs of innovation. As Medicine becomes more data-driven, personalized and precise, embracing AI with responsibility and vision is no longer optional. It is imperative.

Doctors need to be proactively deciding how AI makes its way into the clinical area. This involves changes in the curriculum, new interdisciplinary areas of scholarship, and attempting to

ensure that ethics evolve at the same rate as technology. Medical schools need to produce not just capable physicians, but also digital-age thinkers who can traverse and direct the changing field of intelligent Medicine [8].

Organizations like HITEC Institute of Medical Sciences, which have already started to explore these new frontiers, can take the lead, infusing AI into training programs, driving clinical creativity and forging partnerships with centers of excellence around the world. In doing so, they confirm that Pakistan is not only a victim of technological disruption, but a driver of it.

The Medicine of the future is smart, data-driven, and interconnected. Adopting this technology isn't merely a strategic decision, it's a moral and professional responsibility. The question is no longer whether we are prepared for AI, but whether we are willing to help guide its responsible implementation for the benefit of our patients, our profession and the health-care providers of future generation.

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ORIGINAL ARTICLE

COMPARISON OF THE FREQUENCY OF SEROMA DEVELOPMENT BETWEEN DEAD SPACE CLOSURE WITH QUILTING SUTURES VERSUS WITHOUT QUILTING SUTURES AFTER BREAST SURGERY

Muhammad Ali[1], Farya Aslam[2], Sadia Farhan[3], Sundas Nadeem[4], Muhammad Azhar[5], Muhammad Naeem Ashraf[6]

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ABSTRACT

Objective: To compare the frequency of seroma development between dead space closure with quilting sutures versus without quilting sutures after breast cancer surgery in CMH Rawalpindi.

Study Design: Quasi-experimental.

Place and duration of Study: Department of Surgery, Combined Military Hospital Rawalpindi, 01 year (May 2020 to May 2021).

Methodology: A Total of 60 patients, subjected to either simple mastectomy or a modified radical procedure for breast cancer, were included in the study. Patients who had undergone breast conservation surgery and advanced breast carcinoma were excluded. Randomisation by lottery was used to allocate patients into two groups: Group A, comprising 30 females who received quilting sutures for dead space obliteration, and Group B, of 30 females who did not receive quilting sutures after breast surgery. Seroma formation on the 7th postoperative day was noted.

Results: The overall age range of participants was 35-50 years with a mean age of 42.25 ± 2.83 years. In our study, the frequency of seroma formation in the dead space closure with quilting sutures group was found in 05 (16.67%) vs 20 (66.67%) patients without the quilting sutures group (p=0.0001).

Conclusion: This study found that the frequency of seroma development is less after dead space closure with quilting sutures as compared to without quilting sutures.

Keywords: *Modified radical mastectomy, Quilting sutures, Seroma.*

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INTRODUCTION

The major chunk of operative work on breast-related diseases is secondary to breast cancer. Despite advances in surgical techniques, breast surgery, especially mastectomy, is marred by a multitude of complications, among which Seroma formation is the most common. Seroma is defined as a pocket of clear serous fluid in dead space created during breast and axillary dissection. Its incidence varies from 2.5 to 51% [1,2,3]. Despite being a benign complication, it leads to problems such as discomfort for the patient, delay in adjuvant chemotherapy, risk of infection, and repeated visits to the clinic. Keeping in view that prevention is better than dealing with complications, many techniques are being practiced to prevent seroma development which include using suction drains, shoulder immobilization, minimal use of electrocautery, fibrin sealants and flap fixation using quilting sutures.

Seroma poses a concern for the patient. Multiple aspirations are associated with a risk of infection, thereby prolonging hospital stay. It also delays wound healing and, hence, a delay in commencing adjuvant therapies. Biological mechanisms

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and associated risk factors studied in seroma formation include the patient's age, obesity, the number of axillary lymph nodes dissected, and the type and extent of breast surgery [4]. In the recent past and presently, many publications are in quest for an effective technique/method for preventing seroma formation, and the overall consensus is to strategically obliterate /minimise potential space after mastectomy to achieve seroma-free results[5]. Various methodologies applied include closed drainage, suturing/quilting or application of tissue adhesive glue, shoulder immobilisation and minimal use of electrocautery[6,7]. Studies have revealed that flap fixation, using suturing techniques, has good results in decreasing seroma formation[8,9,10,11].

This study was conducted to measure the efficacy of flap fixing with quilting sutures after breast surgery in terms of decreased seroma formation in the local population.

CAPSULE SUMMARY

The frequency of seroma development in dead space closure with quilting sutures was compared with closure without quilting sutures after breast cancer surgery. Seroma development was found to be less after dead space closure with quilting sutures.

METHODOLOGY

This quasi-experimental study was carried out at the Department of Surgery, Combined Military Hospital, Rawalpindi. The study was conducted over 01 year, from 27th May 2020 to 26th May 2021, with 60 female patients, 30 in each group. The sample size was based on a 5% significance level and 80% power, considering seroma incidence of 78.3% in the group without quilting sutures and 20.0% in the quilting sutures group, as reported previously[12]. Participants were selected via non-probability, consecutive sampling. Inclusion criteria covered women aged 35-50 years, with a BMI of 25-29, undergoing simple or modified radical mastectomy for breast cancer. Exclusions included redo surgery, advanced carcinoma, multiple comorbidities and breast conservation surgery. Permission from the concerned authority and the hospital ethical committee was obtained before commencing the study. Sixty patients were recruited according to the selection criteria after taking history, clinical examination, and after informed, written consent from the patients. Study participants were stratified into Group A, comprising 30 females, having quilting sutures for dead space obliteration, and Group B, of 30 females without quilting sutures after breast surgery. In both groups, some patients had a simple mastectomy and some patients had a modified radical mastectomy, as shown in Table 1. Group A patients, before closing wound skin flaps, were sutured using Vicryl 2/0 interrupted sutures to the underlying muscles equidistant, multiple layers depending on the size of the flaps. The wound was dressed with a standard dressing. In the Group B patients, quilting sutures were not applied; the wound was closed and dressed with a standard dressing. Drain was placed in both groups. Seroma formation on the seventh post-operative day was noted clinically and confirmed on ultrasound. All this data (age, duration of disease, BMI, marital status , stage of carcinoma, and seroma formation was noted in a proforma.

The compiled data were analysed with SPSS version 25.0. Variables like age, duration of breast cancer, and BMI are

Table 1: Patient distribution according to age, duration of disease, Marital status, BMI & tumor Stage (n=60)

Variables	Group A mean±SD	Group B mean±SD	p-value
Age (Years)	42.13 ± 3.93	42.37 ± 3.79	0.233
Duration of disease (Months)	5.37 ± 2.08	5.30 ± 2.17	0.341
BMI (kg/m²)	26.13 ± 2.15	26.27 ± 1.94	0.541
Variables	Group A n(%)	Group B n(%)	
Marital status			
Unmarried	3(10)	2(6.67)	0.64
Married	27(90)	28(93.33)	
Stage			
II	4(13.33)	5(16.67)	0.93
III	14(46.67)	13(43.33)	
IV	12(40)	12(40)	
Type of Surgery			
Simple	18(60)	19(63.34)	0.79
MRM	12(40)	11(36.67)	

shown as mean/standard deviation. Categorical variables like marital status, stage of carcinoma, and seroma formation are tabulated in the form of percentages and frequencies. Influence exerting factors such as age, duration of breast cancer, marital status, stage of carcinoma, and BMI are tabulated through stratification. The chi-square test and independent samples t-test were applied to see the significance. A p-value ≤ 0.05 was considered significant.

RESULTS

In our study, the overall age range was from 35 to 50 years with a mean age of 42.25 ± 2.83 years. The mean age in group A was 42.13 ± 3.93 years, whereas in group B it was 42.37 ± 3.79 years. Forty seven (78.33%) patients were between 35 to 45 years of age. The average duration of disease remained 5.33 ± 2.11 months. Marital status-wise distribution of patients, mean BMI (26.20 ± 2.01 kg/m2), and patients' distribution according to stage of carcinoma are provided in Table 1.

In our study, the frequency of seroma formation in the dead space closure with quilting sutures group was found in 05 (16.67%) vs 20 (66.67%) patients without the quilting sutures group (p=0.0001) (Table 2). Tabulation of seroma formation age-wise, duration of disease, and seroma formation according to marital status, BMI and tumor stage is depicted in Table 3.

DISCUSSION

Conventionally, the wounds are closed after placing a wound drain, commonly a suction type, after mastectomy in an attempt to prevent seroma, which commonly develops after drain removal [13].

Multiple Studies on dead space obliteration using biochemical/natural ingredients such as tetracycline, fibrinogen, glue, and thrombin sealants show variable results [14,15,16,17,18]. Recent studies demonstrate that quilting sutures reduce the incidence of seroma formation[19,20,21,22,23]. Quilting suture consists of suturing the skin flaps to the underlying musculature, thereby obliterating the dead space, and restoring the integrity of tissue planes.

In this study, we compared the frequency of seroma development among patients in whom dead space was obliterated using quilting sutures versus those without quilting

Table 2: Comparison of the frequency of seroma formation between dead space closure with quilting sutures versus without quilting sutures after breast surgery (n=60).

		Group A (n=30)		Group B (n=30)		p-value
		No. of Patients	%age	No. of Patients	%age	0.001
SEROMA	Yes	05	16.67	20	66.67	
	No	25	83.33	10	33.33	

Table 3: Tabulation of seroma (yes/no) according to age, duration, and stage of cancer, marital status, &BMI

Variable	Strata	Group A (n=30)		Group B (n=30)		p-value
		Seroma		Seroma		
		Yes n(%)	No n(%)	Yes n(%)	No n(%)	
Age of patients (years)	15-20	05 (21)	19 (79)	16 (70)	07 (30)	0.001
	21-25	00 (0)	06 (100)	04 (57)	03 (43)	0.026
Duration of Diease (Months)	≤5	03 (19)	13 (81)	10 (67)	05 (33)	0.007
	>5	02 (14)	12 (86)	10 (67)	05 (33)	0.004
Marital status	Unmarried	00 (0)	03 (100)	02 (100)	00 (0)	0.025
	Married	05 (19)	22 (81)	18 (64)	10 (36)	0.001
BMI (kg/m2)	≤27	03 (43)	04 (57)	04 (67)	02 (33)	0.391
	>27	02 (9)	21 (91)	16 (67)	08 (33)	0.0001
Stage of carcinoma	II	03 (21)	11 (79)	08 (62)	05 (38)	0.034
	III	02 (17)	10 (83)	07 (58)	05 (42)	0.035
	IV	00 (0)	04 (100)	05 (100)	00 (0)	0.003

sutures after breast surgery. Frequency of seroma formation in the dead space closure with quilting sutures group was found in 05 (16.67%) vs 20 (66.67%) patients without quilting sutures group, (p=0.0001). The incidence of seroma formation in our study is at par with studies in literature. A study conducted in Japan, among 176 patients (87 managed with conventional closure and 89 quilted), demonstrated a significant reduction in seroma development, i.e 80.5% in the conventional group to 22.5% in the quilted group, p<0.01, OR=0.26, 95% CI 0.08 to 0.86; p=0.03 [24].

In another study conducted in France, evaluating 119 patients operated for breast cancer, it was noted that the overall seroma rate was 15.2% in the quilting suture group, and in the conventional closure group, it was 51.7% [25]. Purushotham et al study also concluded that in breast surgery, suture fixation of flaps was not associated with increased surgical or psychological morbidity, including seroma formation [26].

Upon categorising both groups into demographic strata, to further assess the seroma formation among subgroups, it was found that there was a significant difference in seroma formation across all the included strata of age, duration of disease, marital status, BMI and stage of carcinoma, with the frequencies being higher in Group B.

Considering the age of the patients, our results indicated that age is significantly associated with the frequency of seroma formation, as it differed across both age subgroups (p-value < 0.05). This finding is contrary to a recent study conducted in Pakistan, which reported no association between age and seroma formation among patients who underwent breast cancer surgery (p-value 0.16) [27]. Some of the studies suggest that the frequency of seroma formation generally increases with age. A study found the mean age of patients with seroma to be 62.6 ± 10.4 years, compared to 56.1 ± 10.3 years [28].

Our findings showed that the rate of seroma formation is significantly linked to Body Mass Index (BMI) and the duration of disease among breast surgery patients, as it varied equally across the shorter duration (≤5 years) and longer(>5 years) duration (p-value < 0.05). This differs from the findings of several recent studies. For example, a multicenter study published in "BMC Cancer" investigated factors such as age, smoking, previous radiation history, and COVID-19 infection as reasons for delayed seroma formation, but it did not mention duration of disease as a factor [29]. Data from Lahore, Pakistan, also showed that seroma formation was more closely linked to BMI, axillary lymph node dissection, and postoperative infection than to the length of the disease [30,31]. The "World Journal of Surgical Oncology" published another study that backed this up by showing that the rate of seromas varied more with the type of surgery than with the length of the disease [29,32]. The difference between our results and these reports could indicate that the mechanisms underlying lymphatic response or wound healing varied depending on the population or comorbidities. Further research is needed to investigate this possible link in various situations.

Our study also reported a novel finding that marital status was significantly associated with seroma formation and differed equally between the two groups. The effect of marital status has not been considered previously in such cases. Literature was only found to be related to the fact that being married is associated with better survival rates in breast cancer patients [33].

Our findings revealed a strong association between the stages of breast carcinoma in surgical patients and the rate of seroma formation, with variations observed between both groups across all stages (p-value < 0.05). On the contrary, a study conducted among 50 Indian women reported no association between stages and grading of breast cancer with seroma formation [34].

LIMITATIONS OF STUDY

The results lack generalizability as this was a single-centre study. A multicenter study should be planned to further explore this issue. We used a quasi-experimental design due to limitations of resources; an RCT would provide a higher level of evidence on this topic.

Short follow-up duration upto 7th post operative day may not have captured late onset seroma. Additionally other outcomes like length of hospital stay, volume aspirated, wound infection rate, and wound healing time were not investigated.

CONCLUSION

This study found that in breast surgery, significantly decreased seroma formation is noted after dead space closure with quilting sutures, compared to closure without quilting sutures. Therefore, we conclude that dead space closure with quilting sutures is beneficial after mastectomy, as it decreases seroma formation, thereby improving the quality of life and facilitating an early start to further treatment.

ETHICAL APPROVAL: *Reference number: SGR-2016-120-7971, Date: 18-08-2017*

CONSENT FOR PUBLICATION: *Written, informed consent was obtained from the study participants.*

AVAILABILITY OF DATA: *Data is available from the corresponding author on a justified request.*

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- ***Muhammad Ali:*** *Conception and design*
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ORIGINAL ARTICLE

AWARENESS OF THE MANTOUX TUBERCULIN SKIN TEST AMONG HEALTHCARE WORKERS

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ABSTRACT

Background: The bacterium Mycobacterium tuberculosis (MTB) causes the infectious disease tuberculosis(TB). Mantoux tuberculin skin test (MTST) dates back to the 19th century, and remains widely used as the primary test for TB screening and diagnosis; however, its interpretation continues to be challenging.

Objectives: To determine the knowledge level of the Healthcare Workers (HCWs) about MTST and the knowledge difference among different groups of HCWs.

Study Design: Cross-sectional study.

Place and duration of study: Pakistan Ordinance Factory (POF) Hospital, Wah Cantt, 03 months (January to April 2024).

Methodology: This study involved 200 HCWs comprising medical officers and nurses. The data on knowledge, interpretation, and application of MTST from participants were gathered using a self-administered questionnaire. The understanding level of different groups was determined with the chi-square test.

Results: Healthcare workers had scarce knowledge about MTST, its interpretation, and application. Out of 200 participants, 24(12%) had awareness about MTST, total procedural awareness was seen in 24(12%), while 28(14%) exhibited total interpretation awareness.

Conclusion: The knowledge and interpretation level of HCWs regarding MTST was inadequate. Concrete steps must be taken to enhance its awareness. Regular awareness sessions should be scheduled for healthcare workers to update their knowledge in this area.

Key Words: *Awareness, Healthcare workers, Mantoux Tuberculin Skin Test, Tuberculosis screening*

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INTRODUCTION

Mycobacterium tuberculosis (MTB) causes Tuberculosis (TB), a contagious disease, spread by airborne particles. Being a major cause of global mortality, TB is a significant public health concern [1]. World Health Organisation (WHO) reports 10.6 million fresh TB cases and 1.3 million deaths due to TB in 2022 [2]. In the same year, WHO published the updated guide," Implementing the End TB Strategy: The Essentials, 2022 Update", offering revised resources to support global TB control efforts [3]. The initial steps for decreasing the rate of TB-related ill effects are screening, early diagnosis, and management. All the high-risk Healthcare Workers (HCWs), at risk of contracting TB, even in the low-endemic regions, are required to undergo primary TB screening by using the Mantoux tuberculin skin test (MTST) [4,5]. Additionally, it can pinpoint the high-risk areas within healthcare facilities by analysing the proportion of HCWs diagnosed with TB over several years [6]. The expensive TB confirmatory tests, their low sensitivity, and microscopy being not feasible in low-income endemic areas, make MTST a key screening test in such setups [7]. Latent tuberculosis Infection (LTBI) can be identified through meticulous screening by MTST, and it is recommended for the diagnosis & management of TB in low-income rural populations, where TB is prevalent[8]. This test has its foundation in a delayed hypersensitivity (DTH) response towards the I/D injection of purified protein derivative (PPD), comprising the antigens from MTB, Mycobacterium bovis, Bacillus Calmette-Guerin (BCG) and non-tuberculous mycobacteria (NTM). It shows low sensitivity in immunocompromised patients. Variability in results may be attributed to the requirement for two visits within a 72-hour window following the initial intradermal injection of PPD, as well as potential reader bias during the

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interpretation of the PPD-DTH response [9,10]. Improvement of the PPD skin test can be achieved by conducting a standard procedure, preceded by proper training and supervision of the staff. While the PPD skin test is widely utilized globally, interpreting the results can be difficult[11]. The high-risk groups of TB infection comprise persons directly exposed to the infectious agent, contacts of active pulmonary TB patients, persons suffering from latent tuberculous infection, people living in crowded shelters, and healthcare workers, especially those handling and treating TB patients [12]. Among healthcare workers, pulmonologists and respiratory therapists are particularly at risk and require regular testing due to their high likelihood of exposure [13]. Formal training of HCWs to administer, read, and interpret the results of MTST is a vital requirement for TB screening. Careful measurement of the size of the induration at the site of the injection is mandatory. This can be influenced by elements such as injection technique and the patient's skin condition. Technical difficulties in administering, reading and interpreting the response can lead to false results because of insufficient skills or personal bias [9,14]. Standard, CDC guidelines say that PPD test interpretation encompasses the size of induration as well as individual risk factors. A < 5 mm induration may still be taken as +ve in HIV+ve individuals or those with a recent contact with an active TB patient. An induration of ≥ 5 mm is taken as +ve in the immunocompromised, inclusive of patients on corticosteroid therapy, undergoing chemotherapy, or those who have received an organ transplant. Whereas in the recently immigrated people from countries where TB is common, an induration of ≥ 10 mm is considered +ve. Moreover, workers / residents in risky places like jails, homeless shelters, laboratories and healthcare facilities and, the injection drug users, children under 04 years, individuals with chronic ailments that augment TB reactivation risk, an induration of ≥ 15 mm is considered +ve in disease free adults with low chance of acquiring TB[15,16].

CAPSULE SUMMARY

The knowledge level of the healthcare workers about the Mantoux Tuberculin Skin Test, and the differences in the knowledge of HCWs were assessed. Healthcare workers had insufficient knowledge about MTST, its interpretation and application. Tangible steps, along with regular awareness sessions, must be taken for healthcare workers to update their knowledge in this area.

Our study aimed to evaluate the extent of understanding of MTST by HCWs at POF Hospital, Wah Cantt. The purpose was to check the understanding level of different steps of MTST, including performance and interpretation.

The specific objectives were to determine and compare the knowledge about MTST among different groups of HCWs.

METHODOLOGY

After the approval by the Ethical Review Committee/ Institutional Review Board (ERC/ IRB) of Wah Medical College, a cross-sectional study was undertaken at the same college and POF Hospital, Wah, in 03 months after the approval of synopsis. Sample size calculation was done by the Knowledge, Attitude and Practice (KAP) survey sample size calculator, taking a sample population of 400, keeping 95% confidence level & 5% margin of error. Sample size was 197 (rounded off to 200)[17]. A convenient sampling technique was used.

The House officers (HO), Medical Officers (MO), Post-Graduate Trainees (PGT), Post-Resident Nurses (Post RN), Generic Nursing students (BScN) participated in the study. Questionnaires were distributed to the participants after obtaining their informed consent and were collected within a week. After an extensive literature search, a questionnaire with two sections was constructed. Section 1 was about the demographic aspects like age, gender, work status, academic qualification, etc. Section 2 consisted of 20 questions; 8 were related to the procedure of MTST, and 12 were about the method of reading and interpretation of the result. Close-ended items were used for data collection. It was mandatory to answer all questions to eliminate incomplete forms.

In the study questionnaire, each answer carried a value of "1" if correct and "0" if incorrect. In this way, knowledge of the test procedure carried 8 marks, and knowledge of test result reading and its interpretation carried 12 marks. Each participant's knowledge regarding the test procedure and its interpretation was categorised according to the modified Bloom's cut-off point, where any score from 80%- 100%" was Good", 50% - 79% was "Moderate", and less than 50% score was "Poor".

The software SPSS 23 was used for data analysis. Frequency and percentages of the knowledge score were calculated. To assess the difference in the levels of understanding between various groups, a chi-square test was used. The significance (p-value) was 0.05.

RESULTS

Overall awareness for MTST was good among 24(12%), moderate among 40(20%), and poor in 136(68%) HCWs. The total procedural awareness was good among 24(12%), moderate among 45(22.5%) while 131(65.5%) participants showed poor awareness. The interpretation awareness was good among 28(14%), moderate among 111(55.5%) and 61(30.5%) participants had poor interpretation awareness. Regarding the level of awareness according to designations, the detailed results are given in Tables 1 and 2.

The highest awareness and interpretation awareness levels were observed among MOs(54%), whereas the level of procedural awareness was maximum among HOs (23%)(Table3).

DISCUSSION

The MTST is a dependable and standard method extensively

Table 1: Awareness level according to Designation / Qualification

Designation	Total number of participants	Qualification	Poor n(%)	Moderate n(%)	Good n(%)	p-value
PGT	10	MBBS	4(40)	6(60)	0	
MO	30	FCPS	4(13)	10(33)	16(54)	0.001
HO	44	MBBS	20(46)	16(36)	8(18)	
Post RN	80	Post RN	74(92)	6(8)	0	
Generic BSN	36	Generic BSN	34(94)	2(6)	0	

Table 2: Total level of Procedure awareness according to Designation / Qualification

Designation	Total number of participants	Qualification	Poor n(%)	Moderate n(%)	Good n(%)	p-value
PGT	10	MBBS	2(20)	8(80)	0	
MO	30	FCPS	18(60)	12(40)	0	
HO	44	MBBS	12(27)	22(50)	10(23)	0.001
Post RN	80	Post RN	31(39)	49(61)	0	
Generic BSN	36	Generic BSN	16(44)	20(56)	0	

Table 3: Total level of Interpretation awareness according to Designation / Qualification

Designation	Total number of participants	Qualification	Poor n(%)	Moderate n(%)	Good n(%)	p-value
PGT	10	MBBS	8(80)	2(20)	0	
MO	30	FCPS	4(13)	8(27)	18(60)	
HO	44	MBBS	8(18)	30(68)	6(14)	0.001
Post RN	80	Post RN	76(95)	4(5)	0/0/0	
Generic BSN	36	Generic BSN	35(97)	1(3)	0/0/0	

used for the diagnosis of LTBI. It also has a utility in the estimation of uncertain cases of TB with negative MTB culture. A cross-sectional study conducted in Palestine evaluated the knowledge, awareness, and experiences related to tuberculosis among 383 clinical & pre-clinical medical students. The study found that only 6.5% of all students had ever undergone a Mantoux test, and 29.5% knew that it is administered intradermally. Moreover, only 43.6% correctly understood that a positive Mantoux test does not confirm active TB infection. Clinical students demonstrated significantly better understanding than the pre-clinical students across all TB-related domains, including Mantoux testing. These findings underscore a substantial gap in practical TB knowledge among future healthcare professionals and highlight the importance of targeted educational interventions to reinforce diagnostic concepts such as MTST[18].

From January 2018 to 2020, a study was done in Solan, India. Patients presenting in the OPD for the Mantoux test were included. A related physician referred 789 TB-suspected patients, on whom TSTs were performed. Out of 789 patients, 709 (90%) belonged to the rural population, and 401 (51%) of the rural population were from a low socio-educational status. Patients positive for the MTST were 198 (25%), negative cases were 459 (58%), and 135 (17%) cases did not show up for interpretation[8]. Several surveys were conducted in Pakistan to estimate the knowledge, diagnosis, and management of TB by different methods, including MTST. However, none so far has concentrated on the understanding of the procedure and interpretation of the MTST by HCWs. Considering this void, our study focused on assessing HCWs' knowledge of the MTST, its interpretation and application in detail. Our outcomes will guide the development and implementation of interventions

that assist HCWs regarding the MTST in the diagnosis of TB. Our findings revealed a concerning lack of awareness regarding the MTST. While only 12% of participants demonstrated good awareness and 20% had moderate awareness, a significant majority (68%) exhibited poor awareness. This highlights the urgent need for focused educational interventions and training programs to boost MTST-related knowledge among HCWs, which is critical for timely TB detection and control.

RECOMMENDATIONS

- There is an urgent need for structured training programs to address practical gaps in MTST knowledge.
- Standard operating procedures, hands-on workshops, and routine assessments of MTST knowledge and practices should be integrated into continuing medical education (CME) and infection control programs to ensure updated knowledge and skills among healthcare workers.
- Incorporating qualitative research (interviews/focus groups) could identify the reasons behind poor awareness and perceived barriers to MTST implementation.

LIMITATIONS

This was a single-centre study with a convenience sample, which may have limited generalizability. Self-reporting might have introduced response bias.

CONCLUSION

This study reveals a significant knowledge gap among healthcare workers regarding the MTST. Tuberculosis control relies heavily on accurate screening and early detection. Structured training programs for MTST administration and interpretation must be incorporated into the ongoing professional development initiatives for all HCWs.

ETHICAL APPROVAL: *Reference number: (Letter No =WMC/ERC/IRB/041, Date: 12-01-2024*

CONSENT FOR PUBLICATION: *Written, informed consent was obtained from the study participants.*

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AUTHORS' CONTRIBUTION

- ***Tahira Tehseen:*** *Conception and design, Acquisition of data*
- ***Saba Anwar:*** *Acquisition of data*
- ***Lubna Ghazal:*** *Aanalysis and interpretation of data*
- ***Aniqa Shoukat:*** *Aanalysis and interpretation of data*
- ***Fareena Asim:*** *Drafting the article*
- ***Tariq Masood Malik:*** *Critical revision*

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ORIGINAL ARTICLE

BONE AGE DETERMINATION WITH GREULICH-PYLE METHOD IN 1 TO 20-YEAR-OLD PAKISTANI INDIVIDUALS; A REGIONAL STUDY

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ABSTRACT

Objective: To determine the correlation of mean Bone age (BA), estimated with Greulich-Pyle(GP) method, with Chronological age (CA) in Pakistani individuals.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Diagnostic Radiology, KRL General Hospital, Islamabad, 06 months (April to September 2017).

Methodology: A cross-sectional, observational study was done in Islamabad, comprising 250 individuals of both genders, selected through a non-probability consecutive sampling. Data were gathered on a prescribed proforma, and analysed by SPSS version 23.

Results: Total of 250 individuals participated in this study. Skeletal age (SA) was estimated by observation of hand-wrist radiographs, using the GP atlas. Pearson correlation showed a significant correlation of SA & CA ($r = 0.91$; p-value < 0.0005). Stratification analysis was performed. Pearson correlation was found to be positive and highly significant for different CAs, gender and ethnicity groups.

Conclusion: A positive correlation was found between GP atlas method in assessing SA and CA in the population of Pakistan. It can be used as quick, inexpensive and reliable method for SA estimation.

Key words: *Chronological age, Greulich-Pyle method, Skeletal age.*

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INTRODUCTION

Bone age (BA) indicates skeletal & biological maturity. This differs from the chronological age (CA), based on an individual's date of birth [1]. In Paediatric radiology, the BA assessment is a routine procedure. The BA is evaluated and compared with the CA based on the radiological analysis of the left wrist-hand skeletal development [2,3]. A difference between these two numbers implies improper bone development. The method is commonly used in the management and diagnosis of endocrine problems, and it can also act as an indicator of treatment efficacy [4,5]. In South Asia, over 50% of births are registered after 12 months, highlighting significant delays in birth registration [6]. The precise age estimation is crucial in any situation when a child's age must be accurately determined, such as for immigration, legal proceedings, and competitive sports. Skeletal age (SA) or BA is employed to offer the most accurate estimate of CA [7,8]. Although there are several ways to calculate BA, the Greulich-Pyle(GP) and Tanner-Whitehouse-II methods use radiographs (X-rays) of left hand and wrist for BA assessment [9,10]. Dr. William W Greulich and Dr. Sarah I Pyle created this atlas in 1959. The extent of ossification in different hand & wrist bones is compared, independently for children of both genders, with the closest matching GP Atlas plate to determine BA [11]. Numerous other techniques for evaluating BA are available, such as computerized ultrasonography and magnetic resonance imaging (MRI)[12,13,14,15]. In this study, we used the GP atlas method to assess BA among the Pakistani population. This method is quick, inexpensive, non-invasive and has proven useful in legal and clinical settings. Our objective was the determination of correlation between BA, estimated through the GP method, and CA. Establishing this

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correlation can help to reliably use the GP method for SA estimation, particularly in patients with various endocrine and metabolic disorders.

METHODOLOGY

A cross-sectional, descriptive study was undertaken in the Department of Diagnostic Radiology, KRL General Hospital, Islamabad, from April 2017 to September 2017. It comprised 250 individuals of both male and female genders by non-probability consecutive sampling. The subjects were within the CA range of 1 to 20 years. Individuals with any metabolic disorder confirmed through history and inspection of prior investigation and treatment records. History and inspection of prior investigation and treatment records were performed to exclude Individuals with any nutritional deficiency or with trauma to the wrist or hand. Ethical permission for research work was sought from the hospital. Parents of all children, adults themselves (above 18 years of age), consented to the study(informed consent). Skeletal age by the GP method was estimated by a consultant radiologist, blinded to the CA of the individuals. The consultant examined hand-wrist radiographs of the individual, using the GP atlas. Each radiographic image of the wrist/hand was gender-wise compared with images on the GP atlas, and the closest images were taken into account for SA.

Statistical Analysis: Data were analysed using SPSS 23. Quantitative variables, like CA and SA, were described as mean ± SD and the qualitative ones, like gender, as frequencies and percentages. The correlation coefficient was calculated and interpreted by using Pearson's correlation. Effect modifiers like gender and ethnicity were controlled (by stratification). Any p-value < 0.05 was significant.

RESULTS

The mean CA was 9.24±4.02 years, and the mean SA computed by GP method was 9.98±3.94 years as shown in Table 1. There were 128(51.2%) males and 122(48.8%) females. Major ethnicity was Punjabi. Pearson correlation was significant between SA and CA (r= 0.91; p-value 0.001) as shown in Figure1. Stratification analysis was performed. Pearson correlation was found to be positive and highly significant with respect to different CA, gender and ethnicity groups, as shown in Table 2, 3and 4 respectively.

Table 1: Descriptive statistics of groups

		CA (Years)	SA by GP method (Years)
Mean		9.24	9.98
95% Confidence Interval	**Lower Bound**	8.74	9.48
	Upper Bound	9.74	10.47
Median		8.90	9.20
Std. Deviation(SD)		4.02	3.94
Interquartile Range		6.0	5.8

Table 2: Correlation of CA and SA with respect to CA groups

CA Groups (Years)	n	[r]	p-value
1-5	36	0.874	0.001
6-10	118	0.673	0.001
>10	96	0.664	0.001

Table 3: Correlation of CA & SA for gender

Gender	n	[r]	p-value
Male	128	0.907	0.001
Female	122	0.917	0.001

Table 4: Correlation of CA & SA for ethnicity

Ethnicity	n	[r]	p-value
Urdu Speaking	44	0.865	0.001
Sindhi	72	0.975	0.001
Punjabi	126	0.866	0.001
Pathan	8	0.885	0.003

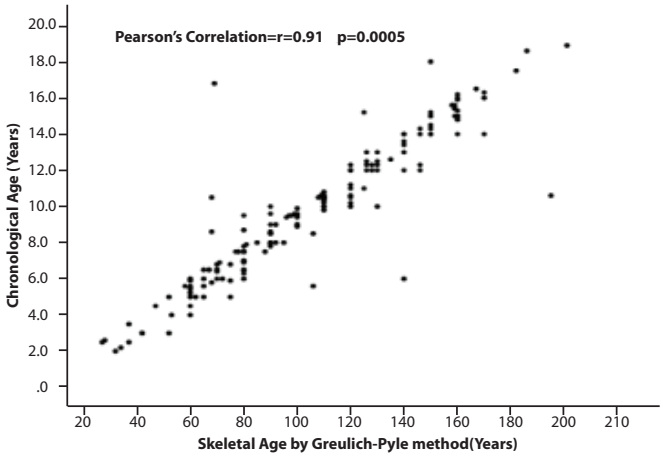

Figure1: Correlation of CA & SA estimated by GP method (n=250).

DISCUSSION

The calculation of BA is frequently used to evaluate childrens' bone growth status. Paediatricians utilise it to diagnose growth problems, for which serial measures are necessary while the patient is under treatment[16]. Moreover, it is required in medico-legal issues like court trials, sports and immigration, and to approximate CA in case of non-availability of a child's birth certificate [17,18,19]. Normal BA criteria ought to fairly depict CA for these reasons. Wrong estimation of BA can lead to unfair punishment, improper growth condition diagnosis & treatment, misplacement in school, or unfair advantages in sports. Different techniques are available to compute BA. In Pakistan, the most commonly used is the GP Atlas[20,1]. Dr. William W Greulich & Dr. Sarah I Pyle created GP Atlas in 1959 with the help of the information from the "Brush foundation study of human growth and development," (led by Professor Wingate Todd), and focused on Caucasian children from higher social stratum of the United States [21] Radiographic pictures of the left wrist and hand from birth to age 19 for men, and age 18 for women, are included for reference in the atlas. Its foundation is the sequential and fixed appearance of ossification centers in the hand and wrist bones. BA is calculated by comparing ossification in hand and wrist bones with the match on the GP Atlas, for males and females. The atlas's applicability varies around the globe because the children chosen for its creation belonged to a specific ethnic and social class. It is thought to calculate BA that is similar to CA in children from Western and Middle Eastern wealthy nations, but there are significant differences between the two in the children from developing nations like India and Iran [22,23,24,25,26,27]. Some studies from Pakistan have assessed the reliability of the GP Atlas. Recall bias may arise from the retrospective study design of one of them; the other has considered only older children (8 to 18 years of age) [11,26,27].

In our study, the mean CA was 9.24±4.02 years and the mean SA computed by the GP method was 9.98±3.94 years. The SA and CA were significantly correlated ($r = 0.91$; $P < 0.0005$) on Pearson correlation.

A recent cross-sectional study with the Egyptian children (aged 8–16 years) using the GP Atlas showed a mean overestimation of SA by 0.04 ± 0.86 years in boys, and a mean underestimation of 0.15 ± 1.32 years in girls, with average error margins slightly exceeding one year in both sexes [28]. A recent systematic review of 20,100 children across different ethnic groups evaluated the GP atlas and found that it overestimates BA in Asian and Arab adolescents and in African youth, highlighting the population-specific variability in skeletal maturation [29]. Other local and regional studies have also reported the reliability GP Atlas for BA assessment [30,31].

CAPSULE SUMMARY

Bone age (BA) indicates skeletal & biological maturity, and it differs from the chronological age (CA). The correlation of mean BA, estimated with the Greulich-Pyle(GP) method, with Chronological age (CA) was determined in Pakistani individuals. This correlation can help reliably use the GP method for SA estimation for various purposes. A strong positive correlation was found in this study.

Nang KM et al reported consistent underestimation with GP Atlas CA by 0.7 years in Sabah, Malaysia, with minimal errors, contrasting with findings from Australia, where males are ahead (by 0.4 years) and females are delayed (by 0.3 years) [32]. Another study in the Canary Islands validates the GP atlas for BA assessment, noting significant underestimation in preschool and school-age groups, while showing closer agreement in teenagers, particularly highlighting the differences between girls and boys [11]. However, statistically significant differences between means and SD of up to 01 year are reported between CA and BA of the Turkish children [33]. Insufficient literature is available on BA assessment in Pakistani children. Our findings agree with Yuh Ys et al, who found significant discrepancies in BA compared to CA for Taiwanese children, with boys showing delayed BA between 6-9 years and girls generally advanced between 7-15 years, differing from the GP standards [32].

CONCLUSION

A strong positive correlation is found between GP atlas method in assessing SA and CA in the population of Pakistan. We can reliably use it in SA estimation in various endocrine and metabolic disorders. This method is quick, inexpensive and non-invasive which provides valuable information in legal cases aswell.

ETHICAL APPROVAL: *Reference number: KRL-HI-PUB-ERC/Jun23/28, Date: 20-06-2023*
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AUTHORS' CONTRIBUTION

- ***Sameeha Ismail:*** *Conception and design, Acquisition of data, Drafting the article*
- ***Maryam Amjad:*** *Acquisition of data*
- ***Muhammad Wasim Awan:*** *Acquisition of data*
- ***Rabia Waseem Butt:*** *Aanalysis and interpretation of data, Drafting the article*
- ***Muhammad Salman Khan:*** *Acquisition of data*
- ***Farkhanda Jabeen:*** *Acquisition of data, Aanalysis and interpretation of data, Critical revision*

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ORIGINAL ARTICLE

FROM NOVICE TO EXPERT: COMPARING PUBLIC HEALTH STUDENTS' KNOWLEDGE OF MONKEYPOX AND ITS RISK PERCEPTION

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ABSTRACT

Objective: To compare monkeypox knowledge and risk perception among the public health students of various educational levels.
Study Design: Cross-sectional study.
Place and Duration of Study: Health Services Academy (HSA), Islamabad, 03 months (June to September 2023).
Methodology: A study was done at HSA, Islamabad, where 800 students of Bachelor of Science in Public Health (BSPH), Master of Science in Public Health (MSPH), and Doctorate (PhD) are enrolled. Two hundred sixty students were selected, by a stratified random sampling technique. Data were gathered by administering a questionnaire (self-developed, pre-tested). Categorisation of monkeypox(Mpox)-related knowledge was good or poor on the basis of scores (percentage). Attitude and risk perception were recorded on a Likert scale. Chi-square test evaluated the association of the educational level of the respondents with study variables.
Results: Knowledge and positive attitudes were seen to improve with advanced academic levels. Association between education level and Mpox knowledge was not significant. Those enrolled in MSPH (59.3%) showed non-significant trends (p=0.31) toward improved knowledge. Moreover, 60.7% of MSPH students had a relatively high perception of knowledge, but the difference was non-significant (p- value 0.16).
Conclusion: Specific educational interventions, involving the community and media, should be done in order to address knowledge gaps, resulting in better preparedness for Mpox outbreaks.
Key words: *Attitudes, Knowledge, Monkeypox, Perception, Public health*
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INTRODUCTION

An Orthopoxvirus causes Monkeypox (Mpox), a zoonotic disease. The affected humans were first recognised in 1970 in Congo. Once a rare infection with comparatively minimal transmission, Mpox was only found in some parts of Africa. Later, the epidemiological picture of Mpox changed substantially. Mpox cases have returned following the global issues by the COVID-19 pandemic, highlighting the need to reevaluate the threat. On May 21, 2022, the World Health Organization (WHO) reported 92 confirmed cases of Mpox in 12 non-endemic countries, along with 28 suspected cases [1]. On May 23, 2022, Pakistan's National Institutes of Health (NIH) sent out alerts about the possibility of breakouts in the region[2]. On August 9, 2022, the WHO deemed the Mpox outbreak, a worldwide health emergency [3].

The largest reservoirs for Mpox virus are the rodents, and the primary hosts are rabbits, lemmings and primates, infrequently passing it to human beings on direct contact while hunting or handling bushmeat. This virus spreads systemically after entering through damaged skin / mucous membrane. Human-to-human transmission occurs via respiratory droplets, lesion contact, or bodily fluids, though it is less efficient than airborne viruses [4]. Recent investigations have also explored the potential for sexual transmission, particularly among men who have sex with men (MSM), a pattern that has emerged in several non-endemic regions during the latest outbreak [5].

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The incubation period of the illness is 5 - 21 days, frequently with nonspecific signs & symptoms of fever, headache, chills, myalgia and lymphadenopathy, before the typical rash erupts. Lesions at different phases of the disease may be present simultaneously. Polymerase chain reaction (PCR) testing of lesion samples is the diagnostic modality of choice, given its sensitivity and specificity, whereas PCR testing of blood is less reliable due to the transient nature of viremia [6]. Management is generally supportive, with an emphasis on symptomatic relief and prevention of secondary bacterial infections. In severe cases or among high-risk populations, antiviral agents developed for smallpox, such as Tecovirimat, have been employed with some success. Mpox prevention and control strategies are diverse, requiring both individual and public health efforts [7].

CAPSULE SUMMARY

Knowledge about monkeypox disease and its risk perception among the public health students of various educational levels was compared. Knowledge and positive attitudes were seen to improve with advanced academic levels. However, the association between education level and Mpox knowledge was not significant. Specific educational interventions should be implemented to bridge the knowledge gaps, resulting in better preparedness for Mpox outbreaks.

Monkeypox causes emotional issues as well. Anxiety, misinformation and stigma can exacerbate the epidemic by deterring patients from getting treatment or collaborating with public health forums. Apprehension as well as societal pressure end up in underreporting, which makes its control arduous. Addressing these psychosocial factors requires a comprehensive approach that integrates mental health [8].

Globally, Mpox has changed from a rare disease to a health problem having notable intercontinental repercussions. Over the past two decades, outbreaks in Nigeria and sporadic cases in the United States, the United Kingdom, Israel, and Singapore have underscored the virus's potential to spread beyond its traditional geographic confines [9]. From 1st January to 30th November 2022, total 92783 verified cases of Mpox, were reported to the WHO (data from 116 countries). One hundred and seventy-one deaths were also confirmed [10].

On a regional level, Pakistan's scenario illustrates the challenges and opportunities of managing Mpox in environments with limited resources. Pakistani health officials increased surveillance and warned medical facilities after receiving early reports of cases from other countries. Despite these proactive measures, the country's healthcare infrastructure, already strained by the COVID-19 pandemic and other infectious diseases, faces significant limitations in terms of diagnostic capacity and clinical management resources [11].

The WHO has demanded the creation of regional and international collaboration that enables quick info sharing, as well as the introduction of standardised procedures for detection, laboratory confirmation and reporting. Such collaborative frameworks are critical for mounting an effective response to Mpox outbreaks and for minimizing the impact of the disease on public health systems worldwide [12].

Notwithstanding the global increase seen in the Mpox cases, there is a scarcity of local data from Pakistan, particularly regarding awareness among public health students. Moreover, assessment of the gaps in knowledge among public health professionals can help to formulate effective protocols for tackling this disease. The study was done with a purpose of finding out the Mpox knowledge, attitudes, and risk perception among Bachelor of Science in Public Health (BSPH), Master of Science in Public Health (MSPH) and Doctorate (PhD) students.

METHODOLOGY

A cross-sectional study was carried out over 03 months (15th June 23 to 15th September 2023) at the Health Services Academy (HSA), Islamabad, an academic institution with about 800 students of BSPH, MSPH, and PhD programs.

Stratified random sampling technique was utilized for the selection of participants, based on students' attendance registers, to ensure proportional representation from different academic programs. Sample size was calculated, using a 50% prevalence assumption to allow for maximum variability, resulting in an initial required sample of 260 participants.

Inclusion criteria were the students aged 18 years or above, who had completed at least one semester at the HSA. Students with serious illnesses or medical conditions that could hinder participation were excluded. Approval regarding the ethical aspects was obtained from the Institutional Review Board (IRB) of the institute.

Data were gathered through structured, direct interviews employing a questionnaire (pre-tested, adapted from the WHO's existing tool, the Centres for Disease Control & Prevention (CDC), as well as from previous peer-reviewed studies on Mpox). The questionnaire underwent expert review and structural revision to enhance clarity and logical grouping of items. To evaluate the reliability of the tool, a pilot study was done with 30 students of Public Health from the National University of Medical Sciences (NUMS). Cronbach's Alpha measured the reliability to be 0.800

The questionnaire comprised sections on sociodemographic characteristics, knowledge and risk perception of Mpox. Knowledge and Risk perception were dependent variables, while the independent variable was the level of education.

Knowledge was assessed through a series of questions covering various aspects of Mpox. Each correct response was awarded one point, with total possible scores ranging from 0 to 10. A

composite knowledge score was created by summing the correct responses. Knowledge levels were categorised as good and poor knowledge based on the total score. Scores > 5 fell in the category of good knowledge, and scores ≤ 5, of poor knowledge.

Risk perception was evaluated using a Likert scale, and responses were categorized into two groups. High-risk perception was indicated by favorable responses, and low risk perception indicated by less favorable or negative responses

Data were recorded and analysed with SPSS 26. Descriptive statistics (frequencies, percentages, means & SD) were utilized for summing up of data. Chi-Square test (χ^2) examined the association of educational levels with knowledge scores and risk perceptions. All p-values of <0.05 were taken as significant.

RESULTS

Two hundred and sixty public health students participated in this study. Participants' age range was 18 - 52 years (mean age 26.0±6.0 years). Over half (55.4%) were enrolled in MSPH program. Regarding residence, the majority (64.6%) lived in urban cities. Occupationally, students comprised the largest group (45.8%), followed by private-sector employees (25.0%). Academic year distribution showed maximum participation (47.7%) from second year (Table 1).

Table 1. Sociodemographic features of public health students (n = 260)

Age	**Mean±SD**	**Maximum**	**Minimum**
	26± 6.0	52	18
Demographics		**Frequency (n)**	**Percentages (%)**
Current education	BSPH	74	28.5
	MSPH	144	55.4
	PhD	42	16.2
Residency	Rural	26	10.0
	Urban town	66	25.4
	Urban	168	64.6
Occupation	Government employee	49	18.8
	Private employee	65	25.0
	Self-employed	11	4.2
	Unemployed	16	6.2
	Student	119	45.8
	Retired	0	0.0
	Other	0	0.0
Academic Year	1st	118	45.4
	2nd	124	47.7
	3rd	8	3.1
	4th	10	3.8
	Other	0	0.0

The majority of participants (87.3%) had heard about Mpox. However, only 27.3% correctly identified its initial discovery

Table 2. Mpox virus knowledge of participants (n = 260)

		Frequency (n)	Percentage (%)
Have you heard about the Mpox virus?	(✓)	227	87.3
	(X)	33	12.7
Do you know when Mpox was first discovered?	(✓)	71	27.3
	(X)	105	40.4
	I don't know	84	32.3
From where you obtained information about Mpox?	Social media	111	42.7
	News media	30	11.5
	Scientific articles	43	16.5
	Health care provider	34	13.1
	Family and friends	20	7.7
	Others	22	8.5
Is contact the most common method of Mpox transmission?	(✓)	202	77.7
	(X)	58	22.3
Can Mpox be transmitted from mother to child?	(✓)	138	53.1
	(X)	122	46.9
Can Mpox virus be transmitted by blood?	(✓)	114	43.8
	(X)	146	56.2
Can Mpox virus be spread through air?	(✓)	118	45.4
	(X)	142	54.6
What is the most common symptoms of Mpox virus?	Fever	32	12.3
	Rash	137	52.7
	Swollen lymph node	56	21.5
	Don't know	35	13.5%
What is the incubation period of Mpox virus?	5-21	118	45.4%
	Don't know	142	54.6%

Note: (✓) means Yes, (X) means No

date. The primary information source was social media (42.7%), followed by scientific articles (16.5%). Regarding transmission, 77.7% recognised close contact as the main route; 53.1% understood vertical (mother-to-child) transmission; 43.8% acknowledged possible blood-borne spread; and 45.4% correctly indicated that airborne transmission can occur. The most frequently cited symptom was rash (52.7%). Correct knowledge of incubation period (5–21 days) came out to be 45.4% (Table 2).

Total 51.9% participants had good overall knowledge of Mpox and a slight majority (53.8%) reported high perceived risk of Mpox (Table 3).

Table 3. Distribution of knowledge scores and risk perception levels among participants (n=260)

		Frequency (n)	Percentage (%)
Knowledge of Mpox	Good	135	51.9
	Poor	125	48.1
Perception	High	140	53.8
	Low	120	46.2

Regarding the association between current education status and knowledge category, a large number (59.3%) of MSPH students had comparatively good knowledge of Mpox among all education levels but the association was non-significant with a p-value of 0.31 (Table 4).

Table 4. Association between education level and knowledge among participants

Knowledge						
Good			Poor		Statistics	
Education level of respondents	**Frequency n=135**	**(%)**	**Frequency n=125**	**(%)**	**X^2**	**p-value**
BSPH	33	24.4	41	32.8	2.36	0.31
MSPH	80	59.3	64	51.2		
PhD	22	16.3	20	16.6		

The relationship between education levels and risk perception indicates that a large number of MSPH students (60.7%) had a significantly high perception of knowledge, with a p- value of 0.16. (Table 5).

Table 5. Association between education level and risk perception among participants (n=260)

	Perception		Statistics	
Education level	**High n(%)**	**Low n(%)**	**χ^2**	**p-value**
BSPH	36(25.7)	38(31.7)	3.61	0.16
MSPH	85(60.7)	59(49.7)		
PhD	19(13.6)	23(19.2)		

DISCUSSION

This study assessed knowledge, awareness, attitudes, as well as risk perception of the Mpox virus among 260 public health students in Islamabad. Overall, 51.9% of participants demonstrated good knowledge, while 48.1% had poor knowledge. The results indicate moderate awareness in our cohort and align with similar research in diverse populations. For example, a Saudi Arabian general population study reported that 52% of respondents had poor Mpox knowledge [13] and an Indonesian survey found that only 10% of general practitioners answered ≥80% of Mpox questions correctly [14]. In Italy, Riccò et al. (2022) observed unsatisfactory Mpox knowledge among medical professionals [8].

Factors contributing to these knowledge gaps likely include limited public health education on rare zoonoses, insufficient coverage in academic curricula, and variability in regional exposure to Mpox outbreaks. In Saudi Arabia, for instance, low case numbers and minimal local media coverage contributed to public unfamiliarity with Mpox [15]. Conversely, a Bangladeshi study reported 63.6% of students with good Mpix knowledge, suggesting that regional educational efforts can yield higher awareness [16].

Within our sample, educational attainment correlated with knowledge levels. MSPH and PhD students demonstrated higher knowledge scores than BSPH students, mirroring findings in other contexts found that clinical dental students in Malaysia had greater understanding of emerging infections than their preclinical counterparts[17]. Similarly, a study reported variable Mpox awareness among Kuwaiti healthcare workers by professional category [18]. In another study Jordanian medical students outperformed non-medical peers in Mpox knowledge and held fewer conspiracy beliefs [19]. These patterns underscore the role of advanced training, research exposure, and specialized curricula in deepening comprehension of infectious diseases.

Risk perception in our study was similarly influenced by educational level. Among MSPH students, 60.7% reported high perceived risk of Mpox was significantly more than BSPH students, of whom only 25.7% reported high risk perception. This trend echoes studies in Saudi Arabia where clinicians with advanced degrees or targeted training exhibited greater risk awareness toward emerging infections [20,21]. Enhanced risk perception among highly educated groups likely reflects greater familiarity with disease severity and transmission dynamics, as well as stronger engagement with evidence-based information sources.

The main sources of Mpox information in our sample were social media (42.7%), research papers (16.5%), and the healthcare community (13.1%), highlighting the need for accurate, authoritative messaging across channels. Social media's dominant role suggests that public health campaigns must leverage these platforms while ensuring content reliability. Healthcare curricula should also incorporate risk

communication along with behavioral science to prepare students for future community health crises.

LIMITATIONS

A cross-sectional design and focus on a single institution might have limited generalizability. Moreover, self-reported data can have recall /social desirability bias. Research with longitudinal designs across multiple universities and qualitative methods to explore underlying reasons for knowledge gaps and perceptions should be undertaken.

CONCLUSION

Higher education alone might not affect the knowledge/ perception of newer diseases. Cohesive awareness strategies should be employed for early diagnosis and coordinated strategies that are vital for future alertness and response to any outbreaks.

ETHICAL APPROVAL: *Reference number: F.No.000265/HSA/ MSPH-2021, Date: 02-05-2023*
CONSENT FOR PUBLICATION: *Written, informed consent was obtained from the study participants.*
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- ***Paras Shaikh:*** *Conception and design, Acquisition of data, Aanalysis and interpretation of data, Drafting the article*
- ***Ejaz Ahmad Khan:*** *Aanalysis and interpretation of data, Critical revision, Drafting the article*
- ***Aysha Mushtaq:*** *Conception and design, Acquisition of data, Aanalysis and interpretation of data*
- ***Saqib Khan:*** *Aanalysis and interpretation of data, Critical revision*
- ***Samia Sheikh:*** *Acquisition of data, Critical revision*

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ORIGINAL ARTICLE

SERUM VITAMIN D, CALCIUM AND PHOSPHATE LEVELS IN PATIENTS WITH ACUTE MANIA: A CROSS-SECTIONAL COMPARATIVE STUDY

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ABSTRACT

Objective: To investigate the levels of serum Vitamin D, Calcium and Phosphate levels in the manic phase of bipolar disorder.

Study Design: Cross-sectional study with comparative groups.

Place and Duration of Study: Rawal General Hospital, Islamabad, 10 months (October 2023 to Jul 2024).

Methodology: Forty patients suffering from manic episode according to the Diagnostic and Statistical Manual of Mental Disorders(DSM)- 5 criteria were included in the study, after informed consent. They were compared to 40 age and gender-matched healthy controls who had no previous psychiatric history. The authorization to conduct the study was given by the Ethical Review Board of the medical college vide the ERB permission letter. Young Mania Rating scale was administered to the patients to assess the severity of mania. Venous blood was drawn from all the participants to determine the serum levels of vitamin D, Calcium and Phosphate. Statistical analysis was done with the help of SPSS-23. For numeric variables, descriptive statistics and mean with standard deviation were calculated, whereas frequencies and percentages were calculated for the categorical variables. For the analysis of categorical variables Chi-square test was used, and for the numerical variables, the Independent samples t-test was utilized. The p- value < 0.05 was considered significant.

Results: With respect to demographic details, the cases and controls were homogeneous. The mean Serum vitamin D was 11.52 ± 5.83 ng/ml for the cases and 17.46 ± 6.18 ng/ml for the controls, and this result was statistically significant(P < 0.01).

Conclusion: In our sample, bipolar patients with a manic episode had significantly lower Vitamin D levels, and this purportedly implicated the latter factor in the pathogenesis of bipolar mania.

Keywords: *Bipolar disorder, Inflammation, Mania, Vitamin D.*

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INTRODUCTION

Bipolar disorder (BD), a mental disorder affecting millions of people worldwide, is an incalcitrant condition[1]. The disorder impairs functioning in the biopsychosocial realms, and currently available psychopharmacological agents only provide symptomatic relief [1, 2]. Active exploration and avenues of research include neuroinflammation, oxidative damage and neurodegeneration in its mechanism[3]. Vitamin D (Vit D) is an essential nutrient with pleotropic actions throughout the body, whose relationship with mood disorders has been investigated. In particular, the role of low Vit D levels and major depressive disorder is well-researched, but this association is less well studied in BD [4].

The potential role of inflammation in the development of BD has been well researched, and it is conceivable that stress may trigger neuroinflammation. This is allegedly implicated in the development of BD [5]. In BD, a number of biochemical parameters associated with inflammation have been explored; however, the connection between manic episodes and serum Vit D levels has not been sufficiently studied. While a handful of studies implicate low Vit D in mania, additional work is needed to validate this association [6].

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Biologically, several factors, including inadequate sunlight, poor dietary intake, seasonal variations and increasing age, influence Vit D levels. Across the world, studies show that low Vit D levels, at all ages, are liable for both physical and mental diseases [7]. There is emerging evidence that Vit D is involved in critical brain functions like neurotransmission, neurogenesis, neuroplasticity and neuroinflammation. As such, researchers have turned their attention towards investigating the potential involvement of Vit D in major neuropsychiatric conditions [8].

CAPSULE SUMMARY

The serum levels of Vitamin D, Calcium and Phosphate in the manic phase of bipolar disorder were determined. Patients in the manic episode had significantly lower Vitamin D levels. The differences in Calcium and phosphate levels were not statistically significant.

Major neuropsychiatric disorders like attention deficit hyperactivity disorder (ADHD), BD and schizophrenia show common executive dysfunction, deficits in social behavior and impaired emotional regulation. Serotonin, a monoamine neurotransmitter, performs crucial functions in the brain, and Vit D, among other micronutrients, is required in its synthesis. Relative deficiency of Vit D during critical periods of development supposedly impairs serotonergic transmission in the prefrontal areas and limbic circuit and leads to major neuropsychiatric disorders. Optimizing Vit D intake throughout the development epoch may help modulate brain functioning, and supplementation with this essential nutrient may decrease the psychosocial impairment associated with neuropsychiatric disorders [9].

In BD, there is acute disturbance during the manic episode, and it is highly desirable to examine the status of Vit D and related parameters of Calcium (Ca) and Phosphate (P) in the peripheral blood. In this regard, only a handful of studies have assessed peripheral levels of Vit D, Ca and P in BD patients. In a review published a few years ago, the authors performed a literature search, investigating Vit D status in BD subjects. They found 10 original studies on this subject, and the overall results showed that there was sub-threshold Vit D deficiency in BD cases, which had an association with the status of symptoms. In addition, Vit D supplementation helped decrease both manic and depressive symptoms [10].

A recent study used novel parameters to examine Vit D status in BD. The researchers measured 25 (OH) D, 24, 25 (OH) D and Vit D metabolite ratio (VMR) [VMR = 100×(24,25(OH)2D/25(OH)D)] in cases and controls. Their findings demonstrated a negative correlation between Vit D parameters and severity of symptoms of mania as calculated by the Young Mania Rating Scale(YMRS). The authors concluded that keeping in view the limitations of the cross-sectional study, a significant inverse relationship occurred between the severity of mania and Vit D levels, and this required further investigation [11]. The aim of our study was to investigate serum Vit D, Ca and P in acute mania and compare those to healthy individuals to examine any association between these variables.

METHODOLOGY

Approval for the study was obtained from the Institution Review Board of Rawal Institute of Health Sciences (RIHS), Islamabad.

In this cross-sectional study with comparative groups, study subjects were patients seen in the outpatient section of the department of Psychiatry of Rawal General Hospital, which is the teaching hospital of RIHS, Islamabad, Pakistan. The duration of the study was from 01/10/2023 to 31/07/2024, a period of 10 months. Patients with BD, suffering from a manic episode, were included in the study through non-consecutive sampling, after an informed consent. Sample size was calculated using open epi calculator for comparing means between two independent groups. The calculations were based on a 95% confidence interval, 80% power and previously reported Vit D levels in group 1, 14.58±11.27 and group 2, 30.97±17.87 mg/ml [12]. The sample size required was calculated to be 14 participants per group. We inducted 40 individuals into each group. A large sample helps mitigate the potential effect of dropouts or outliers and generalizability of the results. The patients in the study group could have an index or recurrent episode of mania, while the comparative group consisted of healthy individuals, matched for age and gender and having no previous psychiatric history.

Inclusion criteria included patients diagnosed as having BD type I, current episode manic according to Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria, giving informed consent, patients of either gender and ages between 18 and 60 years. Exclusion criteria included patients with bone disorders and endocrinological conditions affecting Vit D metabolism, those cases who took Vit D supplementation for 03 months prior to evaluation, pregnant and lactating mothers, patients with acute medical conditions, e.g. infections, patients with chronic medical conditions, for example, diabetes mellitus.

The participants with BD were administered the Young Mania Rating Scale (YMRS) to confirm the diagnosis of mania and rate its severity [13]. This is a well-validated instrument with a high level of reliability. It is the preferred instrument in research work and has been used innumerable times in both national and international studies. To differentiate between cases and non-cases, a cut-off score of 20 on the YMRS was utilized. Demographic variables of the cases and controls were recorded with the help of a separately designed proforma.

With the help of sterile technique, 5 ml of blood from the antecubital vein of all of the subjects was drawn and collected into vacutainer tubes . The samples were centrifuged for 10 min at 2500 revolutions per minute, and the serum was separated. It was analyzed to determine the 25-OHD levels. Serum Vit D levels were interpreted in the following manner [14]:

- normal - 20–100 ng/mL

- insufficient - 10–20 ng/mL
- deficient - <10 ng/mL

From the same sample, serum Ca and P were also determined.

Statistical analysis was done with the help of SPSS-23. For numeric variables, we used descriptive statistics and derived the mean with standard deviation, whereas frequency and percentage were calculated for categorical variables. For the analysis of categorical variables Chi-square test was used, and for numerical variables Independent samples t-test was utilized. The p- value < 0.05 was considered significant throughout the statistical measures.

RESULTS

There was no statistically significant difference between the demographic variables (age, gender, residence, level of education and employment status) of cases and the comparative group (Table 1) The biochemical variables(serum Vit D, Ca and P) of patients and the comparative group are compared in Table 2, which demonstrates that serum Vit D levels are significantly lower in cases with mania as compared to healthy individuals ($p < 0.01$), while serum Ca and P values did not reach statistical significance.

DISCUSSION

The studies examining the link between Vit D and BD are scarce. Relying on the current literature, it can be said that there exists a tentative connection between clinical symptomatology and serum Vit D levels. A comprehensive review, published a few years ago, addressed this matter; an exhaustive search revealed that 10 original studies examined Vit D blood levels in both the manic and depressive phases of BD. Compared to other diagnostic groups, BD cases had no significant differences in serum Vit D levels; nonetheless, the average values of Vit D were in the insufficient range in the BD population. Additionally, it was seen that there existed a relationship between Vit D levels and clinical symptomatology in BD patients, but this could not be regarded as a fully characterized biomarker. Rather, it was a feature shared with other psychiatric disorders, including schizophrenia and major depressive disorder (MDD). Importantly, the addition of Vit D to the treatment regimen was accompanied by a reduction in both depressive and manic symptoms [10]. In our study, the population was homogeneous in the demographic variables. A significantly low serum Vit D was observed in BD patients presenting with mania. These results were in line with previously published studies, and strengthened the general assumption that Vit D had an immunomodulatory and anti-oxidant role, and that its relative deficiency resulted in neuropsychiatric disorders [15].

Table 1: Demographic characteristics of study participants

Variables	BD group n = 40	Healthy individuals n = 40	p-value*
Age (mean ± SD)	31.63±7.49	29.27±8.45	0.358#
Male n(%)	26 (65)	28 (70)	0.154
Female n(%)	14 (35)	12 (30)	0.368
Urban residence n(%)	30 (75)	32 (80)	0.712
Rural Residence n(%)	10 (25)	8 (20)	0.471
No education n(%)	6 (15)	8 (20)	0.217
Matric n(%)	20 (50)	18 (45)	0.761
Higher n(%)	14 (35)	14 (35)	0.358
Employed n(%)	28 (70)	30 (75)	0.269
Unemployed n(%)	8 (20)	8 (20)	0.752
Student n(%)	4 (10)	2 (5)	0.183

P* - Pearson's Chi-square; P# - Independent samples t-test; SD – Standard deviation

Table 2: Comparison of Vit D levels, Ca and P levels between patients with acute mania and healthy individuals

Variable	Manic cases n = 40 mean ± SD	Healthy individuals n = 40 mean ± SD	t-value	p-value
Vit D (ng/ml)	11.52 ± 5.83	17.46 ± 6.18	**2.708**	**< 0.01**
Ca (mg/dL)	9.11 ± 0.83	9.51 ± 0.72	**1.195**	**0.47**
P (mg/dL)	3.19 ± 0.68	3.74 ± 0.68	**1.211**	**0.38**

Ca – Serum Calcium; P – Serum Phosphate; SD. – Standard Deviation; p* – independent samples t-test

An accumulating body of evidence demonstrates that Vit D performs essential functions in the brain. Vitamin D, a neuroactive steroid, has been suggested to modify neurotransmitter pathways in the central nervous system. It is surmised that aberrant neurotransmission is involved in the pathogenesis of principal neuropsychiatric diseases such as schizophrenia, BD and MDD. Vit D performs important actions of calcium homeostasis, and supposedly the amyloid-peptide clearance as well, in addition to having antioxidant and anti-inflammatory functions. Furthermore, it acts as a likely protective factor against the progression associated with Alzheimer's disease, schizophrenia and neurodevelopmental disorders. Several studies indicate that Vit D has a shielding role in neuropsychiatric disorders, such that its regular intake helps in the prevention of these disorders and also reduces the severity of psychiatric ailments. Hence, the bulk of extant research indicates that timely supplementation, keeping Vit D concentrations at adequate levels, is critical in slowing, averting or improving decline in the neurocognitive status [16].

A recently published systematic review highlighted the beneficial effects of regular Vit D intake in neuropsychiatric disorders. A wide-ranging search of the literature was supportive of adding Vit D to the treatment regimens in mood disorders, psychotic disorders, neurodevelopmental and neurodegenerative disorders. The salutary effects of this pleotropic hormone were evident across the spectrum of neuropsychiatric illnesses, such that the monitoring of Vit D levels and its administration were highly recommended [17]. An interesting study was recently published from the People's Republic of China, investigating serum 25-hydroxy Vit D levels in patients diagnosed as suffering from bipolar depression. Vit D levels were measured at the start of the study and 2 weeks after treatment; three sub-groups were identified through latent profile analysis. The study found that participants with adequate levels of Vit D demonstrated a significant improvement in the severity of depression. However, the patients who had low levels of Vit D went on to remain significantly depressed, specifying a requirement for directed Vit D supplementation. The results of this study highlighted the importance of planned and personalized Vit D supplementation to manage the deficiency of Vit D in patients with BD [18].

In an effort to study the part played by inflammation, a recently published study examined the link between serum Vit D levels, C-reactive protein (CRP) and psychiatric illnesses with psychotic symptomatology. The investigators had three clusters of cases, including schizophrenia, psychotic mania and methamphetamine-induced psychosis. In the 3 sets of cases, CRP levels were significantly higher and serum Parathyroid hormone (PTH) levels were significantly lower, compared to the healthy control group ($p < 0.001$). As regards blood levels of Ca, P and Vit D, the differences did not reach statistical significance when patient and control groups were compared. However, in patients with chronic psychosis, serum CRP levels were significantly higher ($p < 0.031$) and Vit D levels significantly lower ($p < 0.044$) compared to patients who had first-episode psychosis. These results proposed that Vit D levels were decreased in subjects with chronic psychosis in comparison to patients with first-episode psychosis, and conceivably, this finding had pathophysiological and therapeutic implications[19]. Neuropsychiatric disorders, including BD are characterized by subtle impairments in cognitive functioning, and it would be interesting to know if Vit D plays a role in this regard. A comprehensive review published recently addressed this issue in the main psychiatric illnesses, including Schizophrenia, mood disorders, Alzheimer's disease and ADHD. The authors noted that while there were many studies specifying the key role of vitamins in cognition, it was still too early to unambiguously assume that Vit D had an effect in the development of cognitive symptoms. More study was needed to confirm this putative association, together with the necessity of improving on the biological veracity of animal prototypes, better defining the key cognitive deficits accompanying the disorders, while determining the optimum way, Vit D is taken [20].

Finally, seasonal affective disorder (SAD) is an illness characterized by depressive episodes in fall and winter, with resolution of the affective symptoms in spring and summer. These patients have an illness where mood episodes occur in a seasonal form for two or more years consecutively. It is surmised that a decrease in sunlight hours during winter months plays an etiological role in SAD, and Vit D status in these patients has been investigated as exposure to sunlight is essential for the synthesis of this substance in the body. A recently published review on the subject of fat and water soluble vitamins in the prevention and treatment of SAD underlined that vitamins taken in the diet, as well as added vitamins, had encouraging effects in both prevention and treatment. However, clinicians dealing with psychiatric ailments faced ambiguity because of the variations present in the study designs, such that any definitive conclusions were hard to make. The authors concluded that there was evidence to support the roles of vitamins B, C and D in the prevention and treatment of mood disorders; nonetheless, additional work was required to explain their modes of action and to find out the most effective means of supplementing these micronutrients [21].

LIMITATIONS

1. Cross-sectional design of the study introduces bias in the interpretation of the results.
2. The fact that many patients were receiving psychopharmacological agents was not controlled for in the study.
3. Dietary habits and exposure to sunlight have an influence on serum Vit D levels, and these factors could have introduced bias in the results.

CONCLUSION

The results of this study can be regarded as preliminary; nonetheless, these are still valuable as it was shown that Vit D levels were unequivocally reduced in BD patients with manic episodes. It is known that immunologic and inflammatory mechanisms are important players in the manic phase of bipolar disorder, and Vit D, with its myriad functions in the CNS, plays a contributory part in the onset and maintenance

of BD. Additional research, which adequately controls for diet, exposure to sunlight and medications, can further elucidate the role of Vit D in the bipolar diathesis.

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AUTHORS' CONTRIBUTION

- ***Ather Muneer:*** *Acquisition of data, Aanalysis and interpretation of data, Drafting the article*
- ***Nargis Muneer:*** *Acquisition of data, Drafting the article*
- ***Mahwish Ahmad:*** *Aanalysis and interpretation of data, Drafting the article*
- ***Zara Inam:*** *Drafting the article, Acquisition of data, Critical revision*

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CASE REPORT

A DIAGNOSTIC CHALLENGE PRESENTING AS NON RESOLVING PNEUMONIA IN A YOUNG FEMALE

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ABSTRACT

This case highlights the diagnostic challenge of a 35-year-old female initially managed as community-acquired pneumonia, who later presented with persistent respiratory symptoms, systemic complaints, and peripheral blood eosinophilia. Further investigations revealed positive peripheral antineutrophil cytoplasmic antibodies (p-ANCA)and pulmonary infiltrates, leading to a diagnosis of Eosinophilic Granulomatosis with Polyangiitis (EGPA), a rare form of ANCA-associated vasculitis. She was managed successfully with high-dose methylprednisolone, methotrexate, and supportive care. Our case illustrates the importance of suspecting rare causes in case of non resolving pneumonia.

Keywords: *Eosinophilic Granulomatosis with Polyangitis, Pneumonia, ANCA*

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INTRODUCTION

Eosinophilic Granulomatosis with Polyangiitis (EGPA), formerly known as Churg-Strauss syndrome, is a rare small-to-medium vessel vasculitis characterized by asthma, eosinophilia, and granulomatous inflammation. Its variable presentation usually causes a delay in its diagnosis. This report illustrates a classic presentation of a patient whose journey through persistent respiratory symptoms and vague systemic complaints eventually led to the diagnosis of this rare autoimmune condition. This case also underscores the importance of considering vasculitic syndromes in patients with unexplained eosinophilia and multi-systemic manifestations. Timely recognition and a multidisciplinary approach are important to prevent irreversible damage to the organs.

CAPSULE SUMMARY

A case is reported that emphasizes the need for high clinical suspicion and a multidisciplinary approach in cases of non-resolving pneumonia, especially when eosinophilia and systemic symptoms are present. Eosinophilic Granulomatosis with Polyangiitis, though rare, should be part of the differential in such cases.

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Case:

A 35-year-old housewife from Mandi Bahauddin presented in Medical out patient department on April 17th, 2024 with a one-week history of intermittent fever (up to 101°F) and productive cough with white mucoid sputum. She had a past medical history of hypothyroidism, for which she was taking Tablet Thyroxine 150 µg daily, and was experiencing asthma-like symptoms for the past one year. On examination, her temperature was 102°F with a pulse of 110 beats per minute. On auscultation, there were crepitations in the right lower chest posteriorly. Chest X-ray showed non-homogenous patchy opacities in the right lower zone. Liver function tests (LFT)and Renal function tests (RFT) were within normal limits. Initial diagnosis of community-acquired pneumonia was made, and she was managed with Inj Rocephin (Ceftriaxone) 1g I/V, 12 hourly, Tablet Leflox (Levofloxacin) 500mg 24 hourly, along with symptomatic treatment. Later her symptoms improved and she was discharged on Tablet Leflox (levofloxacin) 500mg per oral 24 hourly and follow-up advice.

After 02 months, on 16th June 2024, she came in OPD in deteriorated health. This time, she reported persistent cough with hemoptysis. She gave a history of weight loss of almost 3kg in the last 02 months with low-grade fever, numbness in both

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hands and generalized body aches. There were crepitation in the right lower chest and reduced pinprick sensations in her hands. The peripheral blood picture showed Hb 9.2g/dl ,TLC 8.1 ccm and a peripheral eosinophil count of more than 10%. HRCT showed ground glass attenuation in pulmonary parenchyma in mid and lower zones suggestive of an acute infective/allergic etiology. There was no evidence of bronchiectasis. There was no organomegaly, and the absence of any mass in HRCT made malignancy a least likely diagnosis. Sputum for gene expert was negative for tuberculosis. Liver function tests (LFT)and renal function tests (RFT) were within normal limits.

In the light of marked eosinophilia, the rare possibility of autoimmune vasculitis was considered and autoimmune profile was requested which revealed a positive peripheral antineutrophil cytoplasmic antibodies (p -ANCA) and negative anti nuclear antigen(ANA) serology. On the basis of X ray chest/ HRTC findings, peripheral neuropathy, peripheral eosinophila and positive p-ANCA serology she was diagnosed as a case of Eosinophilic Granulomatosis with Polyangiitis (EGPA). Skin biopsy couldn't be done because of the absence of any skin lesion, and the patient refused a lung biopsy.

She was managed with Injection Solu Medrol (Methylprednisolone) 1g/day, Tab Cytotrexate (Methotrexate) 15mg once weekly, supplemental oxygen and nebulization. Her symptoms improved. She was counselled in detail regarding her condition, importance of follow-up and compliance with medications.

DISCUSSION

Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare systemic vasculitis that primarily affects small- to medium-sized vessels and is characterized by asthma, eosinophilia, and tissue infiltration by eosinophils, often accompanied by granuloma formation. The disease typically follows a triphasic clinical course: a prodromal phase with allergic features (e.g., asthma, allergic rhinitis), an eosinophilic phase, marked by peripheral eosinophilia and organ involvement (notably pulmonary and gastrointestinal), and a vasculitic phase, during which systemic manifestations and end-organ damage become evident due to necrotizing vasculitis.[1]

Presentation with stroke or cardiac events may also occur.[2,3] Although only 30–40% of EGPA patients are ANCA-positive, the presence of ANCA often correlates with more pronounced vasculitic manifestations such as glomerulonephritis, neuropathy and purpura, while ANCA-negative patients tend to have more eosinophilic tissue infiltration and cardiac involvement[4]. Our patient's clinical trajectory aligns with an ANCA-positive phenotype, with prominent neurologic and pulmonary findings.

Diagnosis is largely clinical, supported by the American College of Rheumatology (ACR) criteria (Table 1), which include asthma, eosinophilia >10%, mononeuritis or polyneuropathy, pulmonary infiltrates, paranasal sinus abnormality, and biopsy showing extravascular eosinophils.[5] In this case, four of these criteria were met, reinforcing the diagnosis.

Table 1: American College of Rheumatology (ACR) criteria

Considerations when applying ACR criteria:

- These classification criteria should be applied to classify a patient as having eosinophilic granulomatosis with polyangiitis (EGPA) when a diagnosis of small- or medium-vessel vasculitis has been made.
- Alternative diagnoses mimicking vasculitis should be excluded prior to applying the criteria.

Criteria Type	Item	Score
Clinical Criteria	Obstructive airway disease	+3
	Nasal polyps	+3
	Mononeuritis multiplex	+1
Laboratory/ Biopsy Criteria	Blood eosinophil count ≥ 1×10^9/L	+5
	Extravascular eosinophilic-predominant inflammation on biopsy	+2
	Positive test for cytoplasmic ANCA or anti-PN3 ANCA antibodies	-3
	Hematuria	-1

Scoring Guideline:

- Sum the scores for the 7 items, if present.
- A score ≥ 6 is needed for classification of EGPA.

Management of EGPA (Table 2) hinges on disease severity. For non-severe disease, glucocorticoids 0.5mg-1mg/kg/day alone may suffice, but in severe or life-threatening cases—especially those with cardiac, renal, or neurologic involvement—immunosuppressive therapy (e.g., Cyclophosphamide, Rituximab) is warranted. Recent trials have shown promise with Mepolizumab, an anti-IL-5 monoclonal antibody, particularly in relapsing or refractory disease, reflecting a shift toward targeted biologic therapies.[6]

Treatment of EGPA relies on systemic glucocorticoids, in combination with DMARDs. Our patient responded favorably to high-dose corticosteroids and immunosuppressive therapy, highlighting the importance of early recognition and aggressive intervention in preventing irreversible organ damage. However, long-term monitoring remains essential given the potential for relapse and chronic complications, including steroid dependence and treatment-related adverse effects. EGPA has a good prognosis following timely detection and treatment, with a 5 years survival rate of 90%.The relapse rate is estimated to be approximately 20% to 30%, often presenting with fever, joint pain, and constitutional symptoms.[9]

A case involved a 72 years old male with a history of asthma, bronchitis and recurrent sinusitis who presented with shortness of breath and progressively worsening hypoxemic respiratory failure. Similar diagnostic markers p-ANCA positivity d

Table 2 -Management

Step	Category	Details
1	Assess Disease Severity	Non-Severe: No major organ involvement Severe: Cardiac, renal, CNS, or GI involvement[7]
2	Induction Therapy	Non-Severe Disease: • Systemic glucocorticoids (Prednisone 0.5–1 mg/kg/day, tapered slowly) • Consider mepolizumab for relapsing disease Severe Disease: • High-dose corticosteroids + immunosuppressive agent: 1. Cyclophosphamide (oral/IV) for 3–6 months 2. Rituximab (especially if ANCA-positive)
3	Maintenance Therapy	After remission: • Options: Azathioprine, Methotrexate, Mycophenolate mofetil • Consider mepolizumab for relapsing eosinophilic-predominant disease[8]
4	Supportive Measures	• TMP-SMX for Pneumocystis jirovecii prophylaxis (if on high-dose steroids or cyclophosphamide) • Bone protection: calcium, vitamin D, bisphosphonates • Monitor for infections • Regular surveillance for relapse, organ damage, treatment toxicity

eosinophilia supported the diagnosis of EGPA. Treatment with Methylprednisolone and Cyclophosphamide led to clinical remission[10].

Another case involved a 64 year old male with a history of asthma and multiple allergies. Over a long period of time he developed peripheral neuropathy and bronchiectasis. He was admitted with asthma exacerbation. His eosinophil count was 53% with similar diagnostic markers p-ANCA positivity peripheral neuropathy supported the diagnosis of EGPA. Treatment with Methylprednisolone and Methotrexate led to clinical remission but recurrent infections. Progressive respiratory failure developed and he succumbed to pneumonia[1].

Our case and these cases highlight the diagnostic challenge of EGPA due to overlapping symptoms with common respiratory illnesses. Early consideration of vasculitis in patients with asthma, systemic symptoms and eosinophilia is crucial. While treatment regimens varied slightly, both patients responded well to immunosuppressive therapy, underscoring the importance of timely diagnosis and intervention.

Our case also highlights the diagnostic challenge, EGPA poses due to its protean manifestations and overlapping features with other eosinophilic disorders, such as hypereosinophilic syndrome (HES), and vasculitides, including granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). In this patient, the presence of longstanding asthma, marked peripheral eosinophilia, mononeuritis multiplex and pulmonary infiltrates raised the suspicion for EGPA, which was further supported by positive p-ANCA serology.

Infectious agents, allergens and certain drugs are known to precipitate EPGA. In our case it is likely that the initial episode of pneumonia trigged the onset of EPGA and presented as likely unresolved pneumonia.

CONCLUSION

This case contributes to the growing body of literature underscoring the heterogeneity of EGPA and emphasizes the need for high clinical suspicion and multidisciplinary approach in cases of non-resolving pneumonia, especially when eosinophilia and systemic symptoms are present. EGPA, though rare, should be part of the differential in such cases.

CONSENT FOR PUBLICATION: *Written, informed consent was obtained from the study participants.*
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DIAGNOSTIC CHALLENGE

Check the correct answer on page 43

Case 1

Figure 1

A 24 year old girl presents to the outpatient clinic with pain in her left wrist for last 04 months. She does not remember any trauma to the wrist joint. There is no pain in any other joint of the body. The pain is localized, mild to moderate in intensity and increases with weight bearing activities and domestic chores.

On examination of the wrist there is no swelling or deformity of the wrist. There is localized tenderness over the dorsum middle of the wrist. Extremes of flexion and extension are painful.

Her initial rheumatological workup has shown an ESR of 25mm. Her TLC is 5000 and Neutrophils are 50% (within normal range). Her X-ray is shown below:

1. What is your diagnosis?
2. How will you investigate further?
3. How will you treat her?

DIAGNOSTIC CHALLENGE

Check the correct answer on page 44

Case 2

A 45-year-old female presents to the Oromaxillofacial Surgery (OMFS) department at HITEC-IMS with a complaint of gum swelling for the past 3 years. She describes the growth as painless and gradually increasing in size, making it difficult for her to maintain oral hygiene. The patient has a known history of hypertension for the last 15 years and is currently on antihypertensive medication . She denies any history of bleeding, ulceration, or systemic illness.
On intraoral examination, there is generalized gingival enlargement involving both maxillary and mandibular arches. The gingiva appears firm, fibrotic, and pale pink, with bleeding on probing. There is plaque and calculus accumulation, but no signs of ulceration or pus discharge

1. What is the your diagnosis of the case based on clinical findings?
2. What are the common causes for this ?

INSTRUCTIONS TO AUTHORS

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      i. Each person listed as an author is expected to have participated in the study and is accountable for accuracy and integrity of the work.
      ii. He/She should have substantial contribution to:
         1. Conception and design
         2. Acquisition of data
         3. Analysis and interpretation of data
         4. Drafting the article or revising it critically for important intellectual content.
      iii. Those who provide technical support, writing assistance, or department chair who provided just general support should also be mentioned in acknowledgment.
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3. **SCOPE OF PUBLICATIONS:**
   a. Original Articles: Original articles should report original research of relevance to clinical medicine. These include randomized controlled trials, intervention studies, and studies of screening /diagnostic tests, outcome studies and cost-effectiveness analysis. The article should not exceed 4000 words in length (excluding title page, abstract, tables, figures, and references). The article words count for quantitative study should be in range 2000 - 2500 words (excluding references and abstract) with at least 18-25 references

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i. Title page: It should include the following information:
   1. Complete title as well as a short title of the article
   2. Name of author(s)
   3. Department(s)
   4. Institution(s) at which work was performed
   5. Author Affiliation
   6. Subject Specialty
   7. Corresponding authors personal e-mail address and postal address
   8. Short running title for header

ii. Abstract: It should contain a structured abstract of about 250 words and should include following sections
   1. Objective
   2. Study Design
   3. Place and duration of study
   4. Methodology
   5. Results
   6. Conclusion
   7. Keywords 3–10 (Medical Subject Headings – MeSH) in alphabetical order. If suitable MeSH terms are not yet available for recently introduced terms, present terms may be used.

iii. Text
   1. Introduction: This should summarize the purpose and the rationale for the study. It should neither review the subject extensively nor should it have data or conclusions of the study. At the end of the introduction, mention the rationale or scientific significance of the study.
   2. Methodology: This should include exact method or observation or experiment. If an apparatus is used, its manufacturer's name and address should be given in parentheses. If the method is established, give reference but if the method is new, give enough information so that another author is able to perform it. If a drug is used, its generic name, dose and route of administration must be given. Methodology section should contain (without headings) study design, place and duration of study, sample size, sampling technique, inclusion and exclusion criteria, data collection and analysis procedure. Statistical method must be mentioned and specify any general computer programme used. The information system used should be clearly mentioned.
   3. Results: Must be presented in the form of text, tables and illustrations. The contents of the tables should not be repeated in the text. Instead, a reference to the table number may be given. Long articles may need sub-headings within some sections (especially the results and discussion parts) to clarify their contents. Extra or supplementary materials and technical details can be placed in an appendix where it is accessible. It may be omitted from the printed version but may be published in the electronic version of the journal.
   4. Discussion: This should emphasize present findings & the variations or similarities with other work done in the field by other workers. Detailed data should not be repeated in the discussion again. Emphasize the new and important aspects of the study and the conclusions that follow from them. It must be mentioned whether the hypothesis mentioned in the article is true, false or no conclusions can be derived.
   5. Conclusion: Should be in line with the objectives and results and should be same as given in abstract.
   6. Limitations of the study (if any)
   7. Recommendations of the study (if any)
   8. Acknowledgements (if any)
   9. References: References must be numbered as superscript consecutively according to their appearance in the text. References appearing in a table or figure should be numbered sequentially with those in text. Twenty Percent References should be last 05 years and all references listed consecutively as superscript. References should be cited in the correct "Vancouver style".
   10. Tables: All tables should be numbered with numeric numerals. Headings should be placed above tables, left justified.
   11. Figures: All figures should be numbered with numeric numerals. Headings should be placed below figures, left justified.

b. Clinical Case Reports: Must be of academic & educational value and provide relevance of the disease being reported as unusual. It should have a non-structured abstract of about 100-150 words (case specific) with around 5-6 references and 3 keywords.

c. Letters to The Editor (LTE): It is usually a type of short communication that can be written on any topic that attracts the attention of the reader. There are different types of letters to the editor. If the purpose of the LTE is to comment on a published article, the first sentence of the LTE should include the name of the published article's first author along with the title of the published

article and then the comments. If the LTE is a reply to a previously submitted LTE, the first sentence should include the name of the letter's author and cite the letter as a reference. The previously published article should then be referenced as well either in the body of the text or at the end of the response to the LTE.

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e. Systematic Review Article: It should consist of a well-defined research question and should provide detailed review of a specific topic based on the existing literature. It should include the collection and analysis of data from all the relevant research in support of the research question being asked. The text should be 2500-3000 words. It should have a non- structured abstract with a minimum of three keywords.

f. Meta-Analysis: It should comprise a statistical analysis of combined results of numerous scientific studies addressing the same research questions. Meta-analysis is a quantitative and epidemiological study design that should critically analyze the results of previous scientific researches, mostly randomized controlled trials.

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h. Photo Essays: The journal accepts manuscripts for consideration as photo essays. These essays include the visual presentation of material where the prima, emphasis is on the images. These images can include colored images, angiograms, optical coherence tomography, histologic sections, x-rays, ultrasounds, and other studies. The images can be an outstanding presentation of classic findings, atypical findings or new findings. These are not case reports, but rather a visual presentation of material as a teaching tool. The images need to be of the highest quality. The accompanying manuscript should be limited to a total of 300 words. A maximum of 5 separate images and 5 references can be included. Please refer to the rest of the author's instructions for other requirements for manuscripts submitted to HMDJ.

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b. All pages must be numbered starting with the title page being page one.
c. Each figure and table must be submitted separately.
d. All manuscripts must be submitted by email to the address: editor.hmdj@hitec-ims.edu.pk or OJS (https://hmdj.org/).

5. VANCOUVER REFERENCING CONVENTIONS

a. In-text citation

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b. References list

i. References are presented in numerical order by the order in which they appear in the document.
ii. You should only include sources that you have referenced in your work.
iii. If you are asked to include a bibliography (in addition to, or in place of, a references list), you can include further items that were read that informed your research and thinking for the assignment, in addition to those that you directly referenced**.**

c. How to give a reference

i. Act of Parliament

1. Country. Title of Act and year. Chapter. Place of Publication: Publisher.
2. *Example:* Great Britain. Environment Act 1995. Chapter 25. London: The Stationery Office.

ii. Blog

1. Author(s) surname Initial(s). Title of blog entry. Date blog entry written. Title of blog [online]. Year. [Accessed date]. Available from: URL.
2. *Example:* Welle K. Impressions from the Stockholm World Water Week. 25 August. ODI blog: commentary from leading development experts [online]. 2006. [Accessed 9 July 2007]. Available from: http://blogs.odi.org.uk/blogs/main/archive/category/1020.aspx

iii. Book

1. Author surname Initial(s). Title: subtitle. Edition (if it is not the first edition). Place of publication: Publisher; Year of publication.
   a. *Example:* Cooke A. A guide to finding quality information on the Internet: selection and evaluation strategies. 2nd ed. London: Library Association Publishing; 2001.
2. Two to six authors: First author surname Initial(s), second author surname Initial(s),

third author surname Initials. Title: subtitle. Edition (if it is not the first edition). Place of publication: Publisher; Year of publication.

a. Example: Feldman RS, Meyer JS, Quenzer LF. The American Psychiatric Press textbook of psychopharmacology. 2nd ed. Washington DC: American Psychiatric Association; 1998.

3. Seven or more authors/editors: If there are 7 or more authors/editors, only the first 6 are listed followed by et al. First author surname Initial(s), second author surname Initial(s), third author surname Initial(s), fourth author surname Initial(s), fifth author surname Initial(s), sixth author surname Initial(s), et al., editors. Title: subtitle. Edition (if it is not the first edition). Place of publication: Publisher; Year of publication.
   a. Example: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, et al., editors. Harrison's principles of internal medicine. 14th ed. New York: McGraw Hill; 1998.
4. Book with organisation as author:
   a. SCONUL Advisory Committee on Information Literacy. Learning outcomes and information literacy. London: SCONUL; 2004.
5. Edited book:
   a. Editor(s) surname Initial(s), editor(s). Title: subtitle. Edition (if it is not the first edition). Place of publication: Publisher; Year of publication.
   b. Ennis F, editor. Infrastructure provision and the negotiating process. Aldershot: Ashgate; 2003.
   c. Example: Editors should have editor or editors after their name or list of names. If there are no authors or editors given, the title should be listed first, followed by place of publication.
6. Book chapter from an edited book
   a. Author(s) surname Initial(s). Title of chapter: subtitle. In: Author(s) surname Initial(s). Title of book. Place of publication: Publisher; Year of publication. p. page numbers.
      i. Example: Haefner H. Negative symptoms and the assessment of neurocognitive treatment response. In: Keefe RSE, McEvoy JP, editors. Negative symptom and cognitive deficit treatment response in schizophrenia. Washington DC: American Psychiatric Association; 2004. p. 85-110.
   b. When the author's name is the same for the chapter as for the book it does not need to be repeated.
   c. Example: Greenhalgh T. Checklists for finding, appraising, and implementing evidence. In: How to read a paper: the basics of evidence based medicine. London: BMJ Publishing Group; 2000. p. 177-9.

iv. Conference proceedings

1. Individual conference paper
   a. Author(s) Initial(s). Title of contribution. In: Editor(s) surname Initial(s). editor(s). Title of conference proceedings, date, place of conference. Place of publication: publisher; Year. p. page numbers.
      i. Example: Nelmes G. Container port automation. In : Corke P., Sukkarieh S. editors. Field and service robotics: results of the 5th international conference, 29-31 July 2005, Port Douglas. Berlin: Springer; 2006. p. 3-8.
   b. If conference proceedings are published in a journal, the article / contribution should be cited as for a journal article.
   c. If the proceedings have been published as chapters in a book, treat the entire proceedings as a book, and individual presentations as a book chapter. Add details of the conference to the book title.
2. Conference proceedings as a whole
   a. Editor(s) surname Initial(s). editor(s). Title of conference proceedings, date, place of conference. Place of publication: publisher; Year.
      i. Example: Corke P., Sukkarieh S. editors. Field and service robotics: results of the 5th international conference, 29-31 July 2005, Port Douglas. Berlin: Springer; 2006

v. DVD

1. Title. [DVD]. Place of production: Production company; year.
   a. Example: Acland's DVD atlas of human anatomy: the lower extremity. [DVD]. Philadelphia: Lippincott Williams & Wilkins; 2004.

vi. E-book

1. online
   a. Author(s) surname Initial(s). Title: subtitle [online]. Edition (if not the first edition). Place of publication: Publisher; Year of publication [Accessed Date]. Available from: URL of database / location in which the book is held
      i. Example: Greenhalgh T. How to read a paper: the basics of evidence based medicine [online]. London: BMJ Publishing Group; 2000 [Accessed 8 September 2008]. Available from: http://www.netlibrary.com/Ac-

cessProduct.aspx?ProductId=66703

2. e-book reader format, e.g. Kindle
    a. Author(s)/Editor(s) surname Initials(s). Title: subtitle. Edition (if not the first edition). [Name of e-book reader]. Place of publication: Publisher; Year of publication.
        i. *Example:* Llewelyn H, Ang HA, Lewis KE, Al-Abdullah A. Oxford handbook of clinical diagnosis. 2nd ed. [Kindle DX e-book]. Oxford: OUP; 2009.

vii. Film

1. Title of film. [film]. Directed by: Full name of director. Place of production: Production company; year.
    a. *Example:* An inconvenient truth. [film]. Directed by: Davis Guggenheim. USA: Paramount; 2006.
2. If the film is a video recording (on DVD or VHS) use the same format but change [film] to the relevant media. This is because video recording may contain extra footage not shown in the film.

viii. Journal article

1. Journal article (Print)
    a. Author(s) surname Initial(s). Title of article. Abbreviated title of journal. Year of publication;volume number(issue number):page numbers.
        i. *Example:* Meric F, Bernstam EV, Mirza NQ, Hunt KK, Ames FC, Ross M I, et al. Breast cancer on the world wide web: cross sectional survey of quality of information and popularity of websites. BMJ. 2002;324(7337):577-81.
2. Journal article (Electronic)
    a. Author(s) surname Initial(s). Title of article. Abbreviated title of journal [online]. Year of publication;volume number(issue number):page numbers. [Accessed date]. Available from: URL
        i. *Example:* Ross CTF. A conceptual design of an underwater vehicle. Ocean engineering [online]. 2006;33(16):2087-2104. [Accessed 6 July 2007]. Available from: http://www.sciencedirect.com/
    b. When citing online journal articles, it is now widely preferred to include a DOI (Direct Object Identifier) where available rather than a URL.
        i. *Example:* De Pinto M, Jelacic J, Edwards WT. Very-low-dose ketamine for the management of pain and sedation in the ICU. Acute Pain [online]. 2008;10(2):100. [Accessed 8 September 2008]. Available from:<-doi:10.1016/j.acpain.2008.05.023>

ix. Newspaper article

1. Author(s) surname Initial(s). Title of article: subtitle of article. Newspaper title (in full) Year Month and date of publication; section name (if applicable):page numbers of contribution.
    a. *Example:* Rowbottom M. The Big Question: how prevalent is the use of drugs in sport, and can it be defeated? The Independent 2006 Aug 1;Sect. Sport:5

x. Radio broadcast

1. Title of programme/Series title, Episode number, Episode title. Transmitting organisation/channel. Date and year, Time of transmission.
2. *Example:* Desert island discs, Lily Allen. BBC Radio 4. 29 June 2014, 11:15.

xi. Television broadcast

1. Title of programme/Series title, Episode number, Episode title. Transmitting organisation/channel. Date and year, Time of transmission.
    a. *Example:* Yes, Prime Minister, Episode 1, The Ministerial Broadcast. BBC2. 16 January 1986, 20:30.
    b. *Example:* News at ten. ITV. 27 January 2001. 22:00.

xii. Thesis or dissertation

1. Author's surname Initial(s). Title: subtitle. Award level of thesis, Awarding institution; Year of publication.
    a. *Example:* Deb S. Psychopathology of adults with a mental handicap and epilepsy. MA thesis, University of Leicester; 1991.
    b. *Example:* Croser C. Biochemical restriction of root extension under mechanical impedance. PhD thesis, University of Birmingham; 1997.

xiii. Twitter(X)

1. Surname(s), Initial(s) (or organisation). Full text of tweet. [Twitter]. Date and year tweet posted [Date accessed]. Available from: URL
2. *Example:* Cruciform Library. MedTech Week 2014 at UCL Institute of Biomedical Engineering (IBME)16-20 June via @UCL_IBME http://bit.ly/1pbWe53 pic.twitter.com/pzXx3P4DlP [Twitter]. 9 June 2014 [Accessed 2 July 2014]. Available from: https://twitter.com/ucl_crucitwit

xiv. Website or webpage

1. Author(s)/Editor(s) surname Initial(s). Title. [online]. Publisher: place of publication; Year [Accessed date]. Available from: URL
    a. *Example:* SukYin A. Catechol-O-Methyltransferase (COMT) gene and breast cancer. [online]. Human Genome Epidemiology Network, National Office

of Public Health Genomics, Centers for Disease Control and Prevention: Atlanta GA; 2002 Jun [Accessed 8 September 2008]. Available from: http://www.cdc.gov/genomics/hugenet/factsheets/FS_COMT.htm

2. Year can include month if preferred.
3. If a specific author cannot be found, attribute to the organisation or corporation.
   a. *Example:* Overseas Development Institute, Humanitarian Policy Group. Welcome to HPG. [online]. ODI: London; 2007 [Accessed 9 July 2007]. Available from: http://odi.org.uk/hpg/index.html

xv. Wiki

1. Wiki name. Title of article. [online]. Year [Date accessed]. Available from: URL
   a. *Example:* Wikipedia. Jeremy Bentham. [online]. 2014 [Accessed 2 July 2014]. Available from: http://en.wikipedia.org/wiki/Jeremy_bentham

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DIAGNOSTIC CHALLENGE Answers

Case 1

1. **Diagnosis:**
   Kienbock disease.

2. **Investigations**:
   MRI to check for avascular necrosis.

3. **Treatment:**
   Partial wrist fusion.

Discussion:

Kienbock disease is avascular necrosis of the lunate whose definitive cause is not known. Peculiar blood supply of the lunate is mostly held responsible which when obliterated , leads to progressive death and destruction of the bone (Table 1).

Most commonly males, between 20 and 40 years of age are affected. Some of the recognized factors responsible are negative ulnar variance (too short of ulna at the distal radioulnar joint, decreased radial inclination and repetitive trauma). Symptoms are usually gradual and progressive in nature. Treatment is with pain killers in the early stages. Later on the disease progression and stage determines the options available.

Treatment depends upon the stage of the disease. Only in Stage I conservative management is possible. Later on or after failure of conservative management, the patient should be referred to an orthopedic / hand surgeon for the best outcome.

Table1: Lichtman Classification of Kienbock disease.

Stage	Description	Treatment
Stage I	No visible X-ray changes Only changes on MRI	Immobilization NSAIDS
Stage II	Sclerosis of lunate	Joint leveling procedures
Stage IIIA	Lunate collapse No scaphoid rotation	Same as stage II
Stage IIIB	Lunate collapse Fixed Scaphoid rotation	Proximal row carpectomy STT Fusion SC fusion
Stage IV	Degenerated adjacent intercarpal joints	Wrist fusion Proximal row carpectomy Limited intercarpal fusion

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Answers

Case 2

Diagnosis

Drug Induced Gingival Hyperplasia

Drugs causing Gingival Hyperplasia

- Anticonvulsants
  Phenytoin
  Carbamezipine
- Calcium Channel Blockers
  Amlodipine
  Nifedipine
  Verapamil
- Immunosupressants
  Cyclosporin

Discussion

Drug-Induced Gingival Hyperplasia (DIGH) is a pathological enlargement of the gingiva commonly associated with long-term use of specific systemic medications, including anticonvulsants like Phenytoin, immunosuppressants such as Cyclosporine, and Calcium channel blockers like Nifedipine and Amlodipine. Patients typically present with a painless, firm and fibrotic gingival overgrowth that begins at the interdental papillae and may gradually extend to cover the crowns of teeth, most often in the anterior maxillary and mandibular regions. In cases with poor oral hygiene, the gingiva may appear erythematous, inflamed, and prone to bleeding.

The degree of enlargement varies with the type and dosage of the drug, duration of therapy, oral hygiene status, genetic predisposition, and presence of local irritants. The pathophysiology involves increased fibroblast activity leading to excess collagen deposition, compounded by local inflammatory stimuli from plaque.

Diagnosis is primarily clinical and supported by a detailed medical and drug history. Histopathological features include epithelial hyperplasia, elongated rete ridges, and dense collagenous connective tissue with minimal inflammation unless secondarily infected. Management focuses on improving oral hygiene, regular professional cleanings, and if possible, substituting or adjusting the causative medication in coordination with the patient's physician. In severe or unresponsive cases, surgical intervention such as gingivectomy may be required to restore gingival contour and function.
With good plaque control and appropriate treatment, the prognosis is generally favorable, though recurrence is common if risk factors persist, underscoring the importance of long-term follow-up and preventive care.

Our Patient

Our Patient was a severe case of DIGH so a surgical intervention was planned. Gingivectomy was performed under local anesthesia to surgically remove the excess tissue and reestablish a normal gingival contour. In coordination with the patients physician, the causative drug was substituted with an appropriate alternative.
The patient was placed on strict maintenance program with regular follow up visits. At follow up appointments patient demonstrated excellent healing and non recurrence of gingival enlargement.
This successful outcome highlights the importance of combined medical and surgical management ,patient compliance and interprofessional collaboration in treating DGIH.

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