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## The Relationship between Aesthetics and Self-Esteem

Sannia Perwaiz Iqbal

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The aesthetic industry encompasses many products and services dedicated to beauty, cosmetics, and personal appearance. As the demand for minimally invasive cosmetic procedures, such as Botox, fillers, peels, and lasers, rapidly increases, Aesthetic Medicine is gaining recognition as a separate specialty within Pakistan and globally.<sup>1</sup> The prevalence of skin disorders worldwide has increased, leading to many patients seeking skin therapy that utilizes light, ultrasound, and laser-based solutions.

The top five minimally invasive cosmetic procedures, namely botulinum toxin type A, soft tissue fillers, laser skin resurfacing, chemical peels, and intense pulsed light, have recently gained significant popularity. This rise in demand can be attributed to various factors, including reduced treatment risks, cost-effectiveness, and faster results.<sup>2</sup> Technological advancements within the aesthetic industry consistently provide new treatment opportunities and improve the approaches used to address existing indications. Additionally, there is a notable surge in acceptance and popularity of a wide range of non-invasive corrective treatments. Patients increasingly seek these procedures to enhance their physical appearance and improve their mental and emotional well-being.<sup>3</sup>

In a survey of Dermatology residents in Pakistan conducted by Asher et al., 65% of participants expressed interest in pursuing Dermatologic Surgery as a subspecialty after completing their fellowship in Dermatology.<sup>4</sup> Academies offering costly certificate courses in aesthetics have also seen significant growth, while aesthetic practices are predominantly conducted in private setups with minimal regulations. Non-physician operators and allied healthcare professionals have entered the field of aesthetic medicine in large numbers, resulting in a lack of regulation and oversight. After undergoing training, many administer medical procedures to patients without the fundamental knowledge and training required.<sup>5</sup> This editorial aims to provide insight on how aesthetics impacts self-esteem of

people seeking these services.

Aesthetic treatments using injectables have shown substantial improvements in patient-reported psychological and social well-being, along with a decrease in distress related to their appearance. A study examining the use of autologous fat and platelet-rich plasma for facial filling demonstrated that the treatment improved the social and psychological functioning of the patients involved.<sup>6</sup> Many aesthetic clinics have adapted their approach to meet the evolving needs of patients who seek to enhance their appearance and optimize their overall well-being. As a result, aesthetic clinics have transformed into all-in-one wellness centers, offering a comprehensive range of solutions to address patients' concerns. For example, besides providing body contouring treatments, these centers offer opportunities for patients to consult with experts such as dietitians and fitness professionals.<sup>7</sup> This shift reflects a recognition of the interconnectedness of various aspects of health and wellness in achieving the desired look and feeling of individuals.

However, while aesthetic medicine aims to enhance individuals' appearance and build self-confidence, it can unintentionally decrease self-esteem, as indicated by evidence.<sup>8</sup> Unrealistic beauty standards promoted by the media can further erode self-esteem as individuals strive to meet unattainable ideals. While it is challenging to establish a direct causal relationship between unrealistic beauty standards and the increase in the practice of aesthetic medicine, there is evidence to suggest a correlation between the two. Research has shown that societal pressures and cultural norms related to beauty standards can significantly impact individuals' body image dissatisfaction and desire for cosmetic procedures. A study by Hawkins et al, found that exposure to thin-ideal media images was associated with increased body dissatisfaction and a greater desire for cosmetic surgery among women.<sup>9</sup> A study published in JAMA Facial Plastic Surgery highlighted that social media platforms like Instagram, which heavily emphasize appearance through filtered and edited images, have contributed to an increase in facial cosmetic procedures. The study found that patients often requested specific features seen on social media influencers or celebrities.<sup>10</sup>

Body dysmorphia can develop when individuals obsessively focus on perceived flaws, leading to distress and a decline in self-esteem. Social comparison also plays a significant

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role, as individuals compare themselves to others and feel self-doubt and dissatisfaction when they don't meet societal beauty standards.<sup>9</sup> Additionally, the high cost of beauty products, treatments, and surgeries in the aesthetic market can create feelings of inadequacy for those who cannot afford them, impacting their self-esteem. Research shows that the most common surgical cosmetic procedures performed on individuals aged 18 or younger include nose reshaping, breast lifts, breast augmentation, liposuction, and tummy tucks. However, the safety and long-term risks of these procedures to adolescents have not been extensively studied. This is particularly concerning since adolescence is a crucial mental and physical development stage.<sup>10</sup>

In aesthetic surgery clinics, there is a notable occurrence of patients seeking a range of cosmetic procedures, often requesting treatments that may appear disproportionate to their overall needs. Many of these patients may have underlying psychiatric disorders that have been either unrecognized or untreated.<sup>6</sup>

There has been a significant increase in individuals seeking aesthetic treatments to resemble their idols. However, it is important to acknowledge that many images that inspire these patients have been heavily altered, creating an unrealistic perception of what can be realistically achieved through aesthetic interventions. Consequently, these patients are likely to be dissatisfied with the outcomes, and it would be prudent for practitioners to consider carefully whether to proceed with treatment in such cases. Following the ethical principles of non-maleficence and beneficence, refusing treatment to patients with unrealistic expectations may be necessary. This is because the potential risks of the treatment may outweigh the potential benefits in such individuals.<sup>11</sup>

On the other hand, aesthetic interventions can yield clinically significant psychological benefits in carefully chosen patients.

Most individuals who seek aesthetic consultations are typically in good physical health but often report a decline in self-confidence resulting from the deterioration of their facial appearance.<sup>12</sup> To maximize the benefits of aesthetic procedures and minimize the associated risks, it is imperative to prioritize optimal patient selection and uphold a high level of technical expertise. The long-term effects of aesthetic procedures on self-esteem, quality of life, self-confidence, and interpersonal relationships have produced conflicting results in studies. While individuals generally express greater satisfaction with the specific body part they had the procedure on, the overall impact on these aspects remains uncertain and inconclusive.<sup>10</sup> Besides positive outcomes, research has identified a correlation between plastic surgery and unfavorable post-surgical outcomes for certain patients. This is particularly evident among individuals with a personality disorder, those who believed that the surgery would salvage a relationship, and those who held unrealistic expectations regarding the procedure.<sup>9</sup> Certain studies have gone to the extent of establishing a connection between

dissatisfaction with cosmetic surgery procedures and suicidal tendencies.<sup>4</sup>

Several studies indicated a concerning association between breast implants and suicide rates. For example, a study revealed that women with breast implants were four times more likely to commit suicide compared to other plastic surgery patients in the same age range. Similarly, three other studies reported suicide rates two to three times higher in women with breast implants. However, it is important to note that these studies could not establish a direct causal relationship. Some researchers speculate that factors such as certain personality traits or unrealistic expectations among specific individuals who undergo the surgery may have contributed to the heightened risk of suicide.<sup>7</sup>

In the past, mental health experts believed that individuals seeking cosmetic surgery had underlying psychiatric issues.

However, numerous subsequent studies have revealed that there are minimal pathological distinctions between those who choose to undergo cosmetic surgery and those who do not.<sup>11</sup> The primary motivation driving most individuals to undergo cosmetic surgery is dissatisfaction with their body image.

BDD, a condition characterized by an obsessive preoccupation with a specific aspect of one's appearance, involves repetitive behaviors that disrupt daily functioning.

Studies indicate that around 7 to 12 percent of individuals seeking plastic surgery exhibit symptoms of BDD. Furthermore, most BDD patients who undergo cosmetic procedures do not find relief from their BDD symptoms and often pursue multiple surgeries targeting the same or different areas of their body. Cosmetic rhinoplasty is frequently undergone by individuals with Body Dysmorphic Disorder (BDD) due to their common preoccupations with their nose.<sup>12</sup> According to some studies, patients who are dissatisfied with the outcomes of their cosmetic surgery may seek further procedures and may also experience depression, difficulties in adjusting to the changes, social isolation, problems within their family relationships, engaging in self-destructive behaviors, and harboring feelings of anger towards the surgeon and their staff.<sup>5</sup>

Research shows that aesthetic treatments rarely address the core symptoms of BDD and can sometimes make the condition worse. Instead, evidence-based treatments such as serotonin reuptake inhibitors (SRIs) and cognitive-behavioral therapy (CBT) are recommended to help reduce BDD symptoms. In some cases, a combination of medication and treatment may be beneficial.<sup>12</sup> There is a pressing need for comprehensive, large-scale prospective studies that involve representative samples of patients and employ established research tools. While many individuals experience positive psychosocial adjustments after cosmetic procedures, the field must acknowledge that some individuals may not fare as well. It is important to implement screening measures





to identify such individuals. Specifically, exploring the long-term impact of cosmetic surgery on patients' relationships, self-esteem, and quality of life presents numerous research prospects for psychologists. It is important to recognize that the relationship between the aesthetic market and self-esteem is complex, and efforts should be made to promote diverse beauty standards and foster self-acceptance.

**Authors Contribution:**

**Sannia Perwaiz Iqbal:** Conception of design, writing, proof reading

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# Comparison of SOFA and qSOFA Scores in Predicting Infection and Mortality in HDU and ICU Patients at a Tertiary Care Center

Sarah Khan, Jawad Khan, Shaista Khan

## ABSTRACT

**Objective:** The objective of this study is to compare the sensitivity and specificity of the SOFA (Sequential Organ Failure Assessment) and qSOFA (Quick Sequential Organ Failure Assessment) in predicting infection and mortality in ICU (intensive care unit) and HDU (high dependency unit) patients admitted at a tertiary care center of excellence.

**Study Design and Setting:** Prospective observational non-interventional study. Anesthesia Department of Combined Military Hospital, Rawalpindi from Jan 2023-Jun 2023.

**Methodology:** Patients in both ICU (n=220) and HDU (n=220) setups admitted with a suspicion of sepsis were evaluated for onset of sepsis and mortality. Primary variables studied were the sensitivity and specificity for both scores for predicting infection and mortality in the ICU and HDU. Positive predictive value for both scores were calculated as secondary variable.

**Results:** While assessing the primary variables, the sensitivity of SOFA for predicting infection in the ICU was 25.6% with a specificity of 85.3% versus a sensitivity of 76.8% and specificity of 59.0% for qSOFA. In the HDU, It showed sensitivity and specificity with PPV for SOFA being 64.7%, 95.1% and 64.7% versus 79.3%, 85.3% and 46.9% for qSOFA respectively. While assessing for mortality, SOFA values in the ICU for sensitivity, specificity and PPV were 81.8%, 93.5% and 69.2% versus 88.8%, 58.3% and 90.9% for qSOFA respectively.

**Conclusion:** We conclude that qSOFA to be good predictor of mortality in the HDU and SOFA with good specificity for infection and mortality in the ICU.

**Key Words:** HDU, ICU, Infection, mortality, SOFA, qSOFA

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## INTRODUCTION:

Sepsis and sepsis-related complications remain the greatest cause of hospital admissions in the intensive care unit.<sup>1,2</sup> These patients present a challenge to the multi-disciplinary team since most of these patients present with associated co-morbidities and sepsis related derangements causing electrolyte abnormalities, multi organ dysfunction and severe disruption to normal body homeostasis.<sup>3</sup> With advancements in the treatment strategies, the tier of care has also expanded especially in centers of excellence where escalation and de-escalation of therapy requires shifting of patients to and from the intensive care setups.<sup>4</sup> The major bulk of patients

coming to the intensive care setups are either shifted post-operatively requiring ventilator care before extubation or are stepped up from non-critical care setups citing more cautious care to prevent morbidity and mortality.<sup>5</sup>

The mainstay of tiered care is the development of scoring systems to standardize and early detection of cases requiring intensive care or non-intensive care setups.<sup>6</sup> Even though various scoring systems have been developed to diagnose sepsis and its sequelae effectively and efficiently, a single best scoring system with sensitivity and specificity is still lacking.<sup>7</sup> The sepsis-3 task force proposed the Sequential Organ Failure Assessment Score (SOFA) as mainstay to evaluate and diagnose sepsis in the ICU setup in 2016.<sup>8</sup> The score has been a point of interest in ICU setups globally. Since the score requires multiple patient characteristics and metabolic panel details, its use in diagnosing or suspecting sepsis in non-ICU setups is not practically feasible due to lack of advanced test and no routine to carry out critical investigations in the wards. Seymour et al developed the qSOFA including only three basic parameters of respiratory rate, systolic blood pressure and Glasgow Coma Scale to evaluate patients requiring less expertise and investigations.<sup>9</sup> Both these tests represent two points of care, one being the critical care and second being non-critical care setups.

HDU (High Dependency Unit) represent another paradigm

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in point of care, which falls between general ward care and intensive care setups which receives patients from the ICU no longer requiring ventilator care or support and from the wards with suspicion that the patient may end in complications if care is not escalated.<sup>10</sup> It has been proven that HDUs in the tier of care is associated with a significantly reduced hospital mortality in ICU patients, underlining the impact of an HDU as a bridge between the ICU and the regular ward when patient care is concerned. Most of these patients require risk stratification to evaluate for sepsis as they may complicate. The question arises whether to use the SOFA or qSOFA in these patients in the intermediate level of care.<sup>11</sup>

Both the SOFA and qSOFA have been scarcely used to evaluate for infection and mortality in HDU setups. The aim of our study is to compare the sensitivity and specificity of the SOFA (Sequential Organ Failure Assessment) and qSOFA (Quick Sequential Organ Failure Assessment) in predicting infection and mortality in ICU (intensive care unit) and HDU (high dependency unit) patients admitted at a tertiary care center of excellence.

#### **METHODOLOGY:**

This prospective observational non-interventional study was carried out at the Department of Anesthesiology, Combined Military Hospital from Jan 2023-Jun 2023 after approval from the ethical review board vide letter no: BIH-RWP-0010. A total of 440 patients (minimum sample size 163 as per WHO calculator) were included in the study (220 from ICU and 220 from HDU) as per the inclusion criteria furnished keeping the confidence interval at 95%, margin of error at 5% with the global population prevalence of admissions with sepsis requiring ICU/HDU care at 88%.<sup>12</sup> The method of sampling was non-probability consecutive by lottery method.

Inclusion criteria included patients both from the ICU and HDU setups admitted directly or transferred either from the ICU or ward with suspected episodes of infection within 72 hours of admission to the care setting while on broad spectrum antibiotics.

Exclusion criteria included patients with no history or metabolic suspicion of infection, patients with a resolving PCT (procalcitonin) titer, patients where SOFA or qSOFA could not be assessed (lack of investigations or unable to assess GCS) and unwilling to be included in the study.

The study method included all patients as per the inclusion criteria furnished. Patients in both ICU and HDU setups admitted with a suspicion of sepsis were evaluated with episodes of infection defined as the occurrence during the initial 72 hours after starting broad spectrum antibiotics according to institutional protocol. Antibiotics not falling in the category of broad spectrum were not used (ampicillin, colistin, erythromycin, azithromycin, metronidazole etc.). SOFA and qSOFA scores were evaluated and endorsed by

the attending critical care resident after evaluation by a critical care consultant in the ICU thrice a day and by a medicine or anesthesia resident on duty in the HDU by the attending consultant respectively. Median values of both scores were calculated daily and endorsed. For the SOFA score, an increase in two score points from the previous day or a total score of >11 was considered as positive and endorsed. For the qSOFA evaluation, presence of two or more of the parameters was considered positive and endorsed.

Primary variables studied were the sensitivity and specificity for both scores for predicting infection and mortality in the ICU and HDU. Positive predictive value for both scores were calculated as secondary variable. Demographic data were statistically described in terms of mean and SD, frequencies, and percentages when appropriate. Mean values were compared using the independent samples t-test while non-parametric data was compared using the Mann Whitney-U test. A p value of 0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.0.

#### **RESULTS:**

A total of 440 patients were included in the study protocol as per the inclusion criteria furnished with 220 patients each from HDU and ICU setups. Mean age of patients was 56.704.30 years in the ICU group versus 56.694.25 years in the HDU group ( $p=0.982$ ). Mean weight was 65.475.76 kg in the ICU versus 65.125.48 kg in the HDU group (0.514). Mean duration of stay was 8.211.87 days in the ICU versus 5.151.16 days in the HDU group (Table-1).

Frequency of variables studied showed that need for invasive ventilation was required in 84 (38.2%) patients in the ICU versus 05 (2.3%) patients in the HDU group ( $p<0.001$ ). Need for inotropic support was needed in 68 (30.9%) patients in the ICU versus 12 (5.5%) patients in the HDU group ( $p<0.001$ ). Frequency of new onset infection was in 57 (25.9%) patients in the ICU versus 19 (8.6%) patients in the HDU group ( $p<0.001$ ). Overall, 15 (6.8%) patients died in the ICU versus 04 (1.8%) in the HDU group ( $p=0.010$ ) (Table-1).

While assessing the primary variables, the sensitivity of SOFA for predicting infection in the ICU was 25.6% with a specificity of 85.3% versus a sensitivity of 76.8% and specificity of 59.0% for qSOFA. Positive predictive value (PPV) for SOFA was 25.6% versus 89.7% for qSOFA for infection. The same variables for infection in the HDU showed sensitivity and specificity with PPV for SOFA being 64.7%, 95.1% and 64.7% versus 79.3%, 85.3% and 46.9% for qSOFA respectively (Table-2).

While assessing for mortality, SOFA values in the ICU for sensitivity, specificity and PPV were 81.8%, 93.5% and 69.2% versus 88.8%, 58.3% and 90.9% for qSOFA respectively. Same assessment done in the HDU for both scores for mortality showed a sensitivity, specificity and

PPV of 56.0%, 90.3% and 42.4% for SOFA versus 93.4%, 75.0% and 93.9% for qSOFA respectively (Table-2).

Table-1 Demographic Variables (n=440)

Variable	ICU (n=220)	HDU (n=220)	p value
Mean age (years)	56.704.30	56.694.25	0.982
Mean weight (kg)	65.475.76	65.125.48	0.514
Mean stay (days)	8.211.87	5.151.16	<0.001
Need for invasive ventilation	84 (38.2%)	05 (2.3%)	<0.001
Need for inotropic support	68 (30.9%)	12 (5.5%)	<0.001
Frequency of infection	57 (25.9%)	19 (8.6%)	<0.001
Frequency of mortality	15 (6.8%)	04 (1.8%)	0.010

Table-2 Sensitivity, Specificity, Positive and Negative Predictive Values for SOFA and qSOFA in ICU and HDU for Infection (n=440)

Variables	ICU (n=220)		HDU (n=220)	
	SOFA	qSOFA	SOFA	qSOFA
Sensitivity	25.6%	76.8%	64.7%	79.3%
Specificity	85.3%	59.0%	95.1%	85.3%
Positive predictive value	25.6%	89.7%	64.7%	46.9%
Negative predictive value	82.5%	35.4%	95.1%	96.2%

Table-3 Sensitivity, Specificity, Positive and Negative Predictive Values for SOFA and qSOFA in ICU and HDU for Mortality (n=440)

Variables	ICU (n=220)		HDU (n=220)	
	SOFA	qSOFA	SOFA	qSOFA
Sensitivity	81.8%	88.8%	56.0%	93.4%
Specificity	93.5%	58.3%	90.3%	75.0%
Positive predictive value	69.2%	90.9%	42.4%	93.9%
Negative predictive value	93.5%	58.3%	94.1%	73.2%

**DISCUSSION:**

The study was carried out at our institute to better assess the outcome of the SOFA and qSOFA scoring system and whether they can be reliably applied to identify sepsis and mortality in patients admitted to two different treatment setups. While none of the tests proved to be ideal in diagnosing both sepsis and mortality in the ICU and HDU setups; the sensitivity, specificity and positive predictive values were variable for both scores concluding that one score may be better suited to one variable for a given setup. To our knowledge before starting our study, the prospective assessment for both the scoring system has been scarce and majority of the studies done have been retrospective with data pulled out of archives and databases. We present this study as the first one in our institute as well employing a prospective approach to provide more appropriate results.

The SOFA system has been employed by the Sepsis Task Force as both a predictor for sepsis and mortality. The qSOFA on the other hand was originally described by Seymour et al to predict for mortality and not for the

identification of infection or sepsis but our study employed it for both and found results which may prove its use as a tool for diagnosing sepsis in the appropriate setup.<sup>13</sup> We concluded from our study that sensitivity and specificity of the qSOFA score in predicting sepsis in the ICU was not significant and was marginally better for specificity in the HDU. It was in line with studies carried out by X Qiu et al<sup>14</sup> and AK Toker et al<sup>15</sup> They also concluded that the qSOFA score was not effective in the ICU for sensitivity and specificity. However, it has a better predictive value in the ICU for sepsis than the HDU. This was also demonstrated in results of study carried out by H Yu et al.<sup>16</sup> Except for sepsis in the ICU for qSOFA, the predictive power was poor for diagnosing sepsis in the HDU. The SOFA score showed similar results for predictive power for sepsis both in the HDU and ICU, however, it showed good specificity for sepsis both in the HDU and ICU. This was in line with results carried out by BR Adegbite et al.<sup>17</sup> When talking about predicting mortality in the HDU and ICU for both scores, SOFA score was superior to predicting mortality both in the HDU and ICU with good specificity. The specificity of qSOFA was not significant but had a good predictive value for mortality both in the HDU and ICU. Our results were also confirmed by studies carried out by S Liu et al<sup>18</sup> and GL Nugraha et al.<sup>19</sup>

Our predictive values were slightly better with better specificity than some studies done by Koch et al.<sup>11</sup> The reason is attributed to a majority of patients being admitted with medical conditions and less with surgical complications in our study group. This may have resulted in a slightly better predictive power and sensitivity and specificity for both scores. It is also pertinent to mention that since most post-surgical patients present after the operation room with surgical stress related pain, tachycardia and hypertension and a systemic inflammatory response to surgery rather than infection, it becomes challenging in these patients to accurately label sepsis or immune response causing variation in results. We aimed to improve this by carrying out procalcitonin levels to check for titer rise or fall to better identify sepsis from immune response.<sup>20</sup>

**CONCLUSION:**

We conclude that qSOFA to be good predictor of mortality in the HDU and ICU and SOFA with good specificity for infection and mortality in the ICU.

**Authors Contributions:**

- | Sarah Khan: Conception, Design, Acquisition, analysis and interpretation of data, drafting of article
- | Jawad Khan: Conception, Design, Acquisition, analysis and interpretation of data, drafting of article
- | Shaista Khan: Conception, Design, Acquisition, analysis and interpretation of data, drafting of article

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# Experiences and Challenges faced by Orthodontists while Treating Epileptic Orthodontic Patients: A Qualitative Study

Sadia Naureen, Huma Ghazanfar Kiani

## ABSTRACT

**Objective:** This study aimed to explore the experiences and challenges faced by orthodontists in treating patients with epilepsy.

**Study Design and Setting:** This was a qualitative study conducted in the Orthodontic Department at Rawal Institute of Health Sciences, Islamabad.

**Methodology:** The study period was almost three months from 4<sup>th</sup> August 2023 to 30<sup>th</sup> October 2023. Purposive sampling was done and 11 orthodontists with a minimum of 10 years of clinical experience, who had treated at least one patient with epilepsy in the past 5 years, were selected for an interview. Interviews were conducted in person or virtually, and a topic guide was used. Verbatim transcripts were analyzed using framework methodology, with triangulation techniques to minimize bias.

**Results:** All orthodontists were aware of their patients' epilepsy diagnoses, but none knew the specific type. The implementation of the orthodontic treatment strategy was less than optimal. Ceramic brackets were not used in any case. Limited single-arch treatments were preferred by orthodontists in some cases. Seizure and medicine intake history were not taken at every appointment. The emergency anti-epileptic drug was not available in the dental office. The primary challenges reported were patient motivation, poor oral hygiene, gingival hyperplasia, and bracket breakage.

**Conclusion:** Orthodontic treatment of epileptic patients is highly challenging. Modified treatment strategies should be adopted to ensure optimal care for such patients.

**Keywords:** Epilepsy, Gingival hyperplasia, Orthodontist, Seizure.

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## INTRODUCTION:

Epilepsy is a severe neurological condition impacting over 70 million individuals worldwide. Its occurrence follows a bimodal pattern, with the highest risk in infants and older age groups. It is a complex disease with many risk factors and a strong genetic predisposition.<sup>1</sup> According to a recent study by Todaro and Giuliano, the prevalence of epilepsy increases very sharply between 20-29 years of age without any gender predisposition. They also claimed that epileptic patients can be screened for epidemiological research with the help of video consultation.<sup>2</sup> Recent advancements, such as precision medicine coupled with medication, surgery, and the ketogenic diet, have shown promise in managing the disease. The ideal precision treatment would cure the

disease and its comorbidities in the context of individualized genetic factors, of each patient.<sup>3</sup> That is why a significant portion of individuals with epilepsy now seek dental treatment. A comprehensive survey conducted by Schöpfer and Ludolph on 82 epileptic patients revealed that 84% of them regularly visited a dentist (once or twice a year), 79% disclosed their epilepsy to the dentist, 6% faced refusal of treatment due to their epilepsy, and 10% had experienced a seizure while at a dental office.<sup>4</sup> Epilepsy treatment gap according to the latest systematic review was reported to be 5.6% in Norway to 100% in parts of Tibet, Togo, and Uganda. The underlying cause of this treatment gap was found to be the differences in the provision and utilization of treatment care in different regions.<sup>5</sup> Furthermore, a survey conducted in 2023 revealed that epilepsy poses a significant health challenge in low and middle-income countries, regarding availability and accessibility to treatment.<sup>6</sup> Awareness among pre-clinical medical students in Saudi Arabia indicated lesser knowledge and a negative disposition towards epileptic patients, as compared to clinical patients (92% versus 99.0%,  $P$ -value = 0.000). Pre-clinical students although having good awareness, showed a negative attitude towards epilepsy.<sup>7</sup> In another survey in Saudi Arabia, medical students showed better awareness of epilepsy than other health specialty

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students. However, they had less knowledge about the surgical treatment of epilepsy.<sup>8</sup> Dentists often harbor concerns about emergency preparedness, practical skills, availability of life-saving equipment, and staff readiness. A considerable number of dentists do not feel adequately proficient in handling medical emergencies.<sup>9</sup> Dentistry, like many clinical specialties, involves invasive procedures, putting patients at risk of medical emergencies. Thus, heightened attention and emphasis on preventing and managing such incidents is warranted.<sup>10</sup>

Over the past two decades, there has been a notable surge in adult patients seeking orthodontic treatment, many of whom are suffering from chronic diseases. Advances in the management of these conditions have enabled these patients to pursue elective orthodontic procedures that were once considered impossible. One such condition is epilepsy or seizure disorder. While numerous papers and case reports have been written to update orthodontists on the etiology, types, and management of epilepsy in dental settings, the specific problems and challenges faced in a Pakistani context have not been documented. This qualitative study aims to delve into the personal experiences and hurdles encountered by orthodontists when treating epileptic patients. It is anticipated that this research will uncover novel aspects of the disease and patient behavior in the context of orthodontic treatment. This, in turn, will provide valuable insights for future needs and precautionary measures when dealing with epileptic orthodontic patients.

#### **METHODOLOGY:**

A qualitative research project was carried out by two researchers from the Rawal Institute of Health Sciences Islamabad. The study duration was almost three months from 4<sup>th</sup> August 2023 to 30<sup>th</sup> October 2023 after approval from the ethical committee. Ethical permission for the current study was taken by the Ethical Review Committee of Rawal Institute of Health Sciences (RIHS) Islamabad. (Reference no. RIHS/IRB/D/23100). The sample size was attained by scheduling interviews with the practicing orthodontists until no new information about epilepsy was gained for three consecutive interviews. This finally led us to arrange a total of 11 interviews. The researchers initially enlisted 15 orthodontists, who fit the inclusion criteria. The inclusion criteria for orthodontists in the study were a postgraduate qualification and a minimum of 10 years of clinical experience, in the field of orthodontics. All of them had treated at least one patient with epilepsy in the previous 5 years. General dentists and orthodontists having clinical experience of less than 10 years were excluded from the study. Orthodontists were identified through professional networks and academic institutions. Initially, orthodontists were contacted via phone and invited to take part in the study. Face-to-face interviews occurred in a quiet setting, facilitated by an experienced qualitative researcher. Due to geographical constraints, two orthodontists were interviewed

virtually through Zoom. Before the interviews, every orthodontist was fully briefed about the study's purpose, potential risks, benefits, and their right to withdraw at any stage. An informed consent statement that I agree to participate in this study was taken from each orthodontist verbally. During the interview, orthodontists were instructed to draw information solely from their personal experiences and not rely on their academic knowledge of epilepsy.

Interviews were recorded on an iPhone 10 for accurate transcription. To safeguard orthodontist confidentiality, pseudonyms were used, and identifying information was omitted. A Ph.D. scholar, well-versed in qualitative data analysis, assisted with transcribing the recorded files and resolving any discrepancies through discussion and consensus. Researchers also maintained field notes to capture physical gestures not captured by the recorder. Audit trails were conducted to ensure the validity, applicability, reliability, and confirmability of the findings.

The research report, utilizing framework methodology,<sup>11</sup> comprehensively documented the results. This methodology is shown in Figure I. Researchers listened to the interview content transcripts repeatedly, labeling topics identified from each interview as categories and codes, grouping similar codes into themes. Each code was assigned a number for easy identification as in Table II and so the full names of the codes were not written each time onto the transcripts. Any Computer Assisted Qualitative Data Analysis Software (CAQDAS) was not used in our study. Data was charted into a framework table with columns of codes and themes, and rows of participants, and then integrated into the framework matrix. Interpretation of data was effectively carried out by mutual consensus of the researchers. As data analysis is influenced by researchers' knowledge and interests, a triangulation technique<sup>12</sup> was used to minimize interpretation bias through member checking, where participants were allowed to review and confirm the accuracy of their statements.

#### **RESULTS:**

Eleven orthodontists including 5 males and 6 females, with a clinical experience of more than 10 years participated in the study. Table I shows their working experience and gender. Twenty-seven codes (a1-a7, b1-b4, c1-c7, d1-d6, e1-e3) were constructed and grouped under 5 themes (Table 2). All orthodontists were interviewed about their overall experience, and problems faced during treatment of epileptic patients. We will quote the responses of some orthodontists here. None of the orthodontist knew about the type of epilepsy except orthodontist no 1 and 8. I treated two epileptic patients and asked them about the type of epilepsy. One patient showed me his neurologist report. I don't remember his diagnosis now. Orthodontist 1. All others never saw the neurologist's report or communicated with him. There was no need to communicate with the neurologist because the

disease was under control and the patient was willing for orthodontic treatment. I always made sure that the patient brought his medicine along at every appointment. Orthodontist 5

All orthodontists knew that the patient was under medication and had not experienced a seizure since one year as told by the patient, but they never saw the prescription. Three orthodontists (4, and 7) were requested to remove the braces for MRI because of disease relapse or sudden diagnosis of epilepsy during orthodontic treatment. None of the orthodontists used to take a history of any recent seizure at every orthodontic appointment. I just took history at the start of treatment and the patient told me that my disease is controlled. I never thought of taking a seizure or medication history at every appointment. Orthodontist 4

Patient and parent motivation was reported to be extremely compromised by three orthodontists (3,4 and 7) whose patients were newly diagnosed with epilepsy during orthodontic treatment. They requested immediate removal of braces for MRI. Two of them restarted the orthodontic treatment after one year. My patient and his parents were extremely stressed and frightened. They wanted to get rid of braces. I did not use the ceramic brackets, otherwise, the removal of braces in that case could be deferred. Orthodontist 7. Ceramic brackets are tooth colored and do not need removal before MRI unlike metallic brackets.

All the other participants reported the average motivation level of their patients, however, parents' motivation was high which helped a lot in continuing treatment. My patients' disease was controlled, and did not have seizures for the last two years. She was confident, doing a job, and highly motivated to align her teeth. Orthodontist 11

All orthodontists remembered their patients and shared their personal experiences. Orthodontists no 6 and 10 reported that they planned limited single arch treatment with extraction of labially blocked out canine and finished the case in one and a half years. In my epileptic patient, I preferred limited treatment, because the moment we placed the braces, the gingiva became hyperplastic. Orthodontist 3 All others carried out a comprehensive orthodontic treatment for two to three years. Participant no 2 experienced the seizure and said, my patient was jerking and I just timed and observed the seizure to end. I did not call the patient for the next 3 months for an orthodontic appointment. Orthodontist 11 also experienced the seizure and stated, He was my colleague patient and it was a private clinic around 7.00 pm. The seizure was extremely severe and his body was stiff. We removed all the instruments around him and waited for the seizure to end. We did not remember at that time to turn the patient to his side. We related it to the evening appointment and started calling him in the morning. I think it triggers in the evening with fear and anxiety. Orthodontist 11. Orthodontist 3 also experienced the seizure once and said.

I checked the time of the seizure, and unfortunately, buccal /nasal midazolam or any other anti-epileptic drug was not available in the office. The patient hands were tightly closed, and saliva came out of his mouth. The seizure ended after almost a minute or so. The patient had a short-term memory loss after the seizure. He did not remember where he was. I remember that patient later gave history of irregular medicine intake.

All orthodontists except 10 and 11 declared that the biggest challenge was poor oral hygiene. They remembered repeated referrals to the periodontist for scaling, mouthwash prescription, and modified brushing techniques. Patient cooperation was compromised. I as an orthodontist was disappointed to see the oral hygiene and every time counseled the patient, and his parents but it was of no use. Orthodontist 2.

Seven orthodontists reported gingival hyperplasia after the insertion of braces. It was even more so with orthodontic bands, which made it difficult to execute mechanics. I used to refer the patient to the periodontist frequently. My patient could not afford an aligner, but it could be a good option for him. Orthodontist 3.

Orthodontist 10 stated that I avoided using cotton palettes and intense dental chair light in my epileptic patient. Another problem claimed by all participants was bracket breakage which resulted in treatment delays. Premolar brackets were the most frequent to dislodge. I was so annoyed by repeated bracket breakage that I stopped replacing the premolar brackets because bands further aggravated hyperplasia. Ceramic brackets are expensive and not user-friendly, otherwise, I would have preferred them for my epileptic patient. Orthodontist 10.

Nine orthodontists reported increased appointment time and workload because of breakages and poor oral condition. Placing ligatures was a tedious job. I had to remove calculus around brackets at every appointment. Orthodontist 5. Orthodontist no 6 and 9 also reported bad mouth odour and staining of the teeth. All orthodontists recommended frequent workshops, mock exercises, and staff training about treating medically compromised patients.

#### **DISCUSSION:**

This study presents a distinctive opportunity to delve into the challenges and experiences faced by orthodontists in the context of employing fixed mechanotherapy for epileptic patients. While many of the findings align with existing literature, there are noteworthy discrepancies. Here, we will exclusively discuss the shortcomings observed in orthodontic practice that emerged during interviews. The majority of orthodontists employed a standard consent form, however, in cases involving epilepsy, it is imperative to obtain a consent form that expressly highlights the potential for injury associated with intraoral appliances during a seizure episode. Every orthodontist must know the classification and exact



Figure 1: Hierarchy of Framework Methodology

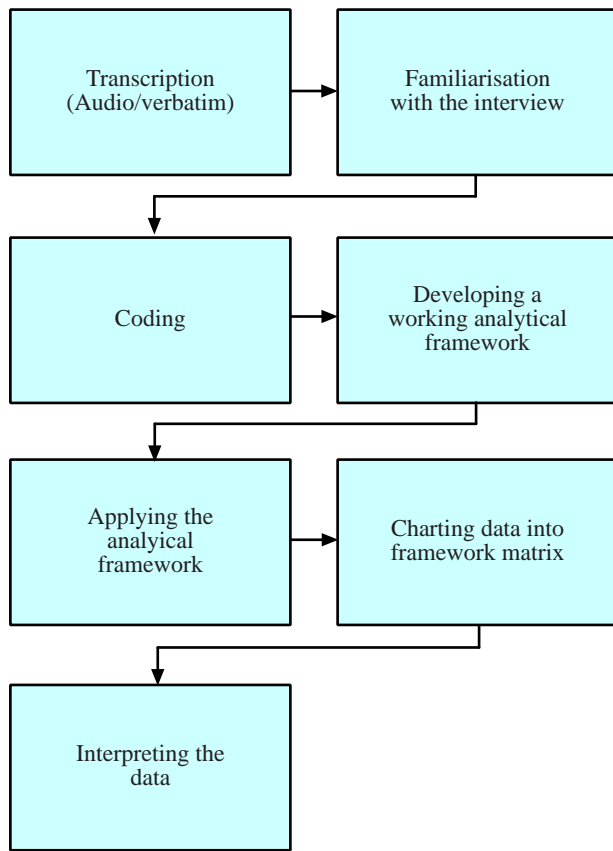


Table 1. List of interviewed orthodontists

No of orthodontist	Gender	Work experience
1	male	11 years
2	male	15 years
3	male	20 years
4	female	10.5 years
5	male	13 years
6	female	11 years
7	female	25 years
8	female	10 years
9	female	13 years
10	male	11 years
11	female	11 years

type of epilepsy, the patient has. For instance, a tonic/clonic seizure or episode of status epilepticus is critical and regarded as a medical emergency if it persists beyond a five-minute threshold.<sup>13</sup> Not all orthodontists uniformly insisted on obtaining a prescription and diagnostic report from the treating neurologist. Previously medicine taken by the patient was mostly phenytoin sodium or Tegretol, however, with advancements in the medical field many other options are available now and neurologists can be communicated regarding change of medication to handle problems like gingival hyperplasia.<sup>14,15</sup>

Table 2. List of Themes and Codes

Themes	Codes
Diagnosis	a1. past medical history a2. the patient had a pre-treatment epilepsy or it started during orthodontic treatment a3 type and frequency of the seizure. a4. When did the last seizure occur? a5. which medicine he is taking a6.MRI done or not, will need removal of braces for MRI. a7. neurologist report studied or not.
Behavior and motivation	b1. Parents and patients interest in treatment. b2. The patient is internally or externally motivated. b3. pretreatment oral hygiene status. b4. overall self-esteem and behavior of the patient.
Treatment Planning	c1. consent of parents and patient about intra-oral injury risks c2. repeated referral to a periodontist c3. medicine and seizure history at every appointment. c4. need for medical emergency help c5. limited treatment goals. c6. more treatment time in extraction cases c7.use aligners and ceramic brackets c8. arrange antiepileptic drugs for emergencies.
Challenges and concerns of the orthodontist.	d1. oral hygiene maintenance. d2. bleeding gums and increased calculus deposits around brackets d3. bracket breakage. d4. gingival hyperplasia. d5. increased treatment time. d6.bad mouth odour and staining of teeth.
Recommendations and Advice	e1. workshops e2. mock exercises for dentists and staff

Echoing prior research, orthodontists in our study exhibited a commendable awareness of precautions pertinent to epileptic patients. However, full-fledged implementation of these precautions was not uniformly evident. Only one orthodontist mentioned that I never use cotton pallets for saliva control in epileptic patients. Insertion of rubber mouthpieces is considered to be a favorable method to cope with the occurrence of epileptic seizures during the bonding of braces.<sup>16</sup> Within our study, prominent challenges in orthodontic treatment encompassed a lack of patient

motivation, gingival hyperplasia, suboptimal oral hygiene, and recurrent bracket breakage. Tiwari and Verma found a strong association between dental caries, gingival enlargement, periodontal disease, injuries of the oral cavity, and seizure-related trauma.<sup>17</sup> However, Alqahtani identified orthodontic facial fractures, dental trauma, gingival hyperplasia stemming from anticonvulsant medications, facial asymmetry, and temporomandibular joint subluxation as primary concerns. It is pertinent to emphasize that patients with poorly managed seizures, particularly those prone to falls or uncontrolled bodily movements, are contraindicated for orthodontic intervention.<sup>18</sup> Notably, while orthodontists in our study acknowledged stress, evening appointments, and missed medication as potential seizure triggers, only 3 of them mentioned that the intense illumination from dental chair lights can also serve as a trigger. It is imperative to utilize dark goggles for all patients in this context.<sup>19</sup> A recent local study by Qasim et al, highlighted a substantial need for enhanced knowledge among Pakistani dentists concerning epilepsy. Notably, 48.2% of respondents erroneously believed that epileptic patients could safely undergo in-office treatment.<sup>20</sup> We posit that such confidence may be misleading, given that seizures can recur even in cases where the condition is well-controlled, particularly in the presence of exacerbating factors so dental procedure should be done in a separate room that is free from loud noises and bright lights. A sphygmomanometer and a portable oxygen cylinder should be kept ready in the dental office.<sup>21</sup> Last but not least, none of the orthodontists mentioned dental drug interaction with anti-epileptic medication. For example, metronidazole, fluconazole, and antibiotics (such as erythromycin) are known to interfere with the metabolism of certain anti-epileptic drugs. Newly introduced drugs like cenobamate and fenfluramine have lesser pharmacokinetic interactions.<sup>22</sup>

While there were variations in the experiences of orthodontists with epileptic patients, the underlying implications are remarkably similar. It is imperative to conduct a comprehensive history, inquire about the current state of the disease and medication, and carefully consider suitable appliances and techniques for orthodontic treatment. Buccal/nasal midazolam should be available in the dental office. Future recommendations are that practical courses for dental professionals and support staff should be frequently arranged.

This study has a few limitations. The research relied on participants' memory during the interview so there may be a potential for recall bias, particularly among orthodontists who treated patients four or five years back. Furthermore, all orthodontists involved in the study were highly qualified, which could potentially influence them to rely more on theoretical knowledge rather than sharing personal experiences exclusively. Nevertheless, this approach's strength lies in the fact that orthodontists were interviewed based on

their direct patient interactions, potentially yielding fresh insights and recommendations for treating epileptic patients.

### CONCLUSION:

We concluded that orthodontic treatment of epileptic patients is highly challenging. Orthodontists experience a lot of problems like gingival hyperplasia, poor oral hygiene, and bracket breakages. Orthodontists should take care of special considerations while treating epileptic patients like use of ceramic brackets, avoiding intense dental lights and intra oral cotton palletes, taking medication history, availability of Buccal/nasal midazolam in the dental office and focus on enhancing the practical implications of their clinical knowledge about epilepsy.

### Authors Contributions:

**Sadia Naureen:** Conception, design, Introduction and discussion

**Huma Ghazanfar Kiani:** Data analysis, Results and conclusion

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## Red Cell Parameters in Beta Thalassemia Trait; Comparison between Iron Deficient and Non-Deficient Carriers

Nazish Tahir, Saeed Akhtar Khan Khattak, Ghulam Murtaza Shaikh, Zunera Sajjad, Tamoor Bin Hanif, Nighat Jamal

### ABSTRACT

**Objective:** To compare hematological parameters in iron-deficient and non-deficient carriers of beta thalassemia trait.

**Study Design And Setting:** Comparative cross-sectional study. This study was conducted at the Department of Hematology at PNS SHIFA Hospital, Karachi for six months (February 2023 to July 2023).

**Methodology:** This comparative cross-sectional study included a total of 304 cases with beta thalassemia trait and was divided into two groups; the Iron-deficient (ID+) and iron-deficient (ID-) group. The study focused on red cell parameters i.e, Hemoglobin (Hb), TRBC, MCV, MCH and RDW. Haemoglobin Electrophoresis results of both groups were also compared. Descriptive statistics were expressed as mean  $\pm$  SD and the Chi-square test was assigned. A p-value = 0.05 was considered statistically significant.

**Results:** Out of the total 304 subjects, 76 (25.0%) had iron deficiency, and 228 (75.0) had sufficient iron stores. Mean age of patients was 18 (Range: 3 – 35) years. HbA levels were similar in both the groups with p-value > 0.05. While all other parameters compared showed marked differences among the two groups and were found to be statistically significant. Hb, TRBC, MCV MCH showed lower values in the ID+ group while RDW was lower in the ID- group.

**Conclusion:** Red Cell parameters and HBA2 levels in beta thalassemia trait vary significantly among the iron deficient vs non-deficient group. Hence due consideration is needed in screening of beta thalassemia trait in patients with iron deficiency anemia.

**Keywords:** Beta Thalassemia, Trait, HbA2, Red Cell parameters, Iron deficient carriers, Iron Sufficient carriers.

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### INTRODUCTION:

Beta thalassemia trait (BTT) is the most common hemoglobin disorder worldwide with the highest number of cases prevalent in Mediterranean, Middle Eastern, and Southeast Asian regions.<sup>1</sup> The prevalence of BTT worldwide is about 1.5% while in Pakistan the prevalence is as high as 5-8%.<sup>2</sup>

BTT is characterized by the reduced or absent synthesis of beta globin chains of hemoglobin molecules (in a heterozygous state). Electrophoresis of haemoglobin is required for a definitive diagnosis of  $\hat{a}$ -thalassemia trait patients. Hb A2 is normally less than 3.2%, however it is greater than 3.5% in  $\hat{a}$ -thalassemia. HbA2 levels can be detected using different techniques such as High-performance liquid chromatography (HPLC), Cellulose acetate membrane electrophoresis, or Capillary electrophoresis. However, in regions where sophisticated diagnostic equipment is unavailable, a simple morphologic criteria has been proposed. It is based on peripheral blood films with microcytic red cells, target cells, and basophilic stippling. The most common technique used for screening is HPLC.<sup>3</sup>

The most prevalent cause of anemia globally is iron deficiency, being particularly common among children and women of childbearing age owing to nutritional deficiencies and menstrual losses respectively. It is also common in old

age due to gastrointestinal blood loss. Body Iron status is determined commonly by serum iron studies that include Serum Ferritin, Iron levels, Total Iron Binding Capacity (TIBC), and Transferrin saturation (TSAT).<sup>4,5</sup> Two of the most common causes of hypochromic, microcytic anemias include beta thalassemia trait and iron deficiency anemia.<sup>6</sup>

Distinguishing between IDA and  $\hat{\alpha}$ -thalassemia trait ( $\hat{\alpha}$ -TT) depends on tests that consume time and money. Not all areas have specialized labs where patients with microcytic anemia can undergo DNA analysis, serum ferritin determination, or hemoglobin electrophoresis. For this reason, different discrimination indices based on various basic red blood cells (RBC) parameters like mean cell volume (MCV), RBC count, and RBC distribution width (RDW) have been suggested since 1973 to differentiate between IDA and  $\hat{\alpha}$ -TT. Red cell parameters in both these conditions (Iron deficiency and BTT) present with specific patterns in the blood complete picture. Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) are low in both conditions. Comparatively red cell distribution width (RDW) is high in iron deficiency anemia (IDA), while in BTT, RBC count is on the higher side.<sup>7</sup>

It is not uncommon for these two conditions to prevail in the same patient i-e a single patient can be having both BTT and IDA and in that scenario spectrum of red cell parameters could significantly change. In addition, the co-existence of IDA with BTT can mask the HbA2 levels on HPLC.<sup>8</sup> This can lead to a missed diagnosis which can later have detrimental implications as a Beta Thalassemia carrier may get married to another BTT, resulting in the possibility (25% chances) of Thalassemia major in the offspring.<sup>9</sup> Our health care system is not capable enough to adequately manage the increasing number of children with Thalassemia major. A better approach is to identify all the cases of BTT so that necessary actions (genetic counseling and prenatal diagnosis) could be timely done to avoid the far-off obvious implications. It is thus important to differentiate the two conditions and to rule out the possibility of their coexistence by assessing red cell parameters on blood complete picture, an early screening test. The distinction is also critical because Hb will not improve in BTT if it is misdiagnosed as IDA and excessive iron is administered by the attending physician.

Considering above, we would try to assess changes in red cell parameters and HbA2 levels by their comparison in known BTT cases with iron deficient and non-deficient states.<sup>10</sup>

#### **METHODOLOGY:**

This comparative random cross-sectional study was conducted at the PNS SHIFA hospital, Karachi for 06 months (February 2023 to July 2023) after getting approval and clearance from the Institutional Ethical Review Committee (ERC/2023/HAEM/37). Sample size (minimum: 114) was

calculated through the WHO calculator, keeping the margin of error at 5%, a confidence interval level at 95%, and a BTT prevalence at 5 to 8%.<sup>6</sup> We included 304 individuals with BTT in our study, sampling was done using the nonprobability convenient sampling technique. Known cases of BTT with HbA2 levels greater than 3.5% with and without Iron deficiency as assessed through Serum Iron, TIBC, and Ferritin levels were included in the study. Whereas cases with co-morbidities like infection, chronic disorders and malnutrition were excluded from the study. Data was collected from patients after taking documented consent.

CBC was done on an Automated CBC analyzer (Sysmex Kx-21) within 2-3 hours after collection of the sample in EDTA bottles, to evaluate the hematological parameters (Hb, MCV, MCH, RDW, and TRBC), followed by HbA2, HbA and HbF levels on HPLC and iron studies (Serum Iron, Ferritin levels, TIBC and Transferrin saturation). The Mentzer index of the two groups was also calculated and compared.

The study was conducted in two groups based on Iron profile results, Cases with low serum ferritin levels (<15ng/ml) and transferrin saturation (TSAT= Iron/TIBC x 100) < 20% were taken in the Iron deficient group (ID+). All others were grouped as subjects with sufficient iron levels (ID-).

To determine the effect of iron deficiency on red cell parameters (Hb, MCV, MCH, RDW, TRBC) the ID- group was compared with the ID+ group. The data was analysed using the Statistical Package for Social Sciences (SPSS) version 26:00. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to ensure that the data was normal. The Mann-Whitney U test was employed to detect the difference between the groups since the data observed varied from the normal distribution. A p-value of 0.05 or less was considered significant.

#### **RESULTS:**

A total of 304 patients were included in this study, Patients were divided into two groups. Group 1 was iron-deficient (ID+) and Group 2 was iron-sufficient (ID-). Out of the total, 76 (25.0%) patients had iron deficiency, and 228(75.0%) patients had sufficient iron. The median age of the patients was 18, ranging from 3 to 35 years. The distribution of individuals with and without iron deficiency based on gender and age is shown in Table-I. The iron-deficient group had a different gender distribution compared to the iron-sufficient group, and there were differences in the median ages of these two groups as seen in Table-I. The mean of various parameters were compared between two groups, iron-deficient (ID+) and iron-sufficient (ID-), as seen in Table II. Notably, the levels of HbA were found to be similar in both groups, with a p-value > 0.05. In contrast, all other parameters (Hb, MCV, MCH, TRBC, RDW, Iron, TIBC, TS, Ferritin, HbF, Mentzer Index) exhibited statistically significant differences between the two groups, as indicated by p-values < 0.05.

Table 1: Demographic variables of the Patients (n=304)

Demographic variables	Iron-deficient (ID+) (n=76)	Iron-sufficient (ID-) (n=228)
Gender		
Male	31 (40.8%)	134 (58.8%)
Female	45 (59.2%)	94 (41.2%)
Age in years	Median (IQR)	Median (IQR)
	16.0 (26.0-9.0)	19.0 (28.1- 9.0)

Table 2: Comparisons of mean values of red cell parameters and other hematologic findings between the groups (n=304)

Parameters	Iron-deficient (ID+) (n=76)	Iron-sufficient (ID-) (n=228)	p-value
Hb (g/dl)	9.1	11.2	< 0.001
MCV (fl)	56.5	66.7	0.043
MCH (g/dl)	19.32	19.60	0.013
TRBC ( $\times 10^{12}$ /L)	5.4	6.0	< 0.001
RDW (%)	17.8	16.0	< 0.001
Iron (micromol/L)	5.9	16.3	< 0.001
TIBC ((micromol/L)	83.92	63.3	< 0.001
TS (%)	18.7	26.2	< 0.001
Ferritin (ng/mL)	7.5	22.7	< 0.001
HBA <sub>0</sub> (%)	83.3	84.7	< 0.201
HBA <sub>2</sub> (%)	3.8	4.5	< 0.038
HBF (%)	1.5	1.2	< 0.001
Mentzer Index	14.1	10.9	< 0.001

## DISCUSSION:

Beta-thalassemias are a group of hereditary blood diseases marked by anomalies in haemoglobin beta chain production, resulting in a wide variety of phenotypes ranging from severe anemia to clinically asymptomatic individuals. The global yearly incidence of symptomatic persons is estimated to be one in 100,000, with the European Union accounting for one in 10,000. There are three types of thalassemia: thalassemia major, thalassemia intermedia, and thalassemia minor. Individuals with thalassemia major typically appear with severe anaemia within the first two years of life. Carriers of BTT are usually symptom free, stresses such as pregnancy can cause the BTT carriers to develop clinically significant anemia sometimes requiring transfusion. Carriers may have mild anemia (Hb: 9-12g/dl). The degree of hypochromia and microcytosis may be comparatively greater than that seen in iron deficiency. Failure to identify BTT antenatally can result in thalassemia major in the offspring, if the partner also carries BTT gene.<sup>11</sup> Thalassemia major patients require regular blood transfusions with many social and economic implications, it occurs when the mutations are inherited in the homozygous pattern.

Iron deficiency anemia (IDA) is the most severe result of iron deficiency and is still regarded the most frequent dietary shortfall globally. The cause of IDA is multi-faceted, but it

typically happens when the body doesn't receive enough iron to meet its needs. People who have IDA may not consume enough iron, experience natural iron losses due to aging or reproduction, have difficulties in absorbing or transporting iron, or suffer from chronic blood loss due to illness. Adults with IDA may encounter various negative effects, such as reduced capacity for work or exercise, impaired immune function, gastrointestinal problems, difficulties regulating body temperature, and impaired cognitive abilities. As in BTT, it presents with Low Hb, MCV, and MCH<sup>6,7</sup> TRBC while contrary to BTT, RDW in the case of IDA is usually increased.<sup>12</sup> Blood CP is the initial screening test for hypochromic microcytic anemias. The co-existence of BTT and IDA is a diagnostic challenge as IDA masks HbA<sub>2</sub> levels on HPLC leading to misdiagnosis. In one study conducted by El-Agouza *et al*, it was noted that repeating HPLC after iron replenishment resulted in a significant rise in HbA<sub>2</sub> levels (from 3.07 to 3.81%) in patients with co-existing IDA and BTT. It is thus very important to understand the spectrum of hematological parameters on CBC in patients with a combination of IDA and BTT. Iron deficiency, once diagnosed, should be adequately managed and patients having borderline HbA<sub>2</sub> levels are often advised to repeat HbA<sub>2</sub> levels after iron replenishment. Understandably, a multidisciplinary approach in hospitals is needed to address the issue.<sup>13</sup>

In our study, cases were grouped into the iron-deficient and non-deficient group based on the results of serum ferritin levels and TSAT. Ferritin levels may be falsely raised in some cases, as it is an acute phase reactant. Hence, TSAT must be calculated to rule out iron deficiency. Out of the total 304 cases enrolled in our study, 72 (24.0%) had iron deficiency and 228 (76.0%) had sufficient iron levels when we compared the red cell indices of iron-deficient (ID+) vs iron-sufficient (ID-) groups of BTT carriers it was noted that ID+ group showed lower values of Hb, MCV, MCH, and TRBC as compared to the ID- group. However, the ID+ group showed higher values of RDW as compared to the ID- group.

The combined effect of defects in globin chain synthesis and additional nutrient deficiency, on erythropoiesis, leads to further reduction in Hb levels in cases with BTT as concluded in a previous study conducted by Saraya *et al*.<sup>14</sup> Similar results were reproduced in our study.

The Mentzer index of both groups was also calculated using the formula; MCV/TRBC. A value greater than 13 is considered suggestive of IDA and vice versa for BTT. This has previously been proved in many studies. One study by Gonul Aydogan *et al*,<sup>15</sup> stated the sensitivity and specificity of the Mentzer index as 100% and 69.4% respectively. However, not much data is available on the effect of Mentzer index values in combined BTT and IDA. In our study it was noted that subjects in the ID+ group showed a Mentzer index value greater than 13 (mean=14.1) which was considered

statistically significant. Other formulas like Green and King ( $MCV^2 \times RDW / (Hb \times 100)$ ), Srivastava ( $MCH/RBC$ ), Ehsani ( $MCV-10 \times RBC$ ), Shine and Lal ( $MCV^2 \times MCH/100$ ), Mentzer ( $MCV/RBC$ ), England & Fraser formula: ( $MCV-RBC-5 \times Hb-3.4$ ) Ricerca, and 11T score have also been previously used to discriminate the two conditions but their sensitivity is too low.<sup>16</sup> Beyan et al calculated the sensitivity, specificity, positive and negative predictive values of the above mentioned formulae and it was concluded that none of these formulae is superior to RBC value in distinguishing IDA from BTT.<sup>17</sup> Similar results were reproduced in another study by Demir et al in which youden's index of all these formulae was calculated. Youden index shows the sensitivity and specificity of any technique, it was the highest for RBC and RDW and these two indices were considered to be of prime importance in distinguishing between IDA and BTT.<sup>18</sup>

Moreover, the HPLC findings of the two groups were also compared that showed lower values of HbA2 in the ID+ group. It was also noted that the ID+ group showed higher levels of HbF compared to the ID- group. HbA levels were similar in both groups.

In a study conducted by Deniz Aslan *et al*, erythrocyte parameters of IDA in BTT were compared, it was seen that the group with co-existing IDA and BTT did not show a significantly lower value of MCV and RBC as compared to the group with only BTT. It was postulated that this might be due to the fact that concomitant IDA in thalassemia carriers poses a basal stress in erythropoiesis that leads to increased HbF levels thus causing erythrocytosis that restrains microcytosis.<sup>19</sup>

While in another study by Aysel Vehapoglu *et al*, it was concluded that RBC count is not a reliable parameter to distinguish between IDA and BTT as patients with IDA can also have a high RBC count, especially in the beginning of starting Iron replacement therapy. In our study, however, both MCV and RBC counts were significantly lower in the ID+ group as compared to the ID- group.<sup>20</sup>

The co-existence of IDA and BTT is not uncommon and very little data has been previously published on the spectrum of hematological parameters that are observed when both these conditions prevail, our study focused on establishing the changes in RBC parameters when BTT and IDA co-exist.

## CONCLUSION

Coexistence of Iron deficiency and beta thalassemia trait results in significant derangements of red cell parameters and HbA2 levels. Therefore, screening of beta thalassemia trait in patients with iron deficiency anemia requires a meticulous approach.

## Authors Contributions:

**Nazish Tahir:** Acquisition, drafting, analysis and interpretation of data for the study

**Saeed Akhtar Khan Khattak:** Concept, design, analysis and interpretation of the study data

**Ghulam Murtaza Shaikh:** Revision of data / statistics for intellectual content production and final approval of the version to be published

**Zunera Sajjad:** Revision of data and proof reading

**Tamoor Bin Hanif:** Revision and proof reading

**Nighat Jamal:** Revision and proof reading

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# Gingival Health Status of Abutment Teeth in Acrylic Removable Partial Denture

Sajjad Hussain, Amna Amjad, Mubashir Sharif, Robina Tasleem

## ABSTRACT:

**Objective:** To determine the change in gingival health status of removable partial dentures abutment tooth/teeth after 1month post-insertion

**Study design and setting :** Quasi-Experimental Study, Department of Prosthodontics, Armed Forces Institute of Dentistry Rawalpindi, from October 2021 to April 2022

**Methodology:** The patients underwent a thorough history and clinical examination after formal consent. Prior to recording the impression for provision of acrylic removable partial denture, the baseline scores for gingival index, plaque index and abutment teeth's periodontal pocket depth were noted. After 30-days of placement of the acrylic removable partial denture, the patient was recalled for follow up and reassessment of score.

**Results:** Out of 90, there were 64 (71.1%) males and 26 (28.8%) females with average age of  $31.1\pm 5.8$  years. The average value of plaque index at baseline was observed to be  $0.39\pm 0.03$ , while mean value of gingival index at baseline was found to be  $0.19\pm 0.01$ . At 30 days follow up, the mean value of plaque index significantly increased to  $1.21\pm 0.07$  ( $p=0.001$ ). Similarly, the mean value of gingival index after 30 days insertion of the acrylic removable partial denture significantly increased to  $1.50\pm 0.09$  ( $p=0.001$ ). No significant difference was observed between 30 days post-insertion indices between smokers and non-smokers, males and females, and  $<30$  and  $>30$  years age groups.

**Conclusion:** It is concluded that the gingival health of abutment teeth significantly gets affected due to removable partial denture. The plaque and gingival index significantly worsen due to use of removable partial denture within a month's time.

**Keywords:** Abutments, Removable partial denture, gingival health status

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## INTRODUCTION:

Tooth loss is a major dilemma that cannot be prevented despite rapid advancement in the field of preventive dentistry and changes in the attitudes of patients in favor of preserving natural teeth rather than their extraction.<sup>1</sup> There are several reasons for loss of teeth, most commonly, tooth extraction occurs as a result of caries and periodontal disease. Other

causes cited for loss of teeth include trauma, infection, malignancies or failed endodontic treatments. Tooth loss may present with different possible adverse consequences on remaining dentition, surrounding soft tissue structures and general wellbeing of individuals.<sup>2</sup> These may include tilting and drifting of adjacent teeth, decreased masticatory efficiency, altered esthetics and appearance, over eruption of opposing dentition, periodontal problems and altered speech.<sup>3</sup>

There is a growing trend for people to try to retain more teeth later in life. For this reason, it is quite commonly seen that patients seek treatment to replace the loss of a significant number of teeth. There are different options available for replacement of these missing teeth including implant retained over-dentures, fixed dental prostheses and removable partial dentures i.e., the acrylic removable partial dentures and cast partial dentures.<sup>4</sup> Removable partial dentures (RPDs) are one of the most widely accepted method of replacing missing natural teeth owing to financial problems, compliance and height of residual ridges. Several studies have been done to review the consequences of placement of removable partial dentures in mouth.<sup>3-5</sup> It has been noted that removable partial dentures significantly alter the oral environment in terms of increased plaque accumulation on tooth surfaces which are

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in contact with it leading to periodontal problems, undue stresses on clasped abutments causing them to become mobile and recurrence of caries owing to food entrapment.<sup>6-7</sup> There are many reported methods to determine the periodontal status of abutment and non-abutment teeth. One of them is to collect data via different indices including Plaque Index (PI), Gingival Index (GI), and Probing Pocket Depth (PPD).<sup>7</sup> Literature supports that patient counselling regarding taking care of removable partial denture can be of significant importance in improving the oral hygiene and gingival health status. Timely follow up is another factor associated with better oral health and hygiene in denture users. The design and material used in formation of acrylic removable partial denture is also reported to be a prominent feature in preserving optimal periodontal health status.<sup>8-9</sup>

This study was conducted to assess the periodontal health status of abutment teeth at 6 months post-insertion of removable partial dentures. Mean average values of plaque and gingival scores were used to assess the gingival health status before and after use of acrylic removable partial dentures in our local population visiting a tertiary care hospital where a specific design of acrylic removable partial denture is used.

#### **METHODOLOGY:**

This quasi-experimental study was conducted at prosthodontics department of AFID (Armed Forces Institute of Dentistry) Rawalpindi for about a period of seven months, spanning October 2021 to April 2022. Minimum required sample size of 90 was calculated by Open-Epi sample size calculator with 95% level of confidence, 80% study power, mean difference in periodontal score of 1.4,<sup>11</sup> standard deviation of 1.2<sup>11</sup> and 10% precision. The study was approved from ethical committee at AFID prior to data collection. All of the patients showing up at Armed Forces Institute of Dentistry, Rawalpindi were screened in general OPD and those patients who fulfilled the criteria were sent to the prosthodontics department.

Non-probability consecutive sampling technique was used to enroll ninety patients of either gender, belonging to 20-40 years of age to whom removable partial denture was advised. Other inclusion criteria included patients in whom no more than 3 teeth were missing in maxillary or mandibular arch unilaterally, patients with no ongoing periodontal disease e.g., periodontitis, gingivitis etc, patients with good oral hygiene (absence of generalized calculus deposits assessed clinically) and with no recent history of periodontal therapy and patients with no supernumerary or retained deciduous teeth. Patients with poor oral hygiene (presence of generalized calculus deposits assessed clinically), history of bruxism or cervical caries or lesions, fixed restoration of abutment teeth (Crowns, Fixed Dental Prostheses), unfavorable residual ridge form (knife edge, flabby ridge or highly resorbed residual ridge), patients with oral lesions like oral cancer,

ulcers, history of diabetes mellitus, epilepsy or any other medical condition and teeth with poor prognosis (mobile teeth) were excluded from the study.

All the patients were undergone history and complete oral examination after taking informed consent. Sociodemographic and clinical data was recorded in data collection tool. Prior to recording the impression for provision of acrylic removable partial denture, the baseline scores for gingival index, plaque index and periodontal pocket depth of the abutment teeth were calculated and recorded. The gingival index and plaque index scores were calculated by Loe and Silness method using a blunt probe. After 30 days of placement of the acrylic removable partial denture, the patient was recalled for follow up and the scores of the abutment teeth for gingival and plaque index of the abutment teeth were again calculated and recorded.

Data analysis was done using IBM-SPSS software (version 20.0). Mean and standard-deviation were calculated for continuous variables like age, gingival index and plaque index. Frequency and percentages were calculated for categorical variables like gender. Confounding factors and effect modifiers like age, gender and smoking were controlled through stratification. Independent samples T-test was used post stratification to compare mean score between the groups. Paired samples t-test was used to compare quantitative variables including score of plaque index and gingival index at baseline and 30 days after the provision removable partial denture. P values of =0.05 was considered to be significant.

#### **RESULTS:**

The sociodemographic characteristics are given in table 1. The minimum value of plaque index at baseline was observed to be 0.35 and maximum of 0.45 was observed with mean score of  $0.39 \pm 0.03$ . Similarly, the minimum value of gingival index at baseline was recorded to be 0.18 and maximum of 0.22 was observed with mean score of  $0.19 \pm 0.01$ .

At follow up, the minimum value of plaque index after 30 days insertion of the acrylic removable partial denture was calculated to be 1.09 and maximum of 1.30 was recorded, with mean score of  $1.21 \pm 0.07$ . Similarly, the minimum value of gingival index after 30 days insertion of the acrylic removable partial denture was found to be 1.34 and maximum of 1.66 was noted with mean score of  $1.50 \pm 0.09$  as given in table 2.

By using Paired sample t-test, difference in mean values of plaque index before and after 30 days insertion of the acrylic removable partial denture was found to be significant ( $p=0.001$ ). There was a significant increase in plaque index score 30 days post insertion. Similarly, mean difference in mean values of gingival index before and after 30 days insertion of the acrylic removable partial denture was also found to be statistically significant ( $p=0.001$ ). There was a significant increase in gingival index score 30 days post insertion as given in table 2.

By the stratification of age, two groups were formed, age group less than 30 years and age group of 30 years and more. It was found that in both groups of age, the mean values of plaque and gingival indices increased after 30 days insertion of the acrylic removable partial denture, but there was no significant difference between plaque and gingival indices scores 30 days post-insertion between two age groups as shown in table 3.

By the stratification of gender, it was found that in both males and females, the mean values of plaque and gingival

Table 1: Sociodemographic characteristics of study participants (n=90)

Characteristics		n(%)
Age in years (mean±SD)		31.1±5.8
Rage range		20 - 40
Age groups	<30	39 (43.3%)
	=30	51 (56.6%)
Gender	Males	64 (71.1%)
	Females	26 (28.8%)
Smoking status	Yes	53 (58.8%)
	No	37 (41.1%)
Socioeconomic status	Low	22 (24.4%)
	Middle	40 (44.4%)
	High	28 (31.1%)
Education status	Illiterate	7 (7.7%)
	Primary	10 (11.1%)
	Graduation	53 (58.8%)
	Post-graduation	20 (22.2%)

Table 2: Mean plaque and gingival indices score at baseline and 30 days post-insertion of acrylic removable partial denture

Parameters	Mean scores		p
	At baseline	At 30-days	
Plaque index (PI)	0.39±0.03	1.21±0.07	0.001
Gingival index (GI)	0.19±0.01	1.50±0.09	0.001

Table 3: Post-stratification comparison of Mean plaque and gingival indices score at baseline and 30 days post-insertion

Strata		Parameters	Mean Scores At 30-days	P	
Age	<30 years	Plaque index (PI)	1.21 ± 0.069	0.526	
	=30 years		1.20 ± 0.07		
Gender	Male		1.21 ± 0.070	0.98	
	Female		1.20 ± 0.071		
Smoking Status	Smokers		1.19 ± 0.074	0.209	
	Non-smokers		1.22 ± 0.064		
Age	<30 years		Gingival index (GI)	1.49 ± 0.09	0.144
	=30 years			1.50 ± 0.10	
Gender	Male	1.51 ± 0.098		0.478	
	Female	1.48 ± 0.093			
Smoking Status	Smokers	1.50 ± 0.098		0.920	
	Non-smokers	1.50 ± 0.097			

indices after 30 days insertion of the acrylic removable partial denture, were significantly increased as compared to baseline but the difference in mean values 30 days post-insertion between males and females was not significant as shown in table 3. By the stratification of smoking status, there was no significant difference in mean values of plaque and gingival indices after 30 days insertion of the acrylic removable partial denture between smokers and non-smokers as shown in table 3.

## DISCUSSION:

Tooth loss is a significant morbidity among older age group people. The desire of restoration of function of lost tooth and aesthetics plays a significant role in adoption of temporary and permanent denture use. Removable partial dentures are more common when there are only a few compromised teeth. According to American College of Prosthodontics, it is estimated that there will be 200 million people using some kind of denture till 2030.<sup>12</sup> With increase utility of temporary and permanent dentures, a primary public health challenge of appropriate oral health is evident. The use of acrylic removable partial denture for a longer period of time predisposes a person's oral health to be compromised which can result in damage to normal teeth upon which the removable temporary denture is anchored to. Plaque and gingival indices are reported to provide valuable indication of the changes associated in the periodontium after the use of an acrylic removable partial denture.<sup>13</sup> In this study, significant difference has been found between the periodontal status prior and after the intervention of acrylic removable partial denture in patients at 6-months follow up.

Many studies from old literature, conducted at various countries but Pakistan, determining the effect of acrylic removable partial denture, reported significant relationship between compromised oral health and partial dentures. A study conducted by Hafeez A et al in Pakistan in 2018 also reported that removable partial dentures significantly affect the oral health and hygiene in denture users and an increase in plaque and gingival score was reported in results of this study.<sup>14</sup>

Similarly, another study conducted by Akaltan F et al on 36 patients reported that at 30-month follow up a significant increase in plaque index was observed in patients undergoing partial removable denture, with more frequent increase in lingual plate treatment group.<sup>15</sup> It was also concluded that timely follow up and regular checkups reduces the poor outcomes in patients using acrylic removable partial denture. In a study conducted by Al Rawi SA et al, the results are quite similar with current study, where baseline Plaque Index for abutment teeth was found to be 0.4±0.05, which increased to 1.2±0.11 after 6 months, similarly baseline Gingival Index was 0.2±0.02 which increased to 1.5±0.16 at 6 months follow up.<sup>11</sup> A study conducted by Kazem NA et al on 26 patients, half of whom were removable denture users and

other half were not, and the results revealed that denture wearers had poor oral hygiene with greater frequency of gingival inflammation, periodontium destruction and plaque accumulation on normal teeth.<sup>13</sup>

In a study conducted by Augustin MM et al, the author studied 4117 persistent teeth in denture and non-denture groups for 5 years and assessed dental status, periodontal status, gingival status and dental plaque. It was reported that dental caries was 6 times more frequently reported in patients with removable partial dentures compared with those not wearing dentures.<sup>16</sup>

In a Pakistani study conducted by Ali M et al, there were 100 subjects enrolled in the study and followed up for 1 year to assess periodontal health status after using removable partial denture. An increased prevalence of periodontitis regardless of age and gender was reported among the removable partial denture users and the most common factor contributing to poor oral health was said to be lack of awareness, followed by low socioeconomic status.<sup>17</sup> Therefore adequate counseling specially of denture users belonging to low socioeconomic class is required to improve their oral health.<sup>18</sup>

In another study conducted by Cankaya ZT included 65 wearers of acrylic removable partial denture to assess the oral health outcomes at three different time intervals. The parameters were compared at day-30 and day-60 with baseline values and confounding factors were stratified for result adjustments. It was reported that periodontal parameters including gingival index, tooth mobility, and clinical attachment loss were significantly affected at day-60 compared with baseline.<sup>19,20</sup>

## CONCLUSION:

It is concluded that the gingival health of abutment teeth is significantly affected due to removable partial denture. The plaque and gingival index significantly worsens due to use of removable partial denture within a month's time.

### Authors Contributions:

**Sajjad Hussain:** Idea conception, data collection  
**Amna Amjad:** Manuscript writing  
**Mubashir Sharif:** Critical Review  
**Robina Tasleem:** Data collection

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# Prevalence of Cognitive Impairment and Risk Factors among Elderly in Rawalpindi, Pakistan: A cross-Sectional study

Hafsah Gul Khattak, Hafsah Arshad, Kinza Anwar, Muhammad Qasim Ali

## ABSTRACT:

**Objective:** The study aimed to find out the prevalence of cognitive impairment and risk factors among elderly.

**Study Design and setting:** Descriptive cross-sectional study was conducted in elderly population of Rawalpindi.

**Methodology:** The study was conducted from October 2020 to February 2021. After getting approval from the ethical committee, data was collected using a semi structured questionnaire. The sample of 446 participants, raised through non-probability convenient sampling technique. Participants aged above 60 years, both genders were included however individuals who had severe head injury, depression, severe hearing and visual impairment, delirium and not willing to participate were excluded from study. Informed consent was obtained from all participants. Data was analyzed by using SPSS v24.

**Results:** The overall mean age of sample was  $69\pm 4.6$  years. Overall prevalence of cognitive impairment was 35.4%. Among them 134 (30%) had mild cognitive impairment and 24 (5.4%) had dementia. The prevalence of cognitive impairment increases with age being higher (64.2%) at 70 years and above than at 60-69 years of age. Females 82 (61%) had high prevalence of MCI than males 52 (39%). Age, gender, hypertension, diabetes, and physical activity were significantly associated with cognitive impairment. Data was analyzed using SPSS version 24. Descriptive statistics were applied. Pearson chi square of independence was used to find the association of various factors. The p value less than 0.05 was considered significant.

**Conclusion:** Cognitive impairment increases with the increasing age and was more prevalent among females. Hypertension, Diabetes, physical activity were modifiable risk factors for cognitive impairment.

**Key words:** cognition, cognitive decline, dementia, elderly, mild cognitive impairment

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## INTRODUCTION:

Aging is associated with decline in whole body functions due to inflammation at cellular level. As the age progresses change in cognitive function of individual are also observed. An increase in the number of older adults is reported worldwide. It is reported that twelve million older adults

are living in Pakistan, and this number is expected to rise to eighteen million by 2050. This can exemplify an increase in number of elderly with increase in morbidity and mortality, particular increase in decline of cognitive functions. Decline in cognitive function (aka cognitive impairment) increases risk of dementia and places the elderly having difficulty in learning, memory and performing daily tasks.

Mild cognitive impairment (MCI) was first described by Petersen et al 1997, refers to impairment in cognition above that which is seen with normal age-related cognitive decline, but not sufficient to cause significantly decreased daily life function, considered as transitional stage from normal cognitive function to dementia. Clinically, the term "age-related cognitive decline" is equivalent with changes in memory and cognition that are typically seen with increasing age or "normal aging." The term mild cognitive impairment (MCI) commonly states a decline in the ability to learn new information or recall stored information. MCI is characterized by attention deficit, memory impairment, disorientation, visuospatial disturbances. People with mild cognitive impairment are at higher risk of developing dementia than older adults with healthy cognition. MCI is regarded as a

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risk factor for developing dementia, previous study indicated that the progression rate of MCI to dementia is approximately 60-100 % over five to ten years.

The worldwide prevalence of MCI was found to be 3% to 42% among individuals of age 60 years and above. Previously published studies conducted in different countries have reported the prevalence of MCI and dementia. A study in United States reported MCI among 22.2% in elder persons of age 71 years and above. The prevalence of MCI in Germany was found to be 3.1%. Population-based studies from India reported 15-33% of estimated prevalence. The difference in prevalence reported in different regions may be due to difference in age of study participants, sample size, tool used for cognitive assessment, difference in inclusion and exclusion criteria, definitions of MCI and dementia. Various risk factors found to be associated with cognitive impairment are advancing age, gender and level of education. Also, low economic status, anxiety, depression, diabetes mellitus and hypertension are some other risk factors reported among older adults with cognitive decline.

Cognitive impairment among older adults decreases the quality of life, independence and increases the burden on society. It also affects daily activities resulting in loss of independence and autonomy. Moreover, such elderly people need a full-time assistance from a caretaker for everyday tasks. There is limited literature on prevalence of cognitive impairment in elderly. Therefore, current study aimed to find out the prevalence and risk factors associated with cognitive impairment among elderly in Rawalpindi, Pakistan.

#### **METHODOLOGY:**

The descriptive cross-sectional survey was conducted on community dwelling older adults from October 2020 to February 2021 after getting approval from Institutional Review board & Research ethical committee of university (IRB/EC/00130). The sample size was calculated by using Rao soft, by assuming elderly population 20,000, by considering the confidence level 95% and margin error 5%, the sample size of our study was 377 while total number of participants who participated in the study was 446. Flow of participants in the study was shown in figure 1.

The sample was raised through nonprobability convenient sampling technique. The inclusion criteria were both male and female gender of age sixty years and above. Individuals who had severe head injury, depression, severe hearing and visual impairment, delirium and not willing to participate were excluded from study. Written informed consent was taken from the participants; the researcher explained the purpose and nature of study to the participants.

The questionnaire included socio-demographic questions: age, gender, marital status, level of education, employment status, living status and family history of dementia.

For cognitive assessment MoCA-Urdu version was used, a

validated instrument for diagnosis of MCI and dementia. It is comprised of several questions grouped into categories to assess specific cognitive functions: visuospatial/executive function, short term memory/ delayed recall, animal naming, attention, language, abstraction, and orientation. The total score Of MoCA- Urdu version was 30. A score of =26 was considered normal. One point was added if years of education are less than 12 years. Scores below 26 and 17 indicate MCI and dementia, respectively. The MoCA- Urdu version was completed by trained investigator for individual participant.

Data was analyzed by using SPSS version 24. Descriptive statistics were applied. For qualitative variables, frequency and percentages, and for quantitative variables mean and standard deviation were calculated. Pearson chi square of independence was used to find the association of various factors. The p value less than 0.05 was considered significant.

#### **RESULTS:**

Out of four hundred and forty-six participants 268 (60.1%) were female and 178 (39.9%) were males. The overall mean age of sample was  $69 \pm 4.6$  years. Most of the study participants 67.1% were in 70 years and above age category. 380 participants were married, and 51 participants were widowed. We found that 138(30.9%) elderly were illiterate, 151 (33.9%) had primary education, 87 (19.5%) had secondary education and 70 (15.7%) were graduate and above. Most of the participants 242 (54.3%) were unemployed, 249 (55.8%) living with spouse. 130 (29.1%) participants had family history of dementia while 316 (70.9%) did not have any family history of dementia. (Table 1)

Overall prevalence of cognitive impairment was 35.4 %. Among them 134 (30%) had mild cognitive impairment and 24 (5.4%) had dementia, using MoCA-Urdu version standard cutoff point less than 26 for MCI and 17 for dementia (figure 2). The prevalence of cognitive impairment increases with age being higher (64.2%) at 70 years and above than at 60-69 years of age. Females 82 (61%) had high prevalence of MCI than males 52 (39%). The prevalence of several risk factors is shown in Table 2. Among them hypertension was 68.8%, diabetes 61.2% and physical activity was 28.5% respectively. Table 3 shows p-value for associated risk factors for cognitive impairment. Most affected sub scores in MCI patients were delayed recall and language as shown in figure 3.

#### **DISCUSSION:**

The prevalence of cognitive impairment among older adults in Rawalpindi was 35.4 %. The prevalence of mild cognitive impairment was 30 % and 5.4% was for dementia. It was higher in female gender, participants with hypertension, diabetes, depression, physically inactive and increased with age. This was similar to that of study conducted in Africa, where prevalence of cognitive impairment was 33.3%. Robabeh Soleimani et al conducted a survey on 393 elderly persons of age 60 years and above. The study reported 37%

Table 1: Sociodemographic characteristic of participants (n=446)

Demographics	Categories	Frequency (Percentage)
Age	60-69 years	147 (32.9%)
	70 years and above	299 (67.1)
Gender	Male	178 (39.9%)
	Female	268 (60.1%)
Marital status	Married	380 (85.2%)
	Widowed	51 (11.4%)
	Divorced	15 (3.4%)
Education	Illiterate	138 (30.9%)
	Primary	151 (33.9%)
	Secondary	87 (19.5%)
	Graduate and above	70 (15.7)
Employment status	Employed	68 (15.2%)
	Retired	136 (30.5%)
	Unemployed	242 (54.3%)
Living status	With spouse	249 (55.8%)
	Alone	13 (2.9%)
	Joint family	184 (41.3%)
Family history of dementia	Yes	130 (29.1%)
	No	316 (70.9%)

Table 2: Prevalence of risk factors

Risk factors	Frequency	Percentage
Hypertension	Yes	307 (68.8%)
	No	139 (31.2%)
Diabetes	Yes	273 (61.2%)
	No	173 (38.8%)
Obesity	Yes	141 (31.6%)
	No	305 (68.4%)
Smoking	Yes	42 (9.4%)
	No	404 (90.6%)
Physical activity	Yes	127 (28.5%)
	No	319 (71.5%)

Table 3: Factors associated with Mild cognitive impairment

Risk factors	X <sup>2</sup>	P value
Age	66.285	0.005
Gender	15.451	0.003
Hypertension	7.978	<0.001
Diabetes	2.675	0.004
Obesity	7.958	0.316
Smoking	6.858	0.247
Physical activity	1.052	0.001

Figure 1: Flow chart for study participants in the study

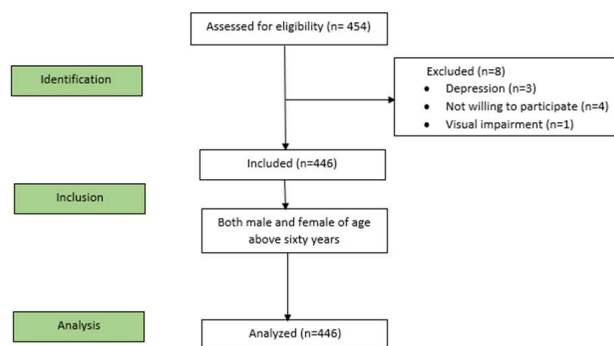


Figure 2: Spectrum of cognitive pattern among study participants (n=446)

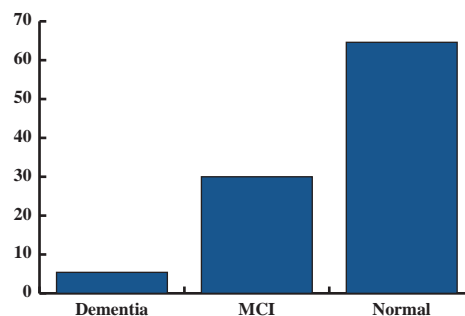
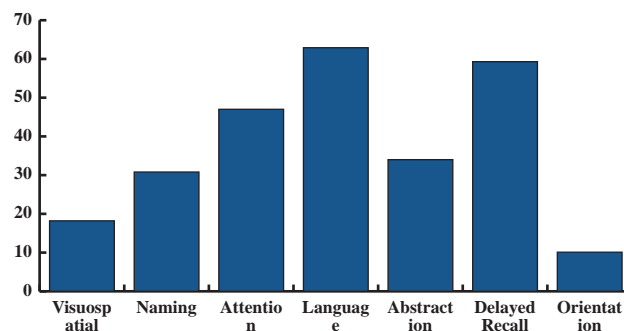


Figure 3: Percentage of MCI patients in various sub scores of MoCA



prevalence of MCI. Moreover, it was observed that females with low education level and participants over 70 years had more cognitive impairment .

Our study results were consistent with a previous study conducted in China, where reported prevalence of cognitive impairment was 30%. They also found that females living alone and belonging to low economic status had increased risk for cognitive impairment. Artero et al conducted a prospective community-based survey in older adults of age 65 years and above. They confirmed that increasing age was the most significant risk factor in the progression from MCI to dementia. Jia et al. in their study observed the prevalence of MCI to be 20.8% and also found that aging was important risk factor for vascular dementia Chinese elderly population.



The present study indicated that physical inactivity was a significant risk factor for mild cognitive impairment among elderly. A previous study conducted in 2017 by Tan et al. found that age related decrease in brain volume and cerebral structures were related to levels of physical activity. They also suggested that this decrease in brain volumes could be prevented by involving elderly in physical activities. The current study has shown that hypertension increases the risk for cognitive problems. Various studies have demonstrated that hypertension is highly associated with the development of ischemic lesions in white matter of brain which results in impaired cognitive function. McDonald et al conducted a five year follow up study in 353 community-dwelling older adults of age 65 years and above. The study concluded that blood pressure variability was significantly associated with impaired cognitive function in older people. Insa Feinkohl et al in their study reported the prevalence of cognitive impairment to be 29.0% in older persons. They also found that cognitive impairment was associated with obesity, hypertension and diabetes, which supports our study results. Qingtao Hou et al in their work reported that abdominal obesity is linked with an increased risk of cognitive impairment in elderly unrelated of conventional sociodemographic, lifestyle, and health-related comorbid factors. current study also revealed that diabetes was also a risk factor that can cause mild cognitive impairment. In another work done by et al concluded that type 2 diabetes myelitis was considered be a risk factor which can progress for MCI into AD. In a work done by et al found that patients with Diabetes at initial develop at severe stages of MCI are more probable to progress towards dementia. They also recommended that patients should be frequently assessed for their cognitive status.

This study may have several limitations. First, this was a cross-sectional study. Due to study design correlations and causal relationships cannot be established. Secondly, the study was conducted only in one setting and so the results of the study were not generalized. Third, in the current study subtypes of mild cognitive impairment were not assessed. Fourth, due to lack of resource neuroimaging studies were not carried out.

#### CONCLUSION:

The current study found prevalence of cognitive impairment to be 35.4% among elderly. Cognitive impairment increases with the increasing age and was more prevalent among females. Hypertension, Diabetes, physical activity was modifiable risk factors for cognitive impairment. Early detection of modifiable risk factors may help health professionals to slow the progression of cognitive impairment to dementia.

#### Authors Contributions:

**Hafsah Gul Khattak:** Designed and Concept, Data collection, Manuscript writing  
**Hafsah Arshad:** Designed and Concept, Statistical Analysis, Interpretation  
**Kinza Anwar:** Literature search, Critical review of Manuscript  
**Qasim Ali:** Data collection, Manuscript writing

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# Current Status of Neurorehabilitation Services in the OIC Countries: Results of an International Online Survey

Zuhaib Hassan, Farooq Azam Rathore, Sermad Mangat

## ABSTRACT

**Objectives:** Neurorehabilitation services are not widely available to most persons with disability (PWD) in the Organization of Islamic Cooperation countries. This study aimed to document status of neurorehabilitation services in OIC countries.

**Study Design and Setting:** Cross-sectional online survey.

**Methods:** Self-administered online survey conducted using Google Forms. Key resource persons for each OIC country working in field of neurorehabilitation were identified from various databases. The questionnaire was emailed to 20 identified resource persons. The response rate was 60% (12/20).

**Results:** Neurorehabilitation services were available in 9 out of 12 surveyed countries. Only 2 countries reported providing access to neurorehabilitation services to 76-100% of their population. Five countries reported less than 25% of population had access to these services. Most commonly available neurorehabilitation services included services for stroke, spinal cord injury, pediatric neurorehabilitation, brain injury, and neuromuscular rehabilitation. Three countries had none of these specialized services. Five countries had neurorehabilitation training programs for physicians and other rehabilitation professionals. Patients had to pay out of pocket for these services in most of surveyed countries, followed by public funding and private insurance. Tele-neurorehabilitation and local disease-specific neurorehabilitation guidelines were not available in most of surveyed countries.

**Conclusion:** Neurorehabilitation services in OIC region are not widely available, with significant variability in availability and quality. There is a need to develop and improve these services. Sharing knowledge and expertise through various forms, such as exchange visits and online sessions, can help improve neurorehabilitation services in these countries.

**Keywords:** Disability management, low middle income countries; online survey; physiotherapy; rehabilitation medicine

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## INTRODUCTION:

Neurological disorders are an important global public health challenge, with an increasing burden of death and disability in the coming decades.<sup>1</sup> Although communicable neurological disorders have declined, mortality has risen by 39%, and disability-adjusted life years have increased by 15% in the past 30 years. There was an estimate that the elderly population would grow from 7 to 65 million by the end of this century, which would increase demands on the health system, including neurorehabilitation.<sup>2</sup> The greatest

burden of neurological disease is in low- and middle-income countries (LIC/LMICs), where an estimated 650 million people with disabilities (PWD) reside, accounting for 65% of the total global disability population.<sup>3</sup> Despite improved care and survival rates, individuals with long-term neurological conditions face physical and functional limitations, psychological issues, loss of productivity and caregiver's burden that require comprehensive management, including rehabilitation, which places an additional strain on healthcare systems that often lack integrated rehabilitation services.<sup>4</sup> Only 5-15% of the people with disability can afford an assistive device.<sup>5</sup> The Organization of Islamic Cooperation (OIC), an intergovernmental organization founded in 1969, comprises 57 Islamic countries,<sup>6</sup> most of which are classified as LMICs or LICs with underdeveloped healthcare systems. Neurorehabilitation programs provide integrated interdisciplinary care that helps PWD achieve and maintain optimal functioning and social reintegration. A standard multidisciplinary neurorehabilitation team consists of various rehabilitation professionals, including Rehabilitation Medicine physicians as team leaders, neurologists, rehabilitation nurses, physical and occupational therapists, speech pathologists, rehabilitation psychologists, social workers, case managers, and other services such as nutrition and respiratory therapy.<sup>7</sup> Each professional

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contributes their expertise to the holistic rehabilitation of PWD. These programs are designed based on the International Classification of Functioning, Disability, and Health (ICF) framework, where activity limitations, participation restrictions, and contextual factors affect functional problems. Interdisciplinary and cross-sectoral efforts are required for neurorehabilitation, involving numerous diverse sectors, professions, and the community to meet patient-centred goals.<sup>8</sup>

Although neurorehabilitation services are well-established in most high-income countries, there is no data on the current status and quality of these services in the OIC region. With a growing and ageing population and an increasing prevalence of major disabling neurological disorders, government commitment to treatment, rehabilitation, and support services for neurologic disorders is crucial. To further explore the challenges and potential solutions in neurorehabilitation in LIC/LMICs, it is essential to understand the unique barriers these countries face. The resources are often limited, and the healthcare infrastructure may not be adequately equipped to handle the complex needs of PWD. Cultural factors, stigma, and lack of awareness about neurological disorders can further impede access to necessary care. In addition, the prevalence of consanguineous marriages in many of these regions contributes to a higher incidence of genetic neurological disorders, compounding the challenge.<sup>9,10</sup>

Investing in research to gather local data on neurological disorders and their impact is crucial for tailoring neurorehabilitation programs to the specific needs of the population in LIC/LMICs. In addition, integrating traditional and community-based rehabilitation methods can provide a more holistic and culturally sensitive approach to care. Such integration not only addresses the medical aspects of disability but also considers the social, economic, and psychological dimensions, facilitating a more comprehensive and effective rehabilitation process.

Therefore, this online global survey aimed to document the availability, details, and types of neurorehabilitation services and training programs in the OIC countries, identifying service gaps and providing a roadmap for future development of neurorehabilitation services in the OIC region. The survey will explore how neurorehabilitation services are integrated within the broader healthcare system, including primary care, specialized neurologic care, and community-based services. It will examine the training and education of healthcare professionals in neurorehabilitation, highlighting areas for improvement and capacity building. The role of technology and innovation in enhancing access to and the quality of neurorehabilitation services in the OIC region will also be a focal point.

#### **METHODOLOGY:**

This study was approved by Ethics Review Committee of the Armed Forces Institute of Rehabilitation Medicine,

Rawalpindi (Case no. 02/2023 dated 16 March 2022). A cross-sectional survey was conducted using a self-administered questionnaire created on Google Forms, a free online tool commonly used for online surveys. The questionnaire consisted of 25 items and four sections. The first section included an informed consent form explaining the aim of the study and ensuring anonymity of participants. The remaining sections included questions related to demographics of disability in the country, availability of general rehabilitation and specialized neurorehabilitation services, details of services, training in neurorehabilitation, availability of local guidelines on neurorehabilitation, and membership in the World Federation for Neurorehabilitation (WFNR). The final question was open-ended, inviting respondents to share their perspectives and views on neurorehabilitation services in the OIC countries.

To identify appropriate resource persons, we explored the national representative and members database of the International Society of Physical and Rehabilitation Medicine (ISPRM)<sup>11</sup> and national society web pages of the WFNR.<sup>11</sup> The email addresses of the concerned persons were noted.

The study was conducted from January 2022 to March 2022. The questionnaire was distributed in the first week of January 2022, and reminders were sent after two and four weeks. Responses received by the first week of February 2022 were downloaded as a Microsoft Excel file. Once the responses were collected and compiled, descriptive statistics were generated for each question in the survey. Frequencies and percentages were used to describe the responses to the closed-ended questions, which included questions related to the availability of general and specialized neurorehabilitation services, details of services, training in neurorehabilitation, availability of local guidelines on neurorehabilitation, and membership of the World Federation for Neurorehabilitation.

#### **RESULTS:**

Key resource persons were identified in 20 out of 57 OIC countries, and 12 of them responded to the survey, resulting in a response rate of 60%. The respondents' current designations varied, with most being associate professors, professors, and heads of departments. Rehabilitation services were reported to be available in all countries, but specialized neurorehabilitation services were only available in 10 countries, with Afghanistan, Benin, and Cameroon reporting their absence. Among the specialized neurorehabilitation services, stroke rehabilitation was available in ten countries, followed by spinal cord injury rehabilitation and pediatric rehabilitation in 8 countries, neuromuscular rehabilitation and traumatic brain injury rehabilitation in 7 countries, and multiple sclerosis rehabilitation in five countries. Three countries reported not having any of these specialized services.

Training programs in neurorehabilitation were available in

11 out of 12 countries, with a percentage of 84.1%. These training programs were available for both PMR physicians and rehabilitation professionals in five countries, only for rehabilitation professionals in three countries, and only for PMR physicians in two countries.

Access to neurorehabilitation services varied across the countries that reported their presence. Only two high-income countries reported 100% access, while less than 25% of the population had access in some countries. In countries where the service is accessible, the range of access was from 26-75%. A professional neurorehabilitation organization was present in nine countries, but most of these organizations were not members of the WFNR. In most countries, rehabilitation medicine physicians were primarily responsible for delivering the neurorehabilitation services, while in some countries, physiotherapists and occupational therapists had the primary responsibility.

The neurorehabilitation services are expensive and many neurological diseases (e.g., multiple sclerosis, motor neuron disease, chronic progressive polyneuropathy) require lifelong services. It can pose a significant economic burden on the patients, their family, public resources and government. The financial cost of providing neurorehabilitation services in this survey varied among different countries, with out-of-pocket expenses by patients being the most common in most countries (10/12), followed by government funding in eight countries and availability of private insurance in six countries. Philanthropic support for these services was available in three countries. (Fig 1).

Different models of neurorehabilitation service delivery include day service, in-patient or outpatient service, virtual, and home service.<sup>13</sup> Most countries (11/12) provided these services as both in-patient and out-patient services, with five countries offering day services. Indonesia and Malaysia had community-based neurorehabilitation services.

Multidisciplinary neurorehabilitation teams are preferred due to their comprehensive care models. In all countries, physical therapists were available, and rehabilitation medicine physicians, occupational therapists, prosthetists, and orthotists, and social workers were available in 11 countries. (Fig 2)

Teleconsultation services for neurorehabilitation were available in only four countries (Pakistan, Bangladesh, Turkey, and Morocco) out of 12, and were not available in the remaining eight countries.

**DISCUSSION:**

In this study, we aimed to assess the availability and quality of neurorehabilitation services, mode of delivery, funding methods, access of population, and training structures for healthcare professionals in OIC countries. The survey found that there are significant disparities in the availability and quality of neurorehabilitation services among OIC member states. While some countries offer advanced and

Figure 1: Funding Sources for Neurorehabilitation Services

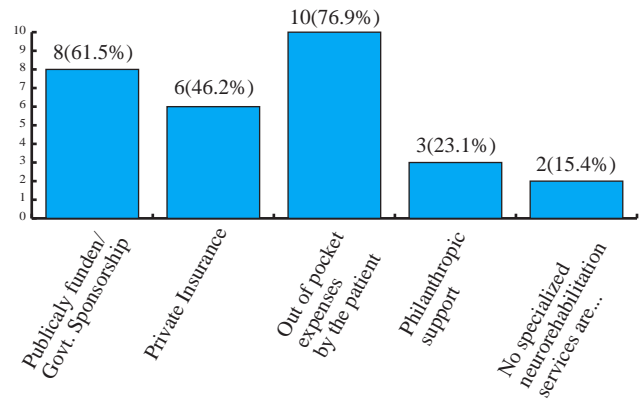
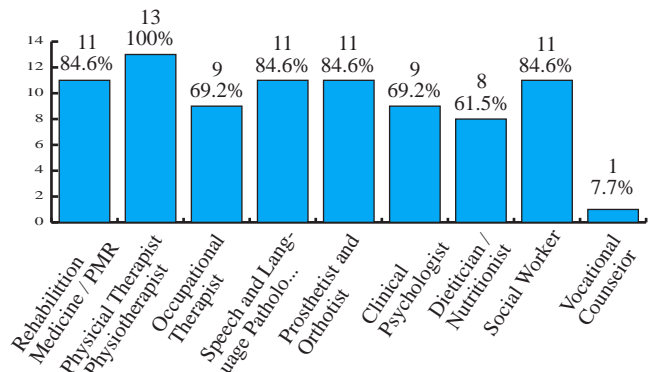


Figure 2: Rehabilitation Team Members Available in the OIC countries



comprehensive services, others lack basic facilities and resources.

While all survey respondents reported the availability of neurological rehabilitation services in their respective countries, the neurorehabilitation services were not comprehensive, highlighting a significant gap in the availability of care for PWD having long term neurological disabilities. National development policies in many LMIC countries have not adequately addressed the concerns of PWD, resulting in a lack of appropriate healthcare services.<sup>14,15</sup> Geberemichael and colleagues have highlighted that in the African region (with all countries classified as LIC/LMIC) , rehabilitation services face significant challenges due to limited political commitments and stakeholder collaborations. Similar challenges have been reported from Bangladesh.<sup>16</sup> Scarce infrastructures and expertise further exacerbate the situation, leading to poorly coordinated efforts. Additionally, community-based rehabilitation programs suffer from fragmentation and lack effective partnerships with healthcare systems.

The survey found that nearly 40% of the study participants reported that only 25% of the total population in OIC countries had access to specialized neurorehabilitation services. The likely reasons for this lack of access may include high treatment costs, lack of public awareness, limited funding, and a scarcity of qualified rehabilitation professionals. While stroke rehabilitation services were

available in most countries, the number of patients who received rehabilitation services following a stroke was alarmingly low.

Training in neurorehabilitation was available in 76.9% of the countries surveyed. Based on the authors experience the training in different OIC and developing countries varies and there are significant variations among different parts of the country. For example, in Pakistan some centres are well equipped and have an adequate infrastructure to offer a comprehensive fellowship training for Rehabilitation Medicine.<sup>17</sup> Whereas some other centres lack many important components of post graduate training. However, it is important to consider that training at the post graduate level alone is not sufficient to address the current gaps in neurorehabilitation services. It is crucial to establish include rehabilitation medicine in undergraduate medical education in the country.

One essential tool that has proven invaluable in developed countries is the establishment of disease registries, which systematically collect data on the prevalence and characteristics of neurological conditions.<sup>18,19</sup> These registries play a pivotal role in enhancing research, understanding disease patterns, and guiding healthcare policies. However, in contrast, many developing countries including the OIC countries lack such comprehensive disease registries, which limits their ability to gather accurate and up-to-date information on local neurological diseases. To bridge this gap and promote equitable access to quality care, it is essential for developing nations to prioritize the establishment of national registries, gathering essential data about the prevalence of neurological disorders and identifying potential variations in their presentations. By implementation of disease registries, these countries can empower their healthcare systems, foster research collaboration, and ultimately improve the neurorehabilitation outcomes for individuals with neurological diseases.

Telerehabilitation has emerged as a transformative approach to bridging the gap in accessing neurorehabilitation services for individuals facing neurological diseases.<sup>20</sup> With a structured effort, telemedicine can facilitate convenient and remote access to specialized care, providing much-needed support to the population in need. This innovative approach enables individuals to receive essential rehabilitation services from the comfort of their homes, overcoming geographical barriers and enhancing the overall accessibility of healthcare.<sup>21</sup> In the developed world, telerehabilitation has already been well established and proven its effectiveness in improving patient outcomes and reducing healthcare disparities.<sup>22</sup> However, in the developing countries, the potential of telerehabilitation remains largely untapped, leaving a significant gap in accessing neurological care for millions of individuals. It is imperative for these nations to recognize the importance of implementing and expanding telemedicine services to meet the growing demand for neurorehabilitation, thereby ensuring equitable and comprehensive care for all

individuals regardless of their geographical location. By embracing telerehabilitation, developing countries can empower their healthcare systems, optimize resources, and offer a lifeline of hope to those in need of neurological care. There are some important limitations of this survey. We were able to reach out to 20 countries and document data from 12 countries only which is less than quarter of the current membership of OIC (57 countries). The data presented represent the view of only one key individual from each country and we did not ask for detailed data and references to support the responses. Respondents filled out a self-report questionnaire, so there is the possibility of incorrectly understanding of the question or misconceptions about their practice. The study design and sample size did not allow for statistical inference, which means that the findings cannot be generalized to the entire OIC region. Rather, the results of this study provide a snapshot of the availability and quality of neurorehabilitation services in the countries that participated in the survey and can be used to identify gaps and areas for improvement in neurorehabilitation services in these countries. Despite these limitations, the current survey is the first formal documentation of the presence, scope, and types of the neurorehabilitation services in the OIC countries. If availability of services is catered for, it can reduce the burden of disability globally. To address the rapidly growing burden of neurological disorders in LMICs, action must be taken at the personal, organizational, governmental, and international levels. It is crucial to establish strong political support, appropriate policies, and good governance for rehabilitation at local, national, and regional levels for efficient service delivery and positive rehabilitation outcomes.

#### **CONCLUSION:**

The results of this international online survey shed light on the current state of neurorehabilitation services in OIC countries. The survey found that there are significant disparities in the availability and quality of neurorehabilitation services among OIC member states. While some countries offer advanced and comprehensive services, others lack basic facilities and resources. The survey also highlighted a shortage of trained professionals in the field of neurorehabilitation, with many countries reporting a lack of specialized physicians, therapists, and nurses. This shortage can have a significant impact on the quality of care provided to patients and may hinder their recovery and rehabilitation.<sup>23</sup>

The findings of the survey underscore the urgent need for greater investment in neurorehabilitation services in OIC member states. This investment should prioritize the development of specialized training programs for healthcare professionals and the establishment of comprehensive and accessible neurorehabilitation facilities. By addressing these issues, OIC member states can provide better care for individuals living with neurological conditions and improve their quality of life

**Authors Contributions:**

**Zuhaib Hassan:** Data analysis, literature review, critical revision and final approval of the version to be published  
**Farooz Azam Rathore:** Conception, data acquisition, drafting work and final approval of the version to be published  
**Sermad Mangat:** Data analysis, literature review, critical revision and final approval of the version to be published

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## Assessment of level of Burnout among Health Professionals in Lahore, Pakistan

Shehnaz Khan, Noor Shahid, Mehrunnisa Hassan

### ABSTRACT

**Objectives:** The prime objective of this study is to assess the level of burnout among healthcare professionals using BAT tool. Also, the association of job satisfaction and workload factors is tested with burnout.

**Study Design and setting:** A cross-sectional multi-centered study in Lahore during the month of August 2022 to Jan 2023. The data was collected from healthcare professionals in three tertiary care hospitals in Lahore.

**Methodology:** The data was collected from clinicians and staff nurses. The required sample size was calculated as 172. Data was collected using Burnout Assessment Tool (BAT) proposed by Schaufeli (2020). BAT was initially proposed with 33 items. BAT-S was the proposed 33-item version with four core dimensions and two secondary dimensions. The average score for each dimension was calculated and interpreted as given by Schaufeli in user manual for BAT-S.

**Results:** Exhaustion was high among 55.8% of the participants. Mental distance was high among 34.3% of the participants whereas it was normal among 46.5%. Nearly 90% of the participants were satisfied from their jobs, committed to their jobs and accept responsibilities. Job satisfaction was significantly associated with burnout level. Lack of organizational influence and poor internal communication were statistically significantly related with level of burnout.

**Conclusion:** The study was conducted to highlight the level of burnout among healthcare professionals. We found that very high level of burnout was observed in cognitive impairment followed by emotional impairment. The average level of burnout was more common among participants with job satisfaction and good internal communication.

**Keywords:** Burnout, healthcare, stress, risk factor

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### INTRODUCTION:

Healthcare industry is no different than other professions in posing multiple pressures on health care professionals. These include a myriad of problems from meeting time restraints to lack of control over work processes, trying relationships and incompatibility with seniors, challenging demands, not to mention the strains of clinical work.<sup>1</sup>

Burnout can occur in any career but is predominantly seen in health-care workers especially in perioperative clinicians.<sup>2</sup>

Freudenberger first defined burnout as an occupational phenomenon in 1974 in his research on volunteers in a free medical clinic due to indeterminable continuous job stress.

It is manifested as frustration, annoyance, anger, distrust, suspicion about colleagues' influence on one's own professional desires, excessive inflexibility in practice and symptoms of depression.<sup>3</sup>

In emotional exhaustion, one experiences fatigue in interacting with other people and feels drained emotionally. In depersonalization, the subject becomes unsympathetic and uncaring towards patients whom he is supposed to look after in terms of service or care, while there is a feeling of lack of accomplishment and incapability towards a relationship with people in reduced personal accomplishment.<sup>4</sup>

Another reason cited as leading to burnout is the electronic health record, which works as a double-edged sword. Rather than facilitating one in managing records it hinders clinical documentation of records, imposes time constraints and decreases usability leading to frustration and burnout.<sup>5</sup>

National research conducted on US physicians over a period of six months, showed that 38.8% of participants experienced high emotional exhaustion, 27.4% depersonalization, and 44.0% had one symptom of burnout in their career.<sup>6</sup>

Stressful medical conditions aggravate burnout even more as can be seen in a study conducted in China during the Covid -19 outbreak where the prevalence of depression in public health workers was recorded as 21.3%, anxiety as

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19%, and poor self-rated health as 9.8% respectively. It was rated as 27.1%, 20.6% and 15% for depression, anxiety and poor self-rated health in CDC (center for disease control) workers respectively. The results for PHI workers (protected health information) were 17.5% for depression, 17.9% for anxiety and 6.8% for self-rated health.<sup>7</sup>

A study conducted in India to systematically review prevalence of burnout among health care professionals showed a collective prevalence of emotional exhaustion of burnout as 24%, depersonalization as 27% and poor personal accomplishment as 23%. Females, young age, being single, and tough working conditions were associated with a bigger risk of burnout.<sup>8</sup> More than half of the post-graduate residents working at The Children's Hospital in Lahore suffered from moderate to severe burnout and 9% had elevated personal and patient related burnout.<sup>9</sup>

Physician burnout is a documented workplace hazard and carries a risk to the societal and professional lives of the health care workers. Therefore, it should be dealt with proactively by running helpful interventions at individual and institutional levels. Improvement in burnout could be achieved by adopting a healthy lifestyle, with enough sleep, balanced diet and some form of exercise. Provision of a conducive work environment would benefit victims of burnout additionally.<sup>10</sup>

The rationale of the study is to observe the factors that are responsible for burnout among healthcare professionals so that the probability of occurrence of these factors can be either fully controlled or minimized. This will facilitate healthcare professionals to work in a stress-free environment. The prime objective of this study is to assess the level of burnout among healthcare professionals i.e. doctors and nurses and to observe those factors that promote burnout at workplace.

#### **METHODOLOGY:**

A cross-sectional multi-centered study was conducted in three tertiary care hospitals in Lahore during the month of August 2022 to Jan 2023. The data was collected from clinicians and staff nurses. The required sample size was calculated as 172 using WHO sample size calculator with 95% confidence coefficient and 12.8% prevalence of severe burnout among healthcare professionals.<sup>11</sup> Doctors and nurses who were working at any hospitals among the three irrespective of age and working experience were included in the study. Paramedic staff other than nurses irrespective of gender were excluded from the study. The data was collected using non-probability convenient sampling technique. BAT-S was filled by interview method from each participant. Nurses or doctors who fulfil the inclusion criteria were asked the items contained in BAT-S and responses were recorded.

Data was collected using Burnout Assessment Tool (BAT) proposed by Schaufeli (2020).<sup>12</sup> BAT was initially proposed

with 33 items. BAT-S was the proposed 33-item version with four core dimensions and two secondary dimensions. BAT-C was 23-item version with only four core dimensions named as exhaustion, mental distance, emotional impairment and cognitive impairment. The secondary dimensions were psychological complaints and psychometric complaints. The responses were measured on five-point likert scale. We included few socio-economic and demographic factors and some other factors found responsible for burnout in the literature. These factors include job satisfaction, decision making power, hierarchy problems, superiority issues and administrative constraint. The average score for each dimension was calculated and interpreted as given by Schaufeli in user manual for BAT-S. The interpretation of average scores of these dimensions is given in Table 1.

The study was approved from Institutional Review Board (IRB) Central Park Medical College with reference number CPMC/IRB-No/1363. The informed consent was obtained prior to the data collection. The objectives of the study were first explained to the participant and their participation will be voluntary with no harmful effects to their jobs. Responses are given in the form of frequency and percentages. Test of association was applied to observe the association of level of burnout with other factors. Data analysis was carried out using SPSS 26.0.

#### **RESULTS:**

The data was collected from 172 participants working at three tertiary care hospitals. The mean age of the participants was 29.20 + 6.60 SD (years). Around 116 (67.4%) of the participants were female. Remaining 56 (32.6%) were male. The educational level of 108 (62.8%) of the participants was graduation or less. Remaining 64 (37.2%) of the participants were post-graduated or above. Around 147 (85.5%) of the participants were from public sector. About 106 (61.6%) of the participants were doctor and remaining 66 (38.4%) were nurses. Nearly 111 (64.5%) of the participants had work experience of 1-5 years followed by 44 (25.6%) of the participants with 5-10 years as working experience. Among the remaining participants, 11 (6.4%) had 10-20 years and 06 (3.5%) had more than 20 years of working experience. Socio-economic class of the participants was assessed by considering number of family members. About 76 (44.2%) of the participants fall in low-socio-economic class where the average household income was not enough for the number of family members. Out of the remaining participants, 51 (29.7%) belong to above average socio-economic class.

The level of burnout can be assessed by observing the average total score, score of exhaustion, mental distance, emotional impairment, cognitive impairment and secondary symptoms. About more than half of the participants had normal total score. Exhaustion was high among 55.8% of the participants. Mental distance was high among 34.3% of

Table 1: BAT -33 scoring for Flemish employees

	Total core	Exhaustion	Mental distance	Emotional Impairment	Cognitive Impairment	Secondary symptoms
Low	1.00 – 1.60	1.00 – 1.75	1.00 – 1.20	1.00 – 1.20	1.00 – 1.80	1.00 – 1.70
Average	1.61 – 2.40	1.76 – 2.70	1.21 – 2.40	1.21 – 2.19	1.81 – 2.59	1.71 – 2.75
High	2.41 – 3.29	2.71 – 3.74	2.41 – 3.59	2.20 – 3.19	2.60 – 3.39	2.76 – 3.50
Very High	3.30 – 5.00	3.75 – 5.00	3.60 – 5.00	3.20 – 5.00	3.40 – 5.00	3.51 – 5.00

Table 2: Frequency (Percentage) of level of burnout of BAT

BAT	Level of Burnout			
	Low	Average	High	Very high
Total score	17	91	51	13
Exhaustion	22	38	96	16
Mental distance	18	80	59	15
Emotional impairment	29	79	44	20
Cognitive impairment	79	33	37	23
Secondary symptoms	-	136	27	09

Table 3: Crosstab of level of burnout and other risk factors

Factor	Categories	Total score				Total	p-value
		Low	Average	High	Very High		
Job Satisfaction	Yes	17	86	42	09	154	<0.001*
	No	0	05	09	05	18	
Commitment to the job	Yes	16	84	46	09	155	0.07
	No	01	07	05	04	17	
Accepting responsibilities	Yes	17	87	42	10	156	0.01*
	No	0	04	09	03	16	
Lack of freedom to make decisions	Yes	03	31	24	05	63	0.15
	No	14	60	27	08	109	
Lack of organizational influence	Yes	02	34	24	07	67	0.05*
	No	15	57	27	06	105	
Few opportunities to participate	Yes	04	41	29	06	80	0.12
	No	13	50	22	07	92	
Hierarchy problems	Yes	03	26	23	04	56	0.11
	No	14	65	28	09	116	
Poor internal communication	Yes	02	12	20	04	38	<0.00*
	No	15	79	31	09	134	
Administrative constraint	Yes	08	29	21	07	65	0.56
	No	09	62	30	06	107	
Pressure from superiors	Yes	03	30	20	07	60	0.18
	No	14	61	31	06	112	

\*p-value <= 0.05 i.e. Statistically significant

the participants whereas it was normal among 46.5%. Secondary symptoms were more normal as compared to other scales (Table 2). Nearly 90% of the participants were satisfied from their jobs, committed to their jobs and accept responsibilities. About 22.1% of the participants felt poor internal communication at their workplace. Around one-third of the participants said that they lack the freedom to make decisions, lack of organizational influence, felt hierarchy problems, administrative constraints were there and pressure from superiors.

Job satisfaction was significantly associated with burnout level. The level of burnout was higher among participants who accept responsibilities. Lack of organizational influence and poor internal communication were statistically significantly related with level of burnout (Table 3). In our sample, average level of burnout was relatively more common among participants without poor internal communication.

#### **DISCUSSION:**

We used the BAT inventory 33-items to assess the level of burnout among healthcare professionals. The BAT-S inventory based on 33 items was five-dimension scale names as exhaustion, mental distance, cognitive impairment, emotional impairment and secondary symptoms which was a combination of psychological complaints and psychometric complaints. In the past literature burnout has been assessed by using Maslach Burnout Inventory (MBI) with 22-items and three sub-dimensions.<sup>14</sup> MBI has been used to assess burnout among healthcare professionals.<sup>15</sup> The three dimensions of MBI was emotional exhaustion, depersonalization and personal accomplishment.<sup>14</sup> The cut-off for various level of burnout was given in the literature.<sup>16</sup> However, BAT was proposed to observe the level of burnout among working or non-working participant. Its core dimensions were different from MBI. In Pakistan, no study has been conducted to assess the burnout using BAT inventory.

In our study, we observed that average burnout was common for mental distance, emotional impairment and secondary symptoms whereas the high level of burnout can be seen for exhaustion among healthcare professionals. Exhaustion was considered an important condition of burnout. However, it was not sufficient to declare burnout. Practitioners considered cognitive and emotional impairment as the core dimension of burnout.<sup>12</sup>

In our study, we find that few opportunities to participate followed by hierarchy problems were the challenges and mostly responsible for burnout. We explored the association of level of burnout with organizational factors. We found that job satisfaction, internal communication, organizational influence and accepting responsibilities were the associated factors.

In the past literature, various factors were seen as responsible for the development of burnout. Organizations stressors were responsible for the existence of burnout.<sup>17</sup> Imbalance between demand and resources obtained from work were responsible for burnout.<sup>18</sup> Demand at job was based on requirement of sustained mental and physical efforts. These were found to be associated with specific psychological cost such as lack of focus or concentration, task requirements and subjective fatigue.<sup>19-20</sup> Growth and development of burnout has been linked with emotional contagions both in or outside the workplace.<sup>21-22</sup> Workload, whether it is qualitative or quantitative, requires sustained efforts and can create costly physiological and psychological impact that results in the experience of burnout.<sup>23</sup>

In the current study, we observed that lack of freedom to make decisions was insignificantly associated with the level of burnout. Higher level of burnout was seen among participants who do not have the power to make decisions. Lack of decision-making power and instability to influence decisions were positively associated with higher level of burnout.<sup>23</sup> Similarly, it was seen workers with more empowerment at work were more likely to have low level of burnout.<sup>24-25</sup>

Pressure from superiors were insignificantly associated with level of burnout. Inappropriate supervision increases the odds of developing burnout.<sup>21</sup> We observed that internal communication was linked with level of burnout. In a past study, social support was considered as a brake for the growth or development of burnout.<sup>26</sup> Various organization factors were found in the current investigation responsible for burnout. However, still there is a need to explore more about in association with demographic factors.

#### **CONCLUSION:**

The study was conducted to highlight the level of burnout among healthcare professionals. For this, BAT-S inventory was used with 33-items to assess the level of burnout among healthcare professionals that access burnout for five-dimension names as exhaustion, mental distance, cognitive impairment, emotional impairment and secondary symptoms which was a combination of psychological complaints and psychometric complaints. We found that high level of burnout was observed among participants due to exhaustion. Average level of burnout was found due to mental distance, emotional impairment and secondary symptoms. The average level of burnout was more common among participants with job satisfaction and good internal communication. Job satisfaction was significantly associated with burnout level. So that it was observed that the participants who were satisfied with their jobs were more likely to have average level of burnout. Internal communication was also significantly associated with level of burnout.

**Authors Contributions:**

**Shehnaz Khan:** Study Design, data collection and Supervision of study

**Noor Shahid:** Write-up, Data Entry and Analysis, Interpretation

**Mehrunnisa Hassan:** Drafting, Data collection and Proof Reading

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# Clinical Characteristics, Prognostic Factors and Outcomes of Paediatric Patients with Haemophagocytic Lymphohistiocytosis

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## ABSTRACT

**Objective:** Haemophagocytic lymphohistiocytosis (HLH) is a multi-system autoimmune disorder. The objective of this study was to find out the clinical characteristics and prognosis of paediatric patients with Haemophagocytic Lymphohistiocytosis.

**Study Design and setting:** Cross sectional study conducted at Pak Emirates Military Hospital, Rawalpindi from July 2021 to June 2023.

**Methodology:** Children with diagnosis of HLH were assessed by including patients who were aged = 13 years during hospitalization. All the patients who had not been diagnosed by using the HLH-2004 criteria were disqualified. Relevant findings were noted by evaluating records pertinent to physical examination, radiology and laboratory markers. Prognosis was assessed by determining the underlying clinical aetiology and whether patient-related factors modulated the overall life expectancy.

**Results:** A total of 32 patient records were evaluated. Mean age at diagnosis was  $44.3 \pm 39.1$  months (Range: 1-132 months) with majority being males [n=23 (71.9%)]. The common clinical characteristics included fever [n=29 (90.6%)], lymphadenopathy [n=27 (84.4%)], splenomegaly [n=23 (71.9%)] and hepatomegaly [n=23 (71.9%)]. Serum ferritin, bilirubin, ALT, AST, and LDH were also raised. All patients were followed for a mean period of 12 months and 18 (56.3%) children failed to survive. Negative prognostic indicators included severe anaemia (p=0.001), neutropenia (p=0.007), thrombocytopenia (p=0.033), and hyperferritinemia (p<0.001). Elevation of liver enzymes (ALT: p<0.001; AST: p=0.031), serum bilirubin (p=0.037), and LDH (p<0.001) also indicated worse disease prognosis.

**Conclusion:** HLH in childhood is a potentially life-threatening disease and carries a significant association with deranged liver function.

**Keywords:** HLH, Liver enzymes; Prognosis; Clinical characteristics

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## INTRODUCTION

Haemophagocytic lymphohistiocytosis (HLH) is characterized as an autoimmune, multisystem disorder, the pathogenesis of which is mediated by a myriad of cytokines including interferon-gamma (IFN- $\gamma$ ), interleukin-2 (IL-2), and tumor necrosis factor-alpha (TNF- $\alpha$ ), that eventually leads to hyper activation of immune system.<sup>1</sup> Persistent and abnormal activation of CD8+ T-lymphocytes and resulting mediators of inflammation are the key mechanism of pathogenesis. Paediatric HLH can either be genetic ( due to familial or immunodeficiency related syndromes resulting from diverse range of genetic pathologies) or acquired. In addition to the role of genetic mutations in mediating the pathogenesis of familial HLH variants i.e., Perforin (PRF1), Munc13-14 (UNC13D), Syntaxin 11 (STX11) and Syntaxin binding protein 2 (STXBP2)<sup>2</sup>, genetic alterations can also be associated with secondary HLH that is seen in Chediak-Higashi syndrome (CHS), Griscelli syndrome and X-linked lymphoproliferative disorders. Infections such as Epstein-Barr virus (EBV) and other herpesviruses, Bacterial, fungal and protozoan infections have also been attributed to the pathogenesis of Secondary HLH.<sup>3,4</sup> Secondary HLH can

also rarely secondary to inborn error of metabolism and drugs such as phenytoin. It is also noteworthy that up to 40% cases of paediatric HLH can arise secondary to systemic infections.<sup>5</sup>

Although paediatric HLH can be manifested at any point during childhood, the condition predominantly impacts children during the initial 18 months of life. Paediatric HLH is marked by a diverse spectrum of clinical manifestations. Depending upon the age at the time of diagnosis, a child may encounter a febrile illness and hepato-splenic enlargement. Characteristic haematological findings include bicytopenia, or even pancytopenia. The reduction in cell counts arises due to the classical feature of haemophagocytosis which potentiates hepatosplenomegaly and widespread lymphadenopathy.<sup>6,7</sup> A few notable biochemical abnormalities include markedly raised triglyceride and ferritin levels associated with significant hypoproteinaemia.<sup>7</sup> Clinical and laboratory criteria have been formulated which includes fever, splenomegaly, cytopenias in two or more lineages (ANC  $<1 \times 10^9$  /L, Hb  $<9$ g/dl or  $<12$ g/dl if age is less than 4 weeks and platelets  $<100 \times 10^9$  /L), Hypertriglyceridemia and/ hypofibrinogenaemia (TG  $>3$ mmol/L, Fibrinogen  $<1.5$ g/dl), Ferritin above 500 ug/L, sCD25  $>2400$ /ml, decreased or absent NK cell activity and evidence of Haemophagocytosis in BM, CSF or LN. Of these 5 out of 8 criterias are required to make diagnosis of HLH.<sup>8</sup> Zhou et al., (2022) have identified a high mortality rate among children, with up to 30% patients dying during the 30-day period following disease onset.<sup>9</sup> Although patient outcomes can be substantially improved through timely diagnosis and provision of critical care, a lot of factors can potentially modulate the overall prognosis of paediatric HLH. In adults, these novel factors include haematological markers, biochemical indicators and background of malignancy-associated HLH. Nonetheless, prognostic data regarding paediatric HLH is rather inadequate.<sup>10</sup>

Given the diminished survival rates observed in HLH<sup>11</sup>, it is imperative to generate a better know-how pertaining to prognostic markers of the disease. In turn, this data can allow clinicians to carry out an efficient prediction of adverse outcomes in childhood HLH and initiate timely treatment. In line with this, the current study was designed to assess the clinical manifestations, prognostic factors, and clinical outcomes of paediatric patients with HLH.

#### **METHODOLOGY:**

The study was organised as a cross-sectional analysis of paediatric cases of HLH and was conducted at Pak Emirates Military Hospital, Rawalpindi. The authors analysed paediatric HLH patients spanning over a period 02 years from July 2021 to June 2023. Data collection, statistical analysis, and report writing were carried out for a period of 03 months from Sep 2023 to Dec 2023. Patients were incorporated into the study by using convenience sampling.

**Inclusion Criteria:** Diagnosed patients of HLH who were aged = 13 years at the time of hospital admission, and had been diagnosed with haemophagocytosis using the HLH-2004 criteria were included in the study. As per HLH-2004, patients had to meet the following diagnostic parameters for HLH: (A) HLH confirmation by genetic analysis or (B) Five out of the following eight criteria have to be fulfilled: (1) Temperature =  $38.5^\circ\text{C}$ ; (2) Splenomegaly; (3) Anemia / Neutropenia / Thrombocytopenia; (4) Hypertriglyceridemia  $>3$ mmol/L and/or hypofibrinogenemia ; (5) Histological evidence of haemophagocytosis in bone marrow, lymph nodes, spleen, or liver; (6) Low or absent natural killer cell activity; (7) Serum ferritin raised above 500 ng/mL; (8) Elevated soluble CD25 (soluble IL-2 receptor alpha) = 2,400 U/mL.<sup>12</sup>

**Exclusion Criteria:** Those paediatric patients whose clinical records indicated only a marked clinical suspicion for HLH without implementing the HLH-2004 criteria, were excluded from the study. Moreover, the patients who could not be contacted to evaluate clinical outcomes were eliminated from the study.

Two separate authors investigated the eligible clinical records for extracting information pertinent to the clinical characteristics, prognostic indicators, and outcomes associated with HLH. With regard to clinical characteristics, patient findings confirmed by physical examination, diagnostic imaging, and laboratory markers were noted. Prognosis was assessed by determining the underlying aetiology of HLH (malignant vs. non-malignant) and whether factors including laboratory markers or childhood malignancy significantly modulated the overall outcome. In addition, clinical outcomes were evaluated by estimating the cumulative mortality rate. Patient survival time was defined as the interval from the point of first admission to the point of subsequent contact during data analysis.

The authors in-charge of data entry and analysis strictly followed the ethical charter set by the Helsinki protocol while the study was also conducted after approval from the institutional review board (ERC no: A/29/EC/414/2022). Statistical analysis was conducted by utilizing IBM Statistical Package for Social Sciences (SPSS) 23.0. The mean  $\pm$  SD values were calculated for quantitative variables including patient age, follow-up intervals, and laboratory values. The independent t-test and the chi-square ( $\chi^2$ ) test were applied to evaluate the statistical correlation of data. A p-value  $<0.05$  was considered significant.

#### **RESULTS:**

A total of 32 eligible cases were accessed and incorporated into the study. Mean age of the participants was  $44.3 \pm 39.1$  months [Range: 1-132 months]. The majority of children were males [n=23 (71.9%)]. The most prevalent clinical characteristics included fever [n=29 (90.6%)], lymphadenopathy [n=27 (84.4%)], splenomegaly [n=23

(71.9%)), and hepatomegaly [n=23 (71.9%)] (Table-2). In terms of haematological parameters, mean haemoglobin levels were  $8.7 \pm 2.4$  g/dL, mean neutrophil count was  $0.6 \pm 0.2 \times 10^3/\text{mm}^3$ , and mean platelet count was equivalent to  $89 \pm 63.0 \times 10^3/\text{mm}^3$ . Serum ferritin levels were significantly elevated at  $3910 \pm 3018$  ng/mL. Serum albumin levels were found in the lower range i.e.,  $2.8 \pm 0.6$  g/dL. As a marker of coagulopathy, mean patient INR was estimated to be  $1.3 \pm 0.4$ . In addition to liver function, liver biochemistry was also found to be deranged with significantly elevated bilirubin

Table-1. Demographic, Clinical, and Aetiological Parameters of Paediatric HLH

Patient-related parameters (n = 32)		Statistical Value	
Demographic variables	Age in months (Mean $\pm$ SD)	44.3 $\pm$ 39.1	
	Gender	Male [n (%)]	23 (71.9%)
		Female [n (%)]	9 (28.1%)
Clinical characteristics	Fever [n (%)]	29 (90.6%)	
	Splenomegaly [n (%)]	23 (71.9%)	
	Hepatomegaly [n (%)]	23 (71.9%)	
	Jaundice [n (%)]	18 (56.3%)	
	Lymphadenopathy [n (%)]	27 (84.4%)	
Clinical aetiology of HLH	EBV infection [n (%)]	12 (37.5%)	
	Non-EBV infection [n (%)]	14 (43.8%)	
	Malignancy [n (%)]	6 (18.8%)	

EBV: Epstein-Barr Virus

Table-2. Laboratory-based Parameters of children with HLH

HLH Laboratory Markers	Statistical Value (Mean $\pm$ SD)
Haemoglobin (g/dL)	8.7 $\pm$ 2.4
Neutrophil Count ( $\times 10^3/\text{mm}^3$ )	0.6 $\pm$ 0.2
Platelet Count ( $\times 10^3/\text{mm}^3$ )	89 $\pm$ 63.0
Ferritin (ng/mL)	3910 $\pm$ 3018
International Normalized Ratio (INR)	1.3 $\pm$ 0.4
Albumin (g/dL)	2.8 $\pm$ 0.6
Bilirubin (mg/dL)	3.5 $\pm$ 3.4
Alanine transaminase (ALT; IU/L)	186.0 $\pm$ 170.7
Aspartate transaminase (AST; IU/L)	136.9 $\pm$ 108.3
Lactate dehydrogenase (LDH; IU/L)	434.2 $\pm$ 329.1

Table-3. Determinants of Clinical Prognosis in Paediatric HLH

Prognostic Indicators		Mortality (n=18)	No mortality (n=14)	p-value
Demographic variables	Age in months (Mean $\pm$ SD)	47.4 $\pm$ 43.4	40.2 $\pm$ 33.8	0.612
	Gender	Male [n (%)]	11 (34.3%)	0.457
		Female [n (%)]	6 (18.8%)	
Clinical characteristics	Fever [n (%)]	16 (50%)	13 (40.6%)	0.702
	Splenomegaly [n (%)]	13 (40.6%)	10 (31.3%)	0.960
	Hepatomegaly [n (%)]	13 (40.6%)	10 (31.3%)	0.960
	Jaundice [n (%)]	9 (28.1%)	9 (28.1%)	0.419
	Lymphadenopathy [n (%)]	15 (46.9%)	12 (37.5%)	0.854
Clinical aetiology	EBV infection [n (%)]	6 (18.8%)	6 (18.8%)	0.581
	Non-EBV infection [n (%)]	7 (21.9%)	7 (21.9%)	0.530
	Malignancy [n (%)]	5 (15.6%)	1 (3.1%)	0.138
Laboratory markers (Mean $\pm$ SD)	Haemoglobin (g/dL)	7.6 $\pm$ 2.0	10.2 $\pm$ 2.1	0.001*
	Neutrophil Count ( $\times 10^3/\text{mm}^3$ )	0.5 $\pm$ 0.2	0.7 $\pm$ 0.2	0.007*
	Platelet Count ( $\times 10^3/\text{mm}^3$ )	65.6 $\pm$ 26.6	119.1 $\pm$ 82.3	0.033*
	INR	1.3 $\pm$ 0.3	1.4 $\pm$ 0.4	0.392
	Ferritin (ng/mL)	6010.6 $\pm$ 2211.8	1210.1 $\pm$ 1171.1	<0.001*
	Albumin (g/dL)	2.7 $\pm$ 0.6	2.9 $\pm$ 0.5	0.384
	Bilirubin (mg/dL)	4.6 $\pm$ 4.1	2.2 $\pm$ 2.0	0.037*
	Alanine transaminase (ALT; IU/L)	273.7 $\pm$ 175.1	73.4 $\pm$ 71.4	<0.001*
	Aspartate transaminase (AST; IU/L)	172.9 $\pm$ 111.0	90.6 $\pm$ 88.2	0.031*
	Lactate dehydrogenase (LDH; IU/L)	640.9 $\pm$ 299.2	168.3 $\pm$ 77.1	<0.001*

Significant determinants of mortality

EBV: Epstein-Barr Virus; INR: International Normalized Ratio



( $3.5 \pm 3.4$  mg/dL), ALT ( $186.0 \pm 170.7$  IU/L) and AST ( $136.9 \pm 108.3$  IU/L) levels (Table-2). High LDH levels ( $434.2 \pm 329.1$  IU/L) were also noted (Table-2).

The HLH patients were categorized on the basis of their clinical aetiology. EBV infection was found to be associated with a total of 12 (37.5%) cases. A total of 14 (43.8%) cases were attributed to non-EBV systemic infections. Moreover, malignancy was the main underlying etiology for up to 6 (18.8%) patients (Table-1). Following their preliminary admission, paediatric patients were subsequently followed for a mean duration of 10 months. Up to 18 (56.3%) children had failed to survive upon follow-up evaluation while a survival period of more than 12 months was estimated only in up to 12 (37.5%) HLH patients. Regarding the clinical prognosis, the severity of anaemia ( $p=0.001$ ), neutropenia ( $p=0.007$ ), thrombocytopenia ( $p=0.033$ ), and hyperferritinemia ( $p<0.001$ ) was significantly associated with poor clinical progression in HLH. Moreover, elevation of liver enzymes (ALT:  $p<0.001$ ; AST:  $p=0.031$ ), serum bilirubin ( $p=0.037$ ), and LDH ( $p<0.001$ ) levels also indicated a poor disease prognosis (Table-3).

#### DISCUSSION:

Our study has assessed the clinical correlation of paediatric patients with haemophagocytic lymphohistiocytosis, most prevalent clinical characteristics included fever, lymphadenopathy and hepatosplenomegaly. Lab findings included cytopenias, elevated ferritin, deranged liver enzymes and raised LDH. A significantly poor long-term prognosis was identified in the sample cohort. Regarding the clinical prognosis, the severity of anaemia, neutropenia, thrombocytopenia, and hyperferritinemia was significantly associated with poor clinical progression in HLH. This is one of the preliminary studies exploring the clinical outcome of paediatric HLH within the developing tertiary healthcare sector of Pakistan.

Similar to our findings, the commonest clinical manifestations in HLH were reported by Zhang et al., (2016) as fever, elevated ferritin, and low platelet count. Compared to adults, paediatric HLH is more likely to potentiate the enlargement of liver and spleen. In line with previous studies, our findings showed that ferritin and/or LDH levels were significantly decreased after 2-3 weeks of treatment, suggesting that serum ferritin and/or LDH may function as sensitive markers reflecting the early treatment response. Deranged liver biochemistry, anaemia, and elevated LDH have also been reported in the literature by Benevenuta et al., (2023). Leucocytosis is not typical of HLH, except in HLH-associated with defined rheumatological conditions/macrophage activation syndrome-HLH (MAS-HLH)<sup>11</sup> Impaired liver function can precipitate Acute liver failure, thereby resulting in a substantially high risk of in-hospital mortality.<sup>13</sup> Although active HLH disease has been considered a relative contraindication to liver transplantation, the latter has been

shown to potentially improve patient prognosis with overall graft and patient survival were 60% at 24 months median age after liver transplantation.<sup>15</sup>

A major etiological condition contributing to childhood HLH is EBV infection. In contrast to adult HLH, paediatric variant of HLH has been shown to be more frequently associated with EBV.<sup>16</sup> This unique vulnerability, as reported by Koh et al., to EBV infection in Asian patients with HLH suggests that different genetic backgrounds can contribute to the development of the disease, even in cases of secondary HLH. Although Zhou et al., (2022) have identified age  $>28$  months as a protective factor in the pathophysiology of HLH.<sup>8</sup> our study has highlighted a non-significant role of increasing age in preventing child mortality where patients experiencing mortality were, on average, 7 months older than the surviving children. Besides, a significant transaminase elevation coupled with coagulopathy has been associated with a markedly poorer clinical prognosis in HLH.<sup>16</sup> Although the authors could not find any significant association between HLH secondary to malignancy and mortality, it has been previously documented that malignancy is a poor prognostic marker of the disease.<sup>9,15</sup>

Our study indicated a poor long-term prognosis among paediatric HLH patients where up to 56.3% of patients had failed to survive when assessed at a mean follow-up duration of 10 months after initial admission. In a broad systematic review and Cochrane meta-analysis, reported by Tan et al., which included a total of 36 studies involving clinical data of up to 493 HLH paediatric patients, a lower mortality rate of approximately 33% was noted.<sup>18</sup> This difference from our findings can be potentially explained by our study being restricted to a single referral hospital where many complicated cases were referred from peripheral hospitals. Nonetheless, early diagnosis and treatment in HLH can drastically reduce the risk of adverse outcomes.<sup>8</sup> In concordance, a study by Xu et al., (2017) up to two-third of HLH cases can undergo remission following 8 weeks of treatment.<sup>19</sup> To boost life expectancy, supportive care is also implicated in HLH since it can effectively reduce the risk of opportunistic infections and other comorbidities in the immunocompromised patients.<sup>20</sup>

A major strength of our study was follow up on patients for assessment of prognosis and clinical outcome. Limitations of this study include the incompleteness of testing for *STXPB2*, *SH2D1A*, *XIAP/BIRC4*, *UNC13D*, *PRF1*, *STX11*, and *ITK* mutations, which was why we adopted the term 'presumed' secondary HLH. This leaves the possibility of causation due to genetic mutation in the patients designated as having non-familial HLH.

#### CONCLUSION

Paediatric haemophagocytic lymphohistiocytosis is a rare and potentially fatal, multisystem disorder. Derangement of liver function and other serum biomarkers is significantly

associated with a poorer clinical prognosis. A multicentre, prospective trial that builds on the present results is warranted to identify subgroups of patients with a poor prognosis and identify optimal treatments.

#### Authors Contributions:

**Sehar Aslam:** Topic selection, study design, data collection, manuscript writing

**Nadeem Sadiq:** Study design, manuscript writing proof reading

**Tariq Nadeem:** Sample collection, study design, methodology

**Awais Arshed:** Sample collection, study design, methodology

**Imrana Atta:** Biostatistics

**Kiran Minhas:** Discussion, conclusion

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# The Association between Estrogen Levels and Prostate Volume in Obese and Non-Obese Benign Prostatic Hyperplasia (BPH) Patients

Afsheen Khan, Naheed Khan, Syeda Bushra, Asma Aijaz, Iffat Raza, Shaheen Haider

## ABSTRACT

**Objective:** To investigate the association between prostate volume and estrogen levels in obese and non-obese individuals suffering from Benign Prostatic Hyperplasia (BPH).

**Study Design and Setting:** Cross-sectional, analytical study

**Methodology:** The International Prostatic Symptom Score (IPSS) was used in the study to recognize sixty participants with BPH. The study examined patients' height, weight, waist circumference (WC), and body mass index (BMI). An IPSS score of less than 7 was seen as healthy. Using standardized BMI (25) and waist circumference (90cm), patients were split into two groups, with obese patients being placed in group A and non-obese patients being placed in group B. Using trans-rectal ultrasonography (TRUS), prostate gland's dimensions were measured, and blood samples were taken to determine serum estrogen levels.

**Results:** In comparison to the non-obesity group, which had a mean prostate volume (PV) of  $31.21 \pm 6.771$  ml, the obese group's PV was  $36.13 \pm 3.673$  ml. It was statistically significant that there was a difference between the two groups ( $p=0.001$ ). In the non-obese group, average level of estrogen was  $309.72 \pm 73.62$  pmol/l, compared to  $328.21 \pm 115.05$  pmol/l in the obese group ( $p=0.462$ ). Correlation study ( $r=0.279, p=0.031$ ) revealed a significantly ideal relationship between participants' blood estrogen levels and PV. Among patients who were obese, there was a significant positive correlation among blood estrogen levels and prostate size ( $r=0.638, p=0.0001$ ).

**Conclusion:** When compared to the non-obese group, obesity significantly raises prostate volume in study participants, leading to benign prostatic hypertrophy. In addition, prostate volume and blood estrogen levels in obese males showed a significant positive association.

**Keywords:** Prostate, Estrogen, Body mass index, Obesity

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## INTRODUCTION:

The lower pelvis contains the prostate gland which is a tubule-alveolar, fibro-muscular, exocrine gland that is situated in the male lower pelvis, surrounding the neck of urinary bladder. Up to 30% of the entire male ejaculate is produced by prostatic fluid. The prostate gland weighs approximately 8gram throughout childhood but over the first 50 years of life, it can weigh up to 150gram. Benign prostatic hypertrophy (BPH) invariably causes it to become heavier after the first 50 years of life. Nocturia, urinary urgency, dribbling, and insufficient bladder emptying are typical signs of BPH. BPH risk factors include aging, family history, and metabolic problems. Urinary tract infections (UTIs), kidney and bladder damage are among the complications. The tests that are advised for diagnosis of BPH include post-void residual urine volume (PVR), digital rectal examination (DRE), and international prostate symptom score (IPSS).<sup>1</sup>

Prostatic enlargement and clinical symptoms are the result of a persistent, progressive, but discontinuous hyperplasia of both glandular epithelial and stromal components in BPH. Additionally, fibroblasts, blood vessels, nerve cells, and inflammatory cells are seen in the stromal components of

BPH. There can be possibility that each of these stromal and epithelial elements will contribute to the development of BPH. The term histological BPH refers to tissue remodeling including fibromuscular matrix and epithelial tissue, as well as proliferation of stromal and epithelial cells in prostate transition zone. Additionally, the gland displays periurethral zone involvement in addition to glandular and stromal hyperplasia. Due to progressive nature of BPH, the greatest risk factor for its occurrence is age. In addition to age, studies have revealed that a number of obesity-related factors also have an impact on prostate volume (PV) of BPH patients. Obesity and metabolic diseases have been associated to BPH.<sup>2,3</sup>

The literature claims that prostate volume differs amongst various racial groupings. Male Asians have lesser PV than male whites.<sup>4</sup> PV measurements are crucial for discussing possible growth in several medical contexts. The median yearly prostate growth in men with PV=30 ml was 1.7%, whereas the median annual prostate growth for men with PV above 30 ml was 2.2%.<sup>5</sup>

Both digital rectal examination and prostate ultrasonography can measure prostate size. Since it evaluates all three dimensions of volume, trans-rectal ultrasonography (TRUS) is a useful method for assessing PV. The peripheral zone (PZ), central zone (CZ), and transitional zone (TZ) constitute roughly 75%, 20%, and 5% of the gland volume, respectively, in adolescents, though these ratios vary with age.

Benign prostatic hypertrophy begins in TZ and eventually may spread throughout the gland completely.<sup>6</sup> In older men, BPH is mainly responsible for voiding issues.<sup>7</sup> This prostatic hypertrophy is benign. It is ranked as the fourth most prevalent disease in males over 50. It affects 90% of men over 80 and about 40% of men over 50 on a regular basis.<sup>8</sup> Patients with familial BPH are more likely to experience the onset of condition earlier.<sup>9</sup>

BPH is caused by a variety of risk factors, including androgenic hormones, genetic predisposition, and changes in the detrusor muscle with aging. According to a new study, systemic inflammation and oxidative stress have been linked to an elevated risk of BPH by serum adipokines, extremely active hormones released by excess adipose tissues. The pathogenesis of BPH may be significantly influenced by systemic metabolic disorders, notably obesity. According to recent investigations genetic, metabolic, neuroendocrine, psychological, and environmental factors all have a role in obesity.<sup>3, 10</sup>

The investigation's findings will aid in the early detection of BPH in elderly individuals (50 years of age and older). This study might help in early identification of BPH patients because the size of the gland has a significant role in deciding patient's future medical treatment and therapy.

#### **METHODOLOGY:**

In this cross-sectional, analytical investigation, 60 BPH patients from Dow University of Health Sciences and Dr. Ruth Pfau's emergency hospital were included. After receiving institutional review board approval (IRB-1182/DUHS/Approval), the study was carried out. To find participants, a non-probability consecutive sampling strategy was used. The sample size was determined with the open Epi calculator. The sample size was calculated using a 95% confidence interval and an 80% test power. The computed sample size was 2 (1 for each group, group A-Obese and group B-Non-obese). To fulfil statistical requirement, 30 samples were taken in each group making a total of 60 (obese 30, non-obese 30).

The study included all BPH patients between the ages of 50 and 80 who had an IPSS score greater than 7 with the condition. The Asian cutoff values of Body Mass Index (BMI) > 25 and Waist Circumference (WC) > 90 cm were used to determine obese men.

Non-obese participants were included on the basis of BMI ranging from (= 25) and (WC < 90cm). Exclusion Criteria included the patients with known prostate cancer, previous prostate surgery and previous pelvic surgery of any type and patients with history of kidney and bladder disorders such as renal stones, bladder stone.

All patients had trans-rectal ultrasonography (TRUS) using an ultrasound machine (Type Doppler machine and Toshiba firm model Nemio XG) to measure the volume and size of the prostate. To determine their oestrogen levels, blood samples from each subject were taken. 5 ml of blood were collected to estimate the amount of estrogenic hormones. The prostate typically has a capacity of 30 ml, and the normal range of oestrogen concentrations is 99.4 to 192 pmol/l.<sup>11</sup>

The baseline characteristics of obese and non-obesity participants were calculated using descriptive statistics, such as mean, standard deviations, frequency, and proportions. The Shapiro-Wilk test was used to determine normality because the distribution of the data wasn't expected to be uniform. The mean differences between age groups were examined using the Mann-Whitney test and the Kruskal Wallis test. Statistical significance was defined as a P-value of 0.05 or less. The data were examined using SPSS, version 21 of the statistical package for the social sciences.

#### **RESULTS:**

A study with 60 participants, on the basis of prostate volume (PV). Specifically, 47 participants have a prostate volume greater than or equal to 30 ml (78.3%), and 13 participants have a prostate volume less than 30 ml (21.7%). Only 8 individuals (13.3%) and 52 participants (86.7%) had serum estrogen levels below 192 pmol/l.

The overall mean prostate volume (of 60 participants) obtained in our study was 33.67± 5.944ml.

The average estrogen concentration was 318.96±96.21pmol/l.

The range of the normal serum estrogen level is 99.400–192 pmol/l. The mean prostate volume in the obese group was 36.13±3.673 ml compared to 31.21±6.771 ml in the non-obese group, with a statistically significant difference (p=0.001) (Table 1). The mean estrogen levels between the obese group and the non-obese group were not different significantly (p=0.462; 328.21±115.05pmol/l vs. 309.72±73.62 pmol/l, respectively). When research participants of different ages were divided into obese and non-obesity groups, the 61-70 age groups had the highest difference. This finding was statistically significant (p-value=0.044).

When individuals with differed PV (30 ml and 30 ml) were divided into the obese group and the non-obese group (Figure 1), the group with PV 30 ml showed the greatest difference, and the result was statistically significant (p-value=0.005) (Table 2). When participants with differed estrogen levels were separated into the obese group and the non-obesity group, a difference was observed in the group with estrogen level 192, but it was not statistically significant (p-value=0.353).

The correlation research revealed a weak correlation (r=0.279, p-value=0.031) between prostate volume and serum estrogen levels .

Further classification based on obesity status revealed a significant positive association between prostate volume and blood estrogen levels in obese individuals (r=0.638, p-value=0.001) (Figure 2). However, among non-obese patients, there is no relationship between prostate volume and serum estrogen levels (r = 0.160, p-value = 0.931) (Figure 3)

Table 1: Obesity and non-obesity differences in mean prostate volume and mean estrogen levels

	Non-obese mean±SD	Obese mean±SD	p-value
Prostate volume (ml)	31.21±6.771	36.13±3.673	0.001*
Serum estrogen levels (pmol/l)	309.72 ±73.62	328.21±115.05	0.462

\*p-value = 0.05 statistically significant , Test applied: Mann Whitney test

Table 2: Study participants' characteristics grouped based by obesity

Features	Obesity		p-value*
	Non-obese	Obese	
	n (%)	n (%)	
<b>Prostate Volume</b>			
< 30 ml	11(37.5)	2(15.4)	0.005*
= 30 ml	19(40.4)	28(59.6)	
<b>Estrogen levels</b>			
< 192pmol/l	3(37.5)	5(62.5)	0.353
=192pmol/l	27(51.9)	25 (25)	

\*p-value = 0.05 statistically significant, Test applied: Chi-square analysis

Figure 1: Trans-rectal ultrasonographic illustration of prostate gland > 30ml volume in A Obese man B Non-obese man

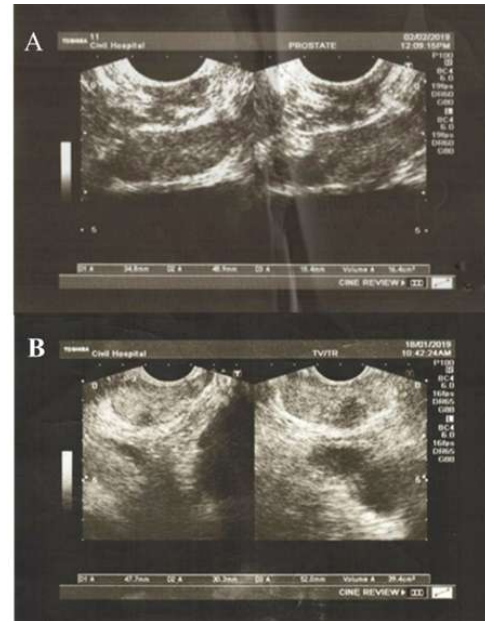


Figure 2: Correlation between prostate volume and estrogen levels in obese patients

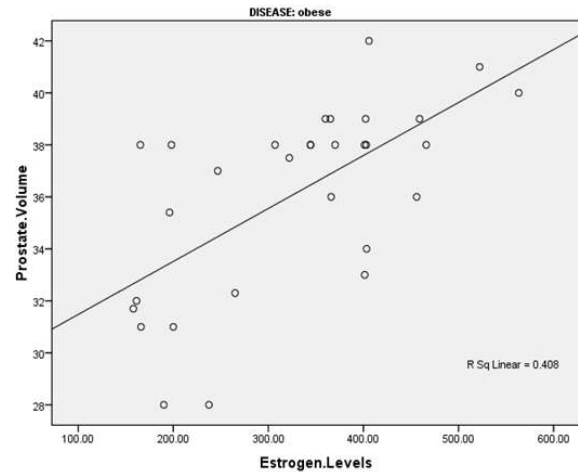
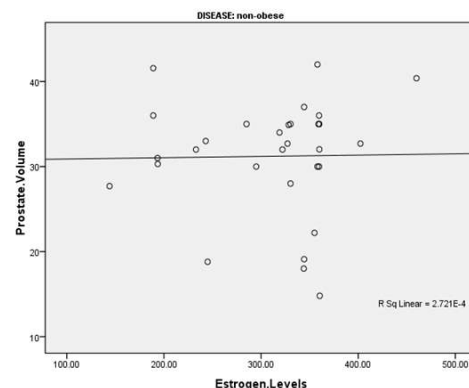


Figure 3: Correlation between non-obese patients' blood estrogen levels and prostate volume



## DISCUSSION

It is well established that several factors, including aging, ethnicity, obesity, genetics, sex steroid hormones, modifiable lifestyle factors, and inflammation, can induce morphological volumetric changes in the prostate gland. The prostate gland can vary for a variety of causes, such as advanced age, obesity, and androgen hormones in men.

People are more likely to experience prostate problems as they get older. Benign prostatic hypertrophy (BPH), or unhealthy prostatic enlargement, is a prevalent issue for elderly men. Lower urinary tract issues are linked to it, can adversely affect quality of life. Age, ethnicity, obesity, genetics, sex hormones, modifiable life factors, and inflammation are generally accepted as known stimulators of morphological volumetric changes and enlargement of the prostate gland. Throughout a man's life, his prostate gland develops and undergo several morphological changes. Future growth and development are strongly correlated with prostatic volume (PV).<sup>12</sup>

The current study, which was conducted on a sample of Karachi residents who were attending a tertiary care hospital, is the first population-based study to demonstrate a positive correlation between PV and estrogen levels in obese participants.

The largest prostate volume in our investigation was found to be 42 ml. In contrast, 103 patients were exposed to benign prostatic hypertrophy in a Pakistani study by Raza et al., of whom 80 had PV smaller than 50 ml and 23 had bigger than 50 ml.<sup>13</sup> In their research, a prostate sample's greatest volume was 90ml. In addition, a 2005 study by Ochiai et al. discovered that 35% of individuals had a prostate volume greater than 50 ml, while 65.6% of patients had one between 25 and 50 ml.<sup>14</sup>

The analysis by volume assessment among people with prostate enlargement has significance in many manners. It is able to detect both the disease's progress and its complications. Numerous studies found that in healthy persons, obesity influences the prostatic volume. The mean prostate volume of obese patients in the current study was 36.13ml, compared to 31.21ml for the non-obese group. The findings are in coherence with the results of Zaza et al who reported higher PV in obese patients compared to normal weight, and underweighted patients, however; contradicts from the study on the Korean population in which 146 men over the age of 40 had mean prostate volume of 18.8 ml in non-obese individuals and 21.8 ml in obese participants.<sup>15</sup>

According to our results, a different study found that obese individuals had larger prostate volume levels than non-obese individuals.<sup>11</sup> The significant association between obesity and prostate volume discovered by other researchers supports the linear relationship between the two variables in investigations.<sup>16</sup>

Due to its impact on prostate development and enlargement, androgen status and obesity is a universal health concern, especially in developing nations, and significance should be given to diagnosis and correction at the community level. It might be because of the fat deposition, which accelerates the adipose tissue's metabolism of estrogen-inducing circulating testosterone into estrogens.<sup>17</sup>

There were no obvious differences between the two groups (obese and non-obese) according to numerous studies that presented their findings about the relationship between estrogen levels, prostate volume, and obesity.<sup>18</sup>

Our study's obese group had mean estrogen levels that were greater (328.21 pmole/l) than the non-obesity group (309.72 pmole/l), which is consistent with previous investigations conducted worldwide.<sup>19</sup> Few studies have found a statistically significant connection between estradiol levels and obesity-related variables including BMI and waist circumference.<sup>20</sup> However, a small number of recent researches did not find any link between estrogen and obesity.<sup>21, 22</sup>

It is important to determine the prostate volume in BPH using the serum oestrogen levels. This may be because the prostate gland needs androgenic hormones to maintain the tissues' normal level of metabolism. According to the current study's findings estrogen levels and prostate volume have a strong positive link. In China, a research with 949 people found no link between estrogen and prostate volume.<sup>20</sup> On Contrary, other researchers found a strong correlation between prostate volume and serum estrogen levels.<sup>23</sup>

The most remarkable finding in the current study's examination of obese males was the elevation of prostate volume with rising serum estrogen levels, which demonstrated a positive association. Due to excess fat, which starts aromatase activity and raises estrogen levels, there may be an increase in prostate volume when oestrogen levels are high.<sup>20</sup> Furthermore, oestrogen can also indirectly affect adipogenesis by controlling important stages in the manufacture of other steroid hormones. This is in reference to estrogen capacity to increase the activity of 11-hydroxysteroid dehydrogenase type 1, a crucial enzyme for the upregulation of adipogenesis in human adipocytes which in turn can lead to a rise in prostate volume.

The majority of the participants were obese with estrogen levels >192pmol/l in the age groups 50–60 years, but no significant differences were seen in the age groups 61–70 years and 71–80 years where the majority of the participants were obese. Previous research has shown that advance age, obesity, and different levels of androgen are risk factors for the pathogenesis of the prostate gland.<sup>20, 22, 23</sup> In the current investigation, men who were obese and older had high estrogen levels. In a study with elevated estrogen levels in men aged 70 and beyond, estrogen changes in obesity and advanced age were also noted, and these results are consistent with our findings.<sup>24</sup> however, Age and estradiol levels have

been found in one investigation to be inversely correlated.<sup>25</sup>

The prostate-related parameters identified at a single moment in time, the limited sample size, the lack of testosterone-related data, and the research was restricted by the lack of a comparison between prostate volume calculated by TRUS and actual findings.

The study has several limitations. It was conducted at a single facility with a limited sample size. We suggest for future studies to compare prostate volume with real specimens such as cadavers and to confirm the influence of estrogen on prostate volume with advancing age, further studies with large sample size are recommended. It is also recommended that clinicians should make a strategy for assessment of prostate gland by correlating International prostatic symptom score with prostate volume measurements by trans-rectal ultrasonography and serum estrogen levels to ensure early detection of disease and prevent adverse outcomes of benign prostatic hypertrophy.

### CONCLUSION:

The study highlighted a significant association between obesity and prostate volume and subsequent development of benign prostatic hypertrophy as compared to non-obese. There is also a significant positive association of estrogen levels with prostate volume that need to be evaluated in obese males for early detection and prevention of adverse outcomes of benign prostatic hypertrophy.

#### Authors Contributions:

**Afsheen Khan:** Study Design and Setting, Drafting of work

**Naheed Khan:** Drafting of work

**Syeda Bushra Ahmed:** Data Collection

**Asma Aijaz:** Data Collection

**Iffat Raza:** Analysis of Data

**Shaheen Haider:** Analysis of Data

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## Effect of Maternal Literacy on Immunization Completeness in Children Under 2 Years of Age – Karachi, Pakistan

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### ABSTRACT:

**Objective:** To assess the association of different levels of education with complete immunization in children under 2 years of age.

**Study Design and Setting:** The study was cross sectional analytical and was carried by online survey of mothers living in Karachi. The study was conducted through a period of 4 months from May 2021 to August 2021.

**Methodology:** The sample size of 270 mothers was calculated using a 95% Confidence Level and using the Epi Info Application. The data was collected using a closed-ended online questionnaire via Google Forms. Due to the COVID – 19 pandemic, the questionnaires had to be distributed online. The data was analyzed using SPSS V23. The statistical test used was Fisher Exact Test to determine whether or not the relationship between maternal education and immunization rate was significant. .

**Results:** A total of 270 responses were recorded from mothers of various socio-economic statuses. It was observed that as the level of education increased from no formal education to a higher level of education, the percentage of children completely vaccinated increased from 76.9% to 92.7%. Upon statistical testing using Fisher Exact Test, the p-value was found to be 0.017 which is less than the alpha value of 0.05 showing that the relationship between the 2 variables is significant.

**Conclusion:** The study had shown that the children of mothers with a higher level of education were associated with a higher likelihood of being fully vaccinated than children of mothers with a lower level of education.

**Keywords:** Children, Immunization, Literacy, Maternal Education, Vaccination.

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### INTRODUCTION:

When a person is made resistant to an infectious disease usually via the application of a vaccine, it is known as immunization. Currently, around 2-3 million deaths are prevented annually from various diseases by immunization.<sup>1</sup> In 1978, the Expanded Program of Immunization (EPI) was introduced in Pakistan by WHO to ensure protection against life-threatening and vaccine-preventable childhood diseases.<sup>2</sup> A child is said to have received complete basic immunization if he has received the following vaccines at the recommended EPI Schedule: one BCG and one dose of oral polio (2-3 drops) of immunization (given at birth or first clinical encounter), three DPT immunizations (given at approximately 6, 10, 14 weeks after birth) and 2 doses of measles subcutaneously with rubella 9 and 15 months of age.<sup>3</sup> One of the most economical public health strategies to reduce child morbidity and mortality is a complete course of vaccinations against devastating diseases. Vaccinations are an important preventive child health tool as their delay increases the susceptibility window for vaccine-preventable diseases; therefore signifying the importance of understanding its factors and their analysis can improve immunization uptake. These vaccines not only decrease the risk of the

diseases for which they provide protection but also decrease the risk of illness and mortality from other causes.<sup>4</sup>

However, despite four decades since the initiation of the EPI Program, it has come across various problems, such as lack of parental literacy, awareness, and socio-economic discrepancies resulting in significant inconsistency in immunization uptake in different areas of the world with lower coverage among children. These occurrences can however be termed vaccine hesitancy. In Pakistan, 15% of the population under five years of age makes up for 50% of the mortality rate. It also has the third-highest burden of mortality.<sup>5</sup> In 2015, 19.4 million children missed out on basic vaccination around the globe.<sup>6</sup> According to WHO, Pakistan ranks third amongst the countries with the highest number of unvaccinated and under-vaccinated children. Of the 3.8 million infants who did not receive their third dose of the DTP3 vaccine in the region in 2015, 40% of those were in Pakistan.<sup>2</sup> Pakistan Economic Survey 2020-21, mentions Pakistan has a low female adult literacy rate of 46.5% (10). In Sindh 44 percent and in Karachi only Karachi's Central District spotted 81.13 percent female are literate, other districts have less than 50 percent rate. This is the very challenging and worrying situation that in spite of so much immunization efforts, they have failed to achieve national and international standards of Vaccination Uptake. The main and primary reason is the maternal education.

Literacy is one of the key aspects of human resource development of the country. Women, who contribute half of our population have the dubious, distinction of maintaining a lower profile in many social, educational and economic aspects.<sup>12</sup> The female adult literacy rate has been defined as the percentage of the female population that can read and write aged 15 and above.<sup>11</sup> The reasons of female illiteracy are many such as socioeconomic and religious, lack of MCH information source, poverty, lack of awareness, family pressure.<sup>7</sup> Maternal illiteracy is the great challenge for the prevention and promotion of healthy life of our future nation. Unawareness adversely affects the child vaccination status via the capacity to obtain, process and understand basic information on the benefits and risks associated with child vaccination, which, in turn, lead to poor adherence to the recommended vaccination schedule, children develop many communicable diseases which may lead to be fatal. Timely and complete course according to the EPI schedule is the key to protect child from many vulnerable and potentially deadly diseases.<sup>8,9</sup>

Since existing literature regarding how different levels of education influence immunization coverage in children is limited in Karachi, this study aims to fill this gap in literature so that this factor can be given more importance and further focus on maternal literacy can make immunization in children more efficient.

## **METHODOLOGY:**

The present research was a cross-sectional study. The study was approved by the Ethical Review Committee of Bahria University Health Sciences Campus, Karachi (ERC number is 40/2021). It was carried out through online survey. The sample size for this study was calculated from StatCalc sample size calculator tool with 95% confidence level and 5% margin of error. The calculated sample size of the study was 369. Before the start of survey, consent was taken from all the participants. Total number of responses received was 446 and finally the valid number of responses among these was 294. Random sampling technique was applied and each respondent was given equal chance of selection. All mothers which have their children aged at least 24 months and who gave consent were our participants and those who had a child with an age of less than and above the age of 24 months and mothers who did not give consent. were excluded from the study. The web-link of the survey questionnaire was shared by the help of text-based instant messaging (WhatsApp). The study was conducted through a period of 4 months from May 2021 to August 2021. The recruited participants were then identified as incomplete child vaccination and also the determinants associated with level of education were noted. The subjects were asked to complete a 22 structured closed-ended questionnaire, the questionnaire was designed and available in both English and Urdu Languages for the ease of use of the subject. The answers were recorded accordingly to reduce bias in the study. It was designed in an online format using Google Forms. Questions were asked regarding socio-demographic, maternal level of education, immunization status. Data was received in the form of excel spreadsheet, was entered and analyzed by using Statistical Package for Social Sciences (SPSS), version 26. Analysis was carried through descriptive statistics to calculate the frequency and percentages of main variables like age, qualification, infant gender, maternal knowledge of immunization, vaccination card, access to health care facilities, socioeconomic status. Multi-variable analysis was done using the Chi-Square test to assess the association of different levels of education with or without complete immunization in children less than 2 years of age. With all variables, the results were considered as significant when p value was =0.05.

## **RESULTS:**

A total of 270 responses were recorded from mothers of various socio-economic statuses in Karachi. Of the respondents, 10% (27) had no formal education, 14.1% (38) had completed primary school, 25.2% (68) had completed secondary school, and 50.7% had graduated from school (Higher). This made a literacy rate of 75.9%. We've defined the criteria for literacy rate as those who have completed secondary school as they can efficiently read and write. Children of those who had no formal education had an

immunization rate of 74.1%, primary education showed 81.6% and secondary education showed 83.8% and higher education showed an immunization rate of 92.7% showing that as the level of education increased percentage of children vaccinated increased from 74.1% to 92.7%. This can also be seen in Table 1. 87% (235) had completed their child’s immunization under 24 months while 13% had not completed it. 87% (235) had a vaccination card belonging to their child whereas 13% did not have it. 71.9% (194) were educated about vaccines while 28.1% (76) were not. 69.3% (187) knew what childhood immunization under 2 years consisted of while 30.7% (83) did not know. 30.9% (64) of those who were educated about childhood immunization were educated by the hospital, 22.2% (46) by their school, 13.5% (28) by their families, 12.6% (26) by television, 9.7% (20) by literature, and other minor sources have been mentioned in Figure 1. One of the main reasons for not getting their child

employed 4% (12) were unemployed, and 0.7% (2) were students. 94.8% (256) of respondents have access to basic healthcare facilities while 5.2% (14) did not. 82 (30.4%) gave birth in Government Hospital, 17 (6.3%) had a home birth, 3 (1.1%) in Military Hospital, 1(.4%) in Naval Hospital, 167 (61.9%) in Private Hospital. 70.7% (191) strongly agreed that vaccination protects their children from diseases. 22.6% (61) agreed. 5.6% (15) were neutral, 0.7% (2) disagreed, and 0.4% (1) strongly disagreed.

**DISCUSSION:**

Child immunization is a very important method of protection against a range of illnesses such as polio, rabies, measles, and tuberculosis. Hence, the discussion of the factors influencing vaccination coverage among children of age below 24 months and how we can improve and sustain the immunization rate. One such factor found to be a major determinant is maternal education and assessing its effect on complete child immunization has been the main focus of this study.

In our study, the 47% mothers did not get their child vaccinated due to a lack of awareness. Another study conducted in Pakistan also showed that the most common reason for un-vaccination was mothers/caretakers lacking awareness of the need for vaccination (35.3%).<sup>14</sup> Another study from India also revealed that 20.4 % of the unvaccinated population in the urban area of Kirti Nagar was due to the low level of maternal education status.<sup>15</sup> A study from Canada also showed that the main reasons for un-vaccination were fears regarding vaccine safety (56.4%) and philosophical or religious reasons (32.8%).<sup>16</sup>

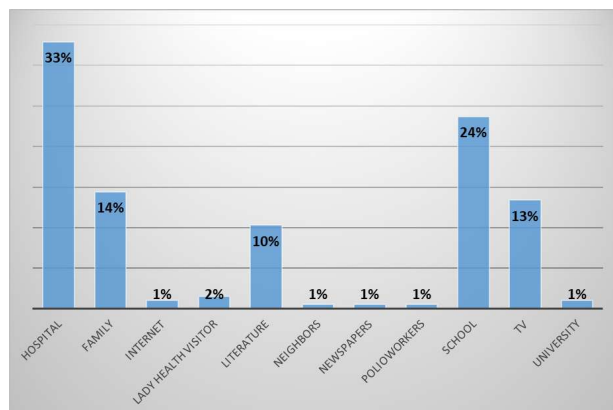
In our study, it could be seen that the major source of knowledge regarding vaccines was the hospital (30.9%) and then the school (22.2%). This is also seen in other studies in Pakistan.<sup>17</sup> Some studies in Pakistan have also shown healthcare workers to be the main source.<sup>18,19</sup> However, in a study in East Asia, media in the forms of television, internet, and radio was a major predictor of increased vaccination.<sup>20</sup> This shows that we should emphasize media more to deliver immunization information more efficiently.

Our studies showed that as education increased from no formal education to a higher level of education (12+), complete immunization in children increased from 74.1% to 92.7%. This pattern has been seen in several developing countries like Pakistan. A similar study conducted in Turkey which is a developing country showed that mothers who completed 8 years of schooling increased the likelihood of receiving the third dose of these vaccines for DPT and Hepatitis by 55% and 92% respectively.<sup>21</sup> In Nepal, the rate of full vaccination uptake showed a clear rise with increasing maternal education from no formal education showing a 67.8% uptake rate to higher education showing a 91.2% uptake rate.<sup>22</sup> Studies from Southern Israel also showed that every year mothers who are not educated, approximately 4-

Table1: Association of child vaccination at different levels of maternal education

		Child complete vaccination		P-Value
		Yes n (%)	NO n(%)	
Mother’s level of Education	No formal education	20(74.1%)	7(25.9%)	0.017
	Primary	31(81.6%)	7(18.4%)	
	Secondary	57(83.8%)	11(16.2%)	
	Higher	127(92.7%)	10(7.3%)	

Figure 1: Information Regarding the Source of knowledge of Mothers of Under Two Children



vaccinated was due to lack of awareness (47%). Other minor reasons for un-vaccination included: Lack of transport, accessibility, and fear of side effects. The statistical test used was Fisher Exact Test. The value of ‘a’ (alpha) was set at 0.05 for significance. Fisher Exact Test gave a “p” value of 0.017 which is less than “a” value of 0.05 showing that the null hypothesis is rejected hence the relationship between maternal education and child immunization is significant. The result can also be seen in Table 1. 74.4% (201) of the respondents were housewives, 15.2% (41) were employed, 5.2% (14) were self-

9% of those mothers delay or skip their children vaccination schedule.<sup>23</sup> On the other hand in Bangladesh, full vaccination coverage increased progressively with greater maternal education.<sup>24</sup>

Another study conducted in Sindh, Pakistan showed that mothers who had an education level of secondary or higher exhibited significant odds ratios (OR, 1.37; 95% CI, 1.04–1.80).<sup>7</sup> A study conducted in Karachi showed there was also a noteworthy association (p-value < .001, Cramer's V= 0.249) found between the level of education and parental perception of vaccination being important for their child.<sup>5</sup> Moreover, In Japan, mothers with a high health knowledge (aOR: 1.337; 95% CI: 1.096–1.631) and high decisional ability (aOR: 1.391; 95% CI: 1.075–1.800) had a higher likelihood to immunize their children.<sup>20</sup> Similar studies conducted in Ethiopia showed that women who had completed their formal education had a 2.45 times greater likelihood to immunize their children as compared to those who had no formal education (OR = 2.45; 95% CI: 1.62–3.72) (25). Furthermore, another study in Nigeria suggested that there is a positive correlation between maternal education and reduction in childhood mortality (PR =1.44; 95% CI: 1.16-1.77).<sup>4</sup> Finally, a meta-analysis of multiple studies in various countries also showed that increasing maternal education increased the overall frequency of vaccination uptake by 57.8% (95% CI: 52.4–63.1) (26).

## CONCLUSION:

The study had shown that the children of mothers with a higher level of education were associated with a higher likelihood of being fully vaccinated than children of mothers with a lower level of education.

### Authors Contributions:

**Usman Saeed:** Literature Review, Data Analysis and Interpretation  
**Asra Saeed:** Literature Review, Data Collection  
**Sandia Matani:** Literature Review, Data Collection  
**Iram Shahzadi:** Literature Review, Data Collection  
**Hooriya Saeed:** Major Data Collection, Minor Literature Review  
**Fareha Shahid:** Guidance, Supervision, Correspondence

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# Challenges of Implementing Gamification in Medical Education: A Scoping Review

Afifa Tabassum

## ABSTRACT

The objective of this scoping review was to identify the challenges in implementing gamification in undergraduate and postgraduate medical education. Three electronic databases, including Google Scholar, PubMed and Pakmedinet were searched for articles published between 2010 and 2021. Eleven articles fulfilled the inclusion criteria. Included articles comprised of 3 original articles, 5 reviews, 1 each of commentary, case study and letter. Majority of the studies (9, 81.8%), addressed administrative and logistic issues. 6 (54.5%) studies analyzed the issues related to learners and 5(45.5%) studies each analyzed the issues due to game design and faculty factors.

In conclusion, the trend of using gamification in medical education is increasing owing to their potential of improvement in learning outcomes and increase in student engagement. But the challenges and barriers to successful gamification implementation need to be analyzed in advance at the institutional level so that strategies to combat these issues may be developed.

**Keywords:** gamification, teaching-learning, medical education, challenges, Educational technology

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## INTRODUCTION:

Gamification is defined as the use of game elements in non-gaming contexts<sup>1</sup>. It is also described as the process of using game mechanics to increase audience engagement, influence behavior and achieve desired outcomes<sup>2</sup>. Game design elements are those elements that are characteristic of games<sup>3</sup>. There are several game elements that can be utilized in creating a gamified experience based on learner needs and goals. They include progression tracking, badges, points, leaderboard, feedback loop etc<sup>4</sup>. It potentially increases motivation and engagement in the learning tasks, while making learning fun and competitive<sup>5,6</sup>. Several theories have been applied to explain gamification, including the Self-determination theory, situated learning theory, achievement goal theory, social cognitive theory<sup>7</sup> and a more focused Theory of Gamified Learning by Landers.<sup>8</sup>

Gamification is at times is confused with game-based learning or serious games but they are essentially dissimilar. Games are utilized in Game-based learning and serious games to achieve learning outcomes, teach specific skills or to bring about change in learner behavior, whereas gamification is utilized to improve the students' learning experience<sup>9</sup>. With the presence of millennial learners, the use of gamification is becoming more popular in education<sup>6,10</sup>. However, it is

only recently that these approaches have been utilized in medical education. Gamification is being incorporated in preclinical and clinical medical education, and patient education<sup>6,10</sup>. To incorporate gamification in medical education, platforms such as Kahoot, Socrative, Mentimeter and others were utilized<sup>11,12</sup>.

Despite its increasing use, evidence on several aspects of implementing gamification in medical education is sparse. One area is the evaluation of gamification in improving learning outcomes<sup>10</sup>. Furthermore, issues of implementing gamification in several educational fields have been studied<sup>13,14</sup> but there is limited analysis of the challenges health educators face or issues that arise in the effective implementation of gamification in medical education<sup>15</sup>. The purpose of this scoping review was to identify the issues and challenges in the implementation of gamification in undergraduate and postgraduate medical education.

The research question was:

- What are the issues or challenges in the implementation of gamification in undergraduate and postgraduate medical education?

## METHODOLOGY

The scoping review was based on the five-step model by Arksey and O'Malley: 1) determining the research question 2) identifying relevant studies, 3) selecting studies, 4) data charting, 5) collating data and presenting the results.

Search strategy

Google scholar, Pakmedinet and Pubmed were used for data search (table 1). Following keywords were used to perform

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data search: "Issues" OR "challenges" AND "Implementation" AND "Gamification" OR "serious games" AND "Undergraduate medical education" OR "postgraduate medical education" OR "medical student"

#### Study selection

Original papers, Review articles, Commentaries, Conference papers, Book chapters, letter to editor and studies on gamification and serious games in undergraduate and postgraduate medical education were included. Working group reports, editorials, articles on simulations and augmented reality games and articles on gamification in other health professions educations were excluded. Based on inclusion and exclusion criteria articles published in English from 2010 to 2021 were retrieved. The article title and abstract were screened. Full text of the screened articles was downloaded. Articles with "challenges or issues" present in title or discussed in results or discussion section were included. The reference section of these articles was manually searched for relevant publications.

#### Data extraction

Main information extracted from final articles included the author, year, study type and main issues highlighted (Table1). The extracted data were analyzed by the author. The PRISMA-ScR checklist was used for reporting.

#### RESULTS:

The process of study selection is shown in Figure1. A total of 353 articles were identified after searching the databases. 340 articles entered the title and abstract review phase after removal of duplicate articles. The final review included nine articles based on relevance. Following a manual reference search, two more studies were included.

Overall, the 11 articles included were composed of 3 original articles, 5 reviews, 1 each of commentary, case study and letter. Majority of the studies (9, 81.8%), addressed administrative and logistic issues. 6 (54.5%) studies analyzed the issues related to learners and 5(45.5%) studies each analyzed the issues due to game design and faculty. Issues/challenges in the implementation of gamification can be grouped into four main categories:

##### *Issues related to learner*<sup>16,17,18,19,20,21</sup>

The challenges discussed from the learner's perspective are a negative attitude and that they may not take a gamified course seriously. Moreover, stress and apprehension about the competition or sub-standard performance will lead to decreased engagement and poor time-on-task, resulting in sub-optimal achievement of learning outcomes.

##### *Issues related to game development and design*<sup>9,17,18,19,22</sup>

The studies discussed that the developers and implementers must be very clear about the context in which gamification is being used, the desired outcomes and the learner characteristics for whom it is intended. If there is no alignment

between the games and the learning outcomes, the learner will not be clear on what he has to achieve from the gamification process.

Studies also highlighted the consequences of poor game design:

- If the game elements chosen are not suitable for the level of learner this will again lead to failure in achieving the learning outcomes.
- It can decrease learners' intrinsic motivation and be too focused on increasing extrinsic motivation leading to a greater importance on satisfying the game elements rather than learning
- It can rely on game elements that result in superficial and not deep learning

Hence poor game design may result in an inadequate experience for both learners and developers.

##### *Issues related to administration and logistics*<sup>16,18,19,20,21,22,23,24,25</sup>

For effective implementation the main issue was achieving support and consent from leadership. The resources needed to develop and implement gamification was another major concern in logistical issues. To develop gamified content that is aligned with the learning objects, suitable for learner with appropriate game elements requires, a lot of time, effort, funding and expertise which pose challenges in effective implementation of gamification. Other barriers identified were; integration into existing technological framework of the institution, time required for integration of these activities in the curriculum and the technology students would need for accessing the gamified content. An interesting issue highlighted was the perception of managers that gamification led to a lack of discipline in students.

##### *Issues related to faculty*<sup>16,20,22,23,25</sup>

The development, integration and conduction of gamified content requires expertise and training. Untrained faculty and lack of awareness regarding the range of options available may be detrimental to the successful implementation of gamification. Other concerns discussed in the studies are lack of support of faculty of gamification because they believe it is frivolous. Developing a complex learning game is also a team effort. Faculty may be reluctant to collaborate and communicate with other team members. Another issue is the feeling of loss of operational autonomy i.e. teacher feels they are losing control of the learning process.

#### DISCUSSION:

The purpose of this scoping review was to investigate the issues and challenges that affect the implementation of gamification in undergraduate and postgraduate medical education. Identifying these challenges can help future educators in effectively designing and implementing gamification in their teaching practices. This review identified a number of challenges at the administrative, faculty and

Table 1: Data extraction table

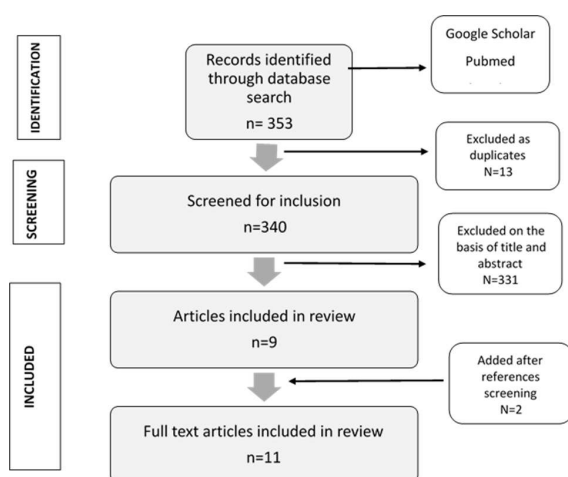
Author/ year	Publication type	Conclusions and Issues highlighted
Rutledge C et al <sup>9</sup> 2018	Review	Poorly designed games may lead to negative effects of competition like stress, poor engagement and poor time-on-task and also affect internal motivation
Bigdeli S and Kaufman D <sup>16</sup> 2017	Review	Logistics issues- extensive collaboration required between subject and game experts, lack of guidelines for gamification, required training, cost and time. Teaching and learning process issues- competitive nature of gamification, boredom potential Different learning styles and negative attitude of learner
Muntasir M et al. <sup>17</sup> 2015	Letter	Gamification should promote intrinsic motivation Outcomes should be defined. The users and context in which gamification is being used is important. Gamification is not a replacement for a well-designed and thoughtful experience
Sánchez Mena AA, Martí Parreño J. <sup>18</sup> 2017	Original Article	Availability of resources Students' lack of interest Subject fit Classroom dynamics
Sandrone S, Carlson C <sup>19</sup> 2021	Review	Alignment between the games and learning outcomes Poor compliance and increased preparation time by learners Trained facilitators and staff Time and resources required
Ellaway RH. <sup>20</sup> 2016	Commentary	Medical students' relative inexperience with games Logistics issues- time, cost, hardware and connectivity Lack of skills
Mesko B et al. <sup>21</sup> 2015	Original Article	Lack of access to the internet Students' preference for different formats Students acceptance of gamification
McCoy L et al <sup>22</sup> 2015	Case study	Challenges include: Support of leadership and faculty. Availability of classroom equipment and student mobile technology Redefining the faculty role Game design promoting deep learning Scheduling of TEAL-MEd activities during class time.
Szeto MD et al. <sup>23</sup> 2021	Narrative Review	Lack of expertise of teachers in development of game-based strategies Extensive collaboration and resources required Expensive and time-consuming
Gentry et al. <sup>24</sup> 2019	Systematic Review	Cost effectiveness is a barrier in the use of gamification
Chan K, Zary N. <sup>25</sup> 2019	Original Article	Time constraints Lack of knowledge of available options Availability of resources

learners' level and also in design and development of gamification. Major issues identified are the support of and collaboration with key stakeholders like faculty and administration. In a study on teachers of various higher education institutes it was found that there was a gap in attitude and practices of these teachers regarding gamification. Despite a strong positive attitude only 11.3 % of the teachers were using gamification on a regular basis<sup>26</sup>. In other studies,

lack of technical skills, fear of losing leading role, difficulties in classroom management, time and scheduling issues have all been identified as contributing factors to teachers' reluctance to use gamification<sup>27,28,29</sup>. McCoy et al in the discussion of TEAL-Med initiative<sup>22</sup> noted that faculty acceptance was an issue initially. The situation improved after pilot testing during which faculty received positive feedback from students. Logistic support was also identified



Figure 1: PRISMA flow chart showing process of study selection



as an important component for successful implementation. In a study that utilized gamification to train pediatric residents in primary survey it was observed that the program faced challenges when administrative resources were reduced due to the pandemic<sup>30</sup>. Similar results about this issue were reported from other educational fields<sup>31,32</sup>.

Another important issue highlighted is that of game design and development. Several components of game design and development have been identified in literature that influence the success of gamification like challenges, feedback<sup>33</sup>, discovery, emotional entailment etc. This also includes alignment of gamification with context of learning and learning outcomes<sup>34</sup>. Studies show that programs with clear outcomes are more successful. For example the use of Gamified Approach to improve clinical reasoning and engagement of emergency medicine residents in video conference resulted in increased learner engagement. Residents also reported that the unpredictability incorporated in gamification design simulated the actual practice of emergency medicine<sup>35</sup>. In another study Doughnut rounds were developed to improve students' and residents' self-directed learning skills. The format included topic selection, formulation of questions, self-study and quiz competition. According to the learners the competitive format resulted in increased motivation for self-study and ultimately increased learning<sup>36</sup>. The review also supports that choice of game elements influence learning, satisfaction and success of gamification. This view is supported by several studies conducted in higher and medical education. In a systematic review of gamification in Distance Learning Platforms in higher education some challenges that were reported were inappropriateness of gamification for the learners' sensory pattern, difficulty level of activities and boredom due to repetition of activities<sup>37</sup>. In medical education, Kerfoot and Kissan<sup>38</sup> found that introduction of game mechanics (leaderboard and prizes) into simulator education significantly increased urology residents' utilization of the skills Simulator.

Nevin CR et al<sup>39</sup> also reported that internal medicine residents found the leaderboard to be the most important motivator for participation. However they found earning badges to be less motivating, resulting in decreased interest over time. According to the authors' this may be due to lack of understanding of what was required to earn badges. In a study investigating medical student perceptions of gamified audience response system on engagement and learning showed that the variety of game elements helped to keep them interested and focused<sup>40</sup>.

Based on the findings of this scoping review, the following recommendations will be beneficial for educational developers and clinicians planning to introduce gamification in their medical education programs:

1. Ensure that the faculty and students are ready for gamification. Sharing the rationale with the students and faculty will help in garnering support and approval<sup>25</sup>.
2. Educational alignment between the learning outcomes and the gamification design needs to be established beforehand so as to achieve maximum learning<sup>41</sup>.
3. The design should be user friendly and customized for the learners. It should include elements and dynamics that are appropriate for achieving outcomes. Consider recyclability of learning resources so that input and additional time of the faculty is effectively utilized. This will facilitate creation of an archive of resources<sup>41</sup>.
4. Pilot - any new initiative should be piloted to identify strengths and challenges before full implementation
5. Provide support- support is essential for successful implementation of any new program. Technical support should be provided to both faculty and students<sup>24</sup>. It may include; training, user guides, help desk/contact person and backup support.
6. Evaluation – this should be an integral part of any educational intervention and should be a planned activity.

Further evidence based on rigorous studies would strengthen our understanding of the utility of gamification in medical education. Research is required in the areas of impact of gamification on student learning at different levels, most effective game elements for different users, the effect of user characteristics on success of gamification and the role of faculty in effective implementation.

## CONCLUSION:

The trend of using gamification in medical education is increasing owing to their potential of improvement in learning outcomes and increase in student engagement. But the challenges and barriers to successful gamification implementation need to be analyzed in advance at the institutional level so that strategies to combat these issues may be developed.

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## Abdominal Pregnancy at Term a Rare Case Report from Jinnah Post Graduate Medical Centre Karachi, Pakistan

Farah Hassan Khan, Tanzila Fahim, Nighat Ali Shah, Fahad Ali

### ABSTRACT:

Abdominal pregnancy is an extreme rare situation and the quoted incidence is 1.4% of all ectopic pregnancies. The diagnosis and management is challenging and requires multidisciplinary input, if not managed in good hands can lead to serious consequences leading to maternal and neonatal mortality. We present a case of 32 years old abdominal pregnancy which presented to us at 31 weeks pregnancy with severe vomiting and mild abdominal pain. The site of pregnancy went unrecognized till 35 weeks pregnancy until she was operated in suspicion of placenta Previa. The patient recovered smoothly after surgery and went home in stable condition. Abdominal pregnancy is challenging to diagnose and manage. It requires not only clinical expertise but also strong radiological guidance to advice management. A rare presentation of persistent nausea and vomiting due to compression of underlying intestines may lead to consider the diagnosis of abdominal pregnancy in later gestation.

**Keywords:** Abdominal pregnancy, Ectopic pregnancy, Laparotomy.

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### INTRODUCTION:

Abdominal pregnancy is a rare type of ectopic pregnancy with presentation around 1 %.<sup>1</sup> It is more common in our part of the world due to poor socio economic conditions and more risk of infections in pelvis.<sup>2</sup> The world wide incidence ranges between 1 in 33,000 and 1 in 10,200 deliveries.<sup>3</sup> The presentation is mostly acute abdomen and is identified in early pregnancy. The early surgical intervention is the key to save maternal mortality.

Abdominal pregnancy at term with a healthy viable fetus is therefore an extremely rare condition and very few of such cases have been published during the last ten years.<sup>2,4</sup> We present an extremely interesting case of abdominal pregnancy with varied presentation that resulted in a term live baby without deformities.

### CASE PRESENTATION:

A 28 years old female G3P2+0 was admitted in emergency room at Jinnah Post graduate medical Centre, ward 9B with severe dehydration and excessive nausea and vomiting at 32 weeks of pregnancy. She also has complains of dull, intense abdominal pain and weight loss. She also complained of constipation. She belongs to a small village of Gwadar, Baluchistan and was a housewife with no formal education. She has 2 previous normal vaginal deliveries and last born was 6 years back. From the 3 rd. month of pregnancy she started to experience abdominal pain and vomiting which was managed conservatively by her local doctor. No early scan was available and according to her estimation she was 8 months pregnant. She was also not sure of her dates.

Physical examination showed wasting and cachexic look with moderate pallor. Pulse was 108 per minute with BP of 100/60 mm Hg. The Chest and heart sounds were normal. Abdominal examination showed distended abdomen with a height of fundus of 29 weeks. There was mild tenderness over the belly. The fetal parts were not appreciated on clinical examination. The fetal heart sounds were audible. Vaginal examination showed a normal cervix with closed Os slightly tilted towards right side.

We suspected intestinal obstruction in view of persistent vomitings and constipation. She was passed NG tube which drained 800 ml of stomach contents. Her Hemoglobin was 6 mg/dl so was corrected by blood transfusion. GS team cleared her from there side and she passed stool after 2 days. Her general condition improved after IV fluids, antibiotics and blood transfusion so she was planned for discharge after ultrasound.

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Ultrasound findings showed an alive intrauterine fetus with breech presentation. The fetal parameters corresponding to 33 weeks. Scanty liquor. Placenta was anterior low lying covering the Os. Dilated, fluid filled, loaded bowel loops seen with sluggish peristalsis. Ultrasound abdomen done showed normal viscera with just prominent bowel loops.

She presented again after one week in OPD with same complains of abdominal pain and constipation. She was again admitted for conservative treatment. Baselines were repeated and ultrasound was done. This time ultrasound showed single alive fetus with breech presentation at 34 weeks pregnancy. AFI of 5.3 cm. Placenta posterior low lying completely covering the Os, loss of interface between bladder wall and myometrium, few vessels are seen running longitudinally and transversely suggestive of placenta Previa.

On view of persistent abdominal pain on /off she was planned for surgery at 35 weeks pregnancy after arrangement of blood and ICU. No suspicion of abdominal pregnancy was given sonographically or clinically. She was planned to be operated on the lines of placenta previa with suspected morbidly adherent placenta.

Operative findings showed on opening the cavity a large feeding vessel was visualized and placenta was found adherent to omentum. A vessel started to bleed so nick given after pushing peritoneum down. The baby was delivered with good apgars (shown in figure 4). Placenta was found adherent to omentum (as shown in figure 1). On exploring pelvic cavity uterus was found tilted towards right side and was normal in appearance corresponding to 14 weeks (as shown in figures 2). The left side of the tube was torn and some portion of placenta was attached to cornu (as shown in figure 3). The damaged tube was removed and whole of

the pedicle was clamped, cut and ligated. GS team was involved which helped in removing all of the placenta with omentum. Bilateral tubal ligation was done and a drain was left in peritoneal cavity after extensive washing with normal saline.

She was transfused 4 pint PC and 4 FFps during surgery as estimated blood loss was 2.5 litres and was shifted to ICU for further monitoring. The Patient was kept on ventilator for 24 hours and was extubated and stable. She was discharged in stable state at 6<sup>th</sup> post-operative day.

Figure 2: 14 Weeks size uterus

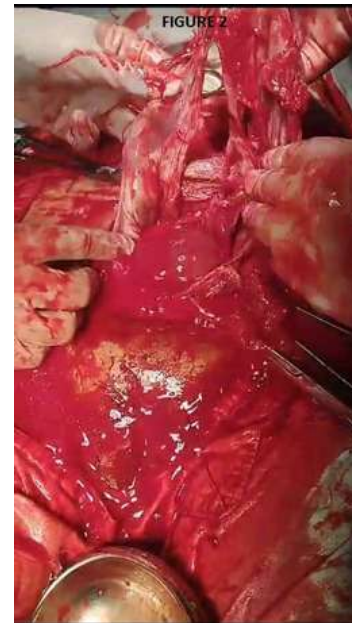


Figure 3: Left tube torn and some portion of placenta was attached to cornu

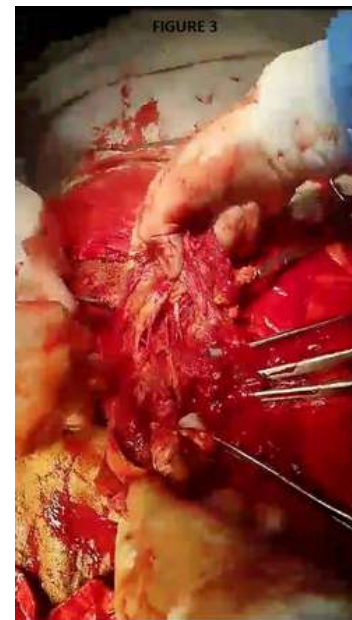
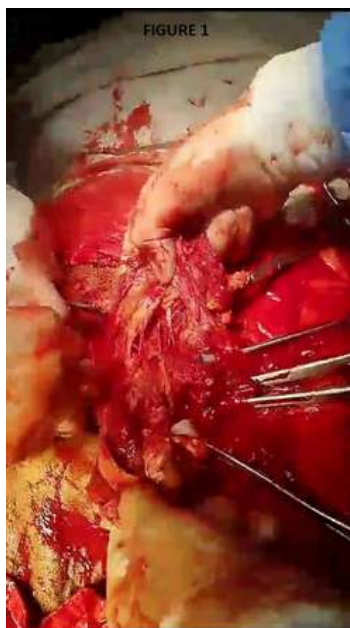


Figure 1: Placenta adherent to omentum



Figures 4: The baby with good apgars scores



**Authors Contributions:**

**Farah Hassan Khan:** Topic selection, study design, data collection, manuscript writing

**Tanzila Fahim:** Study design, manuscript writing proof reading

**Nighat Ali Shah:** Sample collection, study design, methodology

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# Trachea-o-esophageal Fistula following Button Battery Ingestion, Presenting One Month after the Event- A Rare Presentation

Rutaba Tariq, Iftikhar Ahmed Choudhary, Shanza Zaheer, Qaiser Naveed

## ABSTRACT:

Trachea-o-oesophageal fistula (TEF) formation after battery ingestion is a fatal complication with severe consequences. Urgent removal of battery is necessary within few hours. Persistent oral intolerance, respiratory difficulty or clinical deterioration after removal of battery should raise a suspicion of oesophageal rupture/leak or TEF. We present case of a 3-year-old who ingested button battery, which was diagnosed immediately but due to delay in referral to the concerned specialty the battery was removed on the 2<sup>nd</sup> day followed by large oesophageal rupture. However initially the child improved after the repair, the development of TEF was presented much later which was a rare presentation. A large fistula which was not closed by conservative approach was successfully closed surgically. The child was recovered after the repair, and the confirmation of adequate repair by esophagoscopy was done. Button battery ingestion (BBI) should be considered a surgical emergency, requiring urgent removal and vigilant monitoring.

**Key words:** Button battery ingestion (BBI), case report, oesophageal rupture, trachea-esophageal fistula (TEF),

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## BACKGROUND:

As children grow and explore the world, the tendency of putting things in mouth increases. Most foreign bodies pass through the gastrointestinal tract without any intervention, but ingestion of chemicals, medicine and batteries impose a great risk of complications. Ingestion of batteries has been less publicized and taken lightly by both parents and health care providers. Button battery ingestion (BBI) is a predictor for severe morbidity presumably due to leakage of highly caustic potassium or sodium hydroxide contained in these electric cells.<sup>1</sup> A literature review of complications after paediatric BBI showed esophagus is the most common organ affected by BBI complications.<sup>2</sup> serious complications arise in cases with oesophageal impaction.<sup>3</sup>

## CASE PRESENTATION:

A three-year-old previously healthy male child was brought to A&E department with history of BBI., while playing with his toys. The child was completely asymptomatic at that time. Initially, the parents visited a nearby hospital. On clinical examination there was no respiratory distress and child was vitally stable. The chest x-ray showed a radio opaque shadow at the level of neck. He was referred to tertiary care hospital where on arrival x-ray was repeated and urgent consultation was sought from the ENT department. Child was prepared for esophagoscopy. On endoscopic examination foreign body was found in the proximal oesophagus which was not retrieved and pushed into stomach, otherwise oesophagus was normal, the procedure was terminated, and Paediatric surgery opinion was sought. (fig1)  
The child who was initially stable had now developed high grade fever, and was not tolerating anything orally, he also started to deteriorate and was not able to maintain oxygen saturation on room air. On repeat chest and abdominal x-rays, the battery was found in stomach but by that time, the child had developed right sided Pneumothorax. On chest tube intubation purulent, foul-smelling pus was drained. We suspected oesophageal rupture. Gastrografin swallow was done which showed leak in distal 1/3<sup>rd</sup> of oesophagus. (fig2)  
Gastrostomy was done to remove foreign body and a feeding tube was placed. The child remained stable initially. He was observed for next 48 hours in intensive care for the clinical response. The child over the period did not improve and became septic. Repeat chest x-rays showed collapsed/trapped right lung with pyo-pneumothorax despite chest tube in place. Urgent thoracotomy was planned. It revealed empyema

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and fibrous tissue causing entrapment of right lung for which decortication was done and fibrous exudates were sent for culture. A 3.5cm longitudinal perforation was found in lower oesophagus. The defect was closed in two layers with absorbable sutures (4/0 PDS Polydioxanone Suture) and secured with pleural flap. The chest tube was removed on the 5th post op day. Baby had a smooth post op recovery. Fever settled with antibiotic cover as per sensitivity. On 8<sup>th</sup> post op day gastrograffin study was repeated, it showed bilateral bronchogram but no leak throughout the oesophagus. There was no free leak in pleural cavity. Child was therefore allowed to begin with clear liquids orally. The parents complained that the child vomited and coughed every time they gave him water. The child was kept under observation and kept NPO as he was not tolerating anything orally. He gradually became septic and had multiple fever spikes. To ascertain any leakage, gastrograffin study was repeated after a week. It again showed bilateral bronchogram with a suspect of minor leak at the level of cricopharynx. Virtual bronchography and CECT chest (contrast enhanced CT scan) and Flexible esophagoscopy was done and it revealed a 2cm oesophageal fistulous connection with trachea around 16cm from incisors.<sup>(fig3)</sup> These clinical squeals had taken a period of few weeks; the child was malnourished and

emaciated by that time. His chest infection had worsened and was septic. This entire scenario made the situation at high risk. Conservative management that took whole one month was a total failure and there was less chance of the fistula to close spontaneously. Surgery was planned. We successfully repaired the fistula with Oblique cervical approach and mini sternotomy. Esophageal and tracheal defects repaired separately with PDS 5/0, and a strap muscle flap placed in between.<sup>(fig4)</sup> Our patient remained intubated for 2 days and was extubated on 3rd post op day. He had slow but smooth post op recovery. Baby was discharged 2.5 months later, and feeding was advised through gastrostomy tube. One month later, repeat esophagoscopy was performed which showed normal mucosa and the child was started gradually on oral feed.

**DISCUSSION:**

In our patient, a large tracheoesophageal fistula developed and was diagnosed almost after a month the ingested battery was retrieved from the stomach via gastrostomy. In this child, button battery was impacted initially for tissue damage to occur, the battery was removed on 2<sup>nd</sup> day of the initial event. The delay in removing the battery led to complications. Recently, the North American Society for Paediatric

Figure 1; initial position of battery B; Battery in stomach and rt sided pneumothorax C; after chest intubation

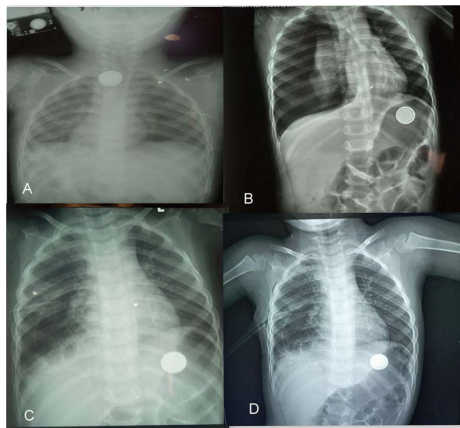


Figure 2: Gastrograffin study showing major esophageal rupture in lower 1/3<sup>rd</sup>

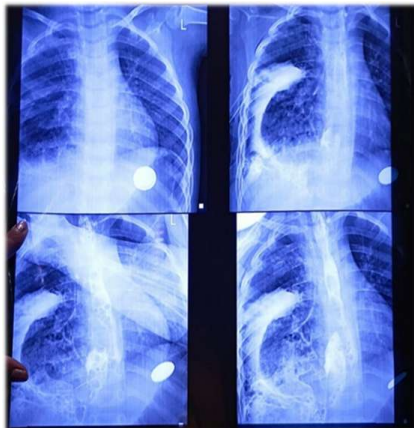
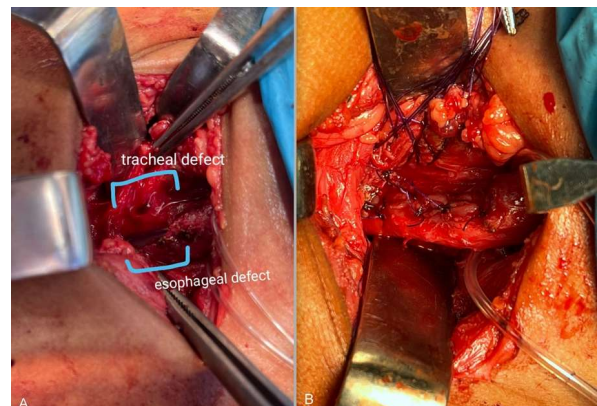


Figure 3: TEF identified on CECT Chest at the level of T3/4 in different positions A coronal section B sagittal section



Figure 4 Per-operative pictures of TEF (A) tracheal & esophageal defects (B) after repair





Gastroenterology, Hepatology, and Nutrition Endoscopy Committee revised the recommendations pertaining to the timing of endoscopic intervention. The presence of oesophageal button batteries mandates emergency removal within 2 hours regardless of the presence of symptoms.<sup>4</sup> We conducted literature search in pub med to search for development of TEF followed by button battery ingestion from the year 2010-2022. A similar case report was reported from, India, in which a child of one year of age ingested the battery and due to delay in diagnosis large fistula developed which was repaired surgically in the same way.<sup>5</sup> A case of 1 year old with BBI and was diagnosed on the 4th day was reported from UK. He developed TEF above the carina. Near total esophagectomy, cervical oesophagostomy and gastrostomy were performed with a patch repair of the trachea, followed by a bio-absorbable tracheal stent.<sup>6</sup> Another case reported in 2020 from Japan in which a 16-month-old ingested lithium button battery, on day 8 after retrieval, endoscopy and fluoroscopy identified a (TEF), 6 mm in diameter. Conservative management was conducted with periodic follow-up endoscopies, which showed signs of healing in the esophagus.<sup>7</sup> In all the above-mentioned cases the delay in the diagnosis lead to the devastating complications like oesophageal rupture and TEF formation. In our case the diagnosis was made immediately but due to delay in referral to the concerned specialty the battery was removed on 2<sup>nd</sup> day. However initially the child improved after the repair, the development of TEF was presented much later which was a rare presentation.

#### CONCLUSION:

Button batteries are the second most frequently ingested foreign bodies and can lead to serious clinical complications within hours of ingestion.<sup>8,9</sup> In a study conducted in Birmingham they concluded the use of Trauma I activations for suspected button battery ingestions has led to more expedient evaluation and shortened time to removal of impacted oesophageal batteries.<sup>10</sup> TEF induced by BBI is one of the most challenging issues for paediatric surgeons. Timely diagnosis, referral and intervention are important to avoid the complications. Once the complication has occurred; appropriate decision making, and timely decision making is necessary. If operated then vigilant post operative management, oesophageal rest with sufficient nutrition and after discharging careful and long follow-up are keys to success of management.

#### Authors Contributions:

**Rutaba Tariq:** Topic selection, study design, data collection, manuscript writing  
**Iftikhar Ahmed Chaudry:** Study design, manuscript writing proof reading  
**Shanza Zaheer:** Sample collection, study design, methodology  
**Qaisar Naved:** Sample collection, study design, methodology

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## Unusual Presentation of Extra Pulmonary Tuberculosis in Middle aged Female: A Unique Case Report.

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### ABSTRACT:

Pulmonary tuberculosis (TB) is a leading cause of morbidity and mortality among all infectious diseases especially in Pakistan where TB is endemic while extra pulmonary TB often encountered. However, primary salivary gland specifically unilateral parotid gland involvement is exceedingly uncommon. We present a case of 38-year old woman with six months duration of right parotid lump. The lump was firm and non-tender with bilateral cervical lymphadenopathy. No other constitutional symptoms of TB in our patient except weight loss. We presumed it a parotid neoplasm but after workup it reveals parotid TB which responds to first line anti-tuberculous therapy (ATT). So, careful exclusion of parotid neoplasm prevented unwanted surgery in our patient and patient recovered without any residual disease. We proposed that the differential diagnosis of a parotid gland swelling should include the infrequent possibility of parotid gland tuberculosis.

**Keywords:** Anti-tuberculous therapy, Extra-pulmonary Tuberculosis, Fine needle aspiration cytology, Parotid tuberculosis.

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### BACKGROUND

TB is a chronic necrotizing granulomatous disease caused by *Mycobacterium tuberculosis* primarily affecting the lungs known as Pulmonary Koch's. TB is endemic in Pakistan with the incidence of 264 per 100,000 people. Out of which

20% of cases have extra-pulmonary presentation<sup>1</sup>. TB rarely involves salivary glands with less than 200 cases of parotid TB reported yet<sup>2</sup>. The involvement of the salivary glands is even more uncommon because the constant flow of saliva prevents tubercular bacilli from building up in them. Owing to slow salivary flow, the parotid glands are more susceptible to be affected than other salivary glands<sup>3</sup>. Diagnostic challenges arise from the fact that parotid gland TB presents similarly to a parotid tumor<sup>4</sup>, and also when there is no relevant clinical history of TB.

### CASE PRESENTATION

A 38-year-old housewife presented at the outpatient clinic with the complaint of a rounded painless swelling below and in front of the right ear lobule for last 6 months, swelling was insidious in onset and gradually increased in size and attained a size of 3 x 3 cm. It was not associated with pain or change in size while chewing food. No history of asymmetry of face, difficulty in closing eyes, difficulty of chewing food, or drooling of saliva from mouth. No history of other swelling. There was a history of weight loss. She lost 6 kg over these months. She had no prior surgery or hospital admission. She was known hypertensive for which she has been taking verapamil for last 2 years. No history of autoimmune disease, mumps in childhood, earache, fever, and dental infection. No history of other symptom like fever, malaise, anorexia, cough, and discharge from swelling except her family history was positive for pulmonary tuberculosis, and there was no history of addiction or smoking.

On examination, there was a well-defined smooth surface spherical swelling of about 6 x 5 cm on right parotid region displacing right ear lobule upwards and outwards, it was firm in consistency with no signs of inflammation. The

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swelling was not fixed to the underlying masseter or overlying skin. No sign suggestive of facial nerve palsy. Oral examination was unremarkable with normal parotid duct opening. There were multiple mobile right sided cervical lymph nodes.

On routine blood test, her total leukocyte count was 18.4 (Normal Range  $4-11 \times 10^3$  /ul) with predominately lymphocytosis, Erythrocyte Sedimentation Rate was 80 mm/hour.

Her ultrasound neck showed an enlarged right parotid gland having a heterogenous texture with small hypoechoic focus, on Doppler increased vascularity was seen and this suggested parotitis. And there were multiple subcentimetric right cervical lymph nodes.

Her contrast enhanced CT scan (CECT) from base of skull to root of neck showed a mildly enlarged parotid gland without any necrosis and calcification, and no evidence of sialolithiasis. Multiple subcentimeter right cervical lymph nodes were seen. (Figure: 1). Fine needle aspiration cytology (FNAC) of right parotid gland and cervical lymph node both were carried out. FNAC of right parotid showed acellular smears comprising necrotic debris showing a caseous appearance. (Figure: 2). FNAC of right cervical lymph node (LN) showed cellular smears comprising two small collections of epithelioid histiocytes, having lymphoid cells in varying stages of maturation. (Figure: 3). It raised suspicion of tuberculosis so an excisional biopsy and high-resolution computed tomography (HRCT) of the chest was performed to rule out pulmonary tuberculosis. Excisional biopsy of cervical LN showed chronic granulomatous inflammation with necrosis. (Figure: 4). Her HRCT of the chest showed few calcified sub-centimeter-sized mediastinal and bilateral hilar lymph nodes.

Excluding benign and malignant growth and other infective etiologies patient was diagnosed with Primary Tuberculosis of unilateral Parotid gland involving cervical LN without lung involvement.

Meanwhile, Mantoux test became positive (30 mm in 72

Figure: 1. CECT scan shows only Right-sided Parotid gland enlargement and contralateral side is normal



Figure: 2. FNAC of right Parotid shows Caseous necrosis.

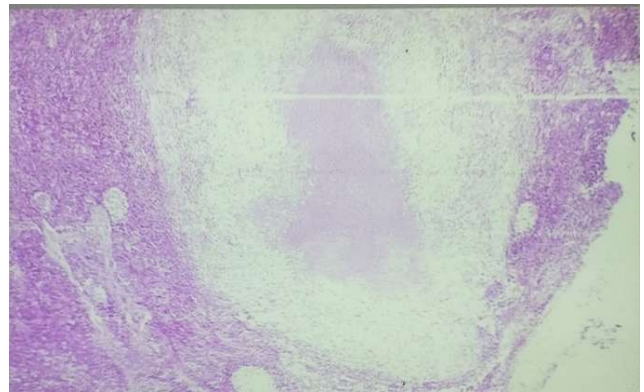


Figure 3: FNAC of Cervical Lymph node shows epithelial histiocytes.

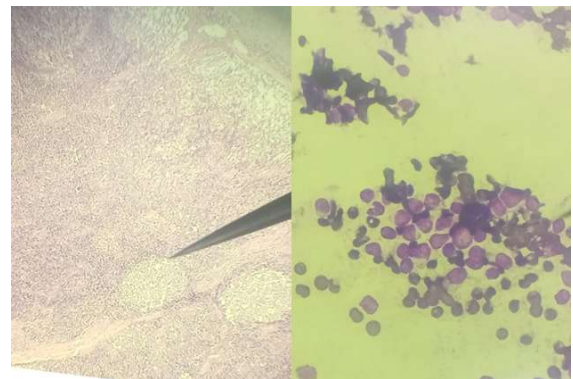
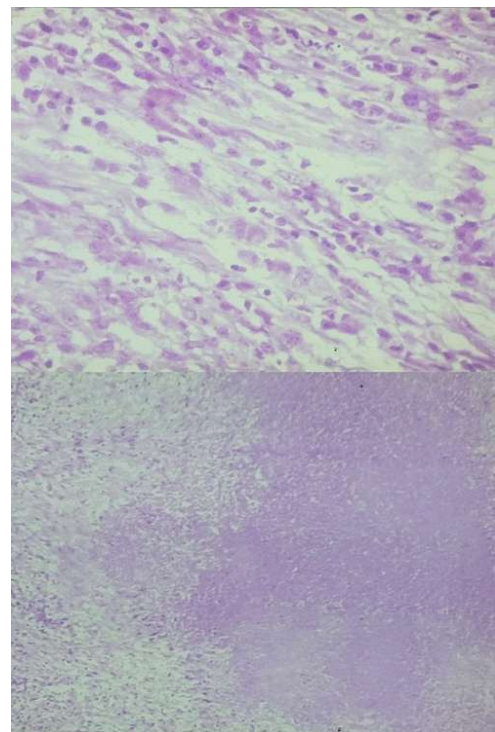


Figure: 4. Excision Biopsy of Lymph node shows Chronic Granulomatous inflammation.



hours with vesicle formation) which strongly support our diagnosis. The patient was prescribed first line ATT for 1 year with liver function monitoring and counseling for strict compliance of therapy. Result was satisfactory.

### DISCUSSION:

The long-known cause of chronic necrotizing granulomatous disease is *Mycobacterium tuberculosis*. Ten percent of extra-pulmonary sites are in head and neck area, with cervical lymph nodes being the most frequently affected. The larynx, deep neck space, and otitis media are the next most frequently affected regions. The skin, mouth cavity, oropharynx, nose, thyroid, salivary glands, and mandible are some less frequent sites. The first case of secondary parotid TB was documented in 1893. And the first case of primary parotid TB was reported in 1894, a year later<sup>3</sup>. Even in Pakistan, where tuberculosis is ubiquitous, salivary gland involvement is uncommon. The constant flow of saliva and presence of proteolytic enzymes like lysozymes and thiocyanate ions in salivary gland secretions may be the cause of this<sup>4</sup>.

Parotid TB is comparatively more common in males<sup>5</sup>, but in our case it found in female. Rarely does the localization occur in both parotid glands simultaneously; it is typically unilateral<sup>8</sup>. The majority of cases of parotid TB occur in adults, with a median presentation age of 45 years<sup>5</sup>. Parotid tuberculosis does not have any particular symptoms or clinical signs; it typically manifests as a slowly growing painless parotid lump<sup>5,8</sup> mimicking benign parotid tumor<sup>6</sup>. Sometimes, fistulization of the swelling can lead to the direction of tubercular pathology, but most of the time cutaneous plane remains intact with minimal or no evidence of inflammation. Rarely, tubercular sialadenitis results in trismus. Since parotid swelling is linked to cervical adenopathy, it may happen on its own. It is rare for primary disease to exhibit tubercular symptoms such as fever, asthenia, weight loss, and nocturnal sweats<sup>8</sup>. Parotid abscess is another possible presentation. Long-standing parotid abscess incision and drainage should delay until tuberculosis has been ruled out since doing so could cause a fistula or sinus formation<sup>7</sup>. In 2022, the first incidence of bilateral parotitis with facial nerve palsy was documented by Jameel Z et al which are extremely rare presentation of primary parotid TB<sup>9</sup>.

Along with FNAC, ultrasonography and CECT are effective methods for diagnosis confirmation; however, the FNAC report may not be definitive if the infection is active. Better findings are obtained when aspirated material is stained with AFB in conjunction with cytological studies<sup>7</sup>. In cases where FNAC and imaging yield conflicting results, surgical intervention is required to collect tissue for histological analysis. Typically, an excisional biopsy is carried out; however, if the entire parotid is affected, a total parotidectomy can be necessary<sup>7</sup>. There are two pathological types of parotid tuberculosis based on histology: the diffuse form and the nodular or circumscribed form. The nodular type involves

either periglandular or intraglandular lymph nodes. A cyst or cold abscess could be the appearance of it. This variety is more frequent. Pathological alterations may occur in glandular or interstitial tissue. The less frequent diffuse variety is characterized by both large and small caseation or abscesses that affect the gland parenchyma as a whole<sup>5,7</sup>.

The only course of treatment after diagnosis is ATT. Belatik H et al. in 2018 report two cases of parotid TB on histology after excision of parotid gland<sup>8</sup>. But in our case, we diagnosed on FNAC and antimicrobial treatment alone is beneficial, allowing the parotid swelling to subside and the tubercular focus to be eliminated. So, use of parotidectomy for diagnostic and/or therapeutic purposes is no longer a hot topic. For drug-sensitive tuberculosis, the World Health Organization suggests a six-month therapy regimen. The recommendations also apply to extra-pulmonary tuberculosis, with the exception of TB of the central nervous system, joint, or bone<sup>3</sup>.

### CONCLUSION:

Because of its rarity, diagnosis of parotid TB needs high level of suspicion<sup>1</sup>. It diagnosed accurately with the help of microbiology, histopathology and radiology<sup>1,5,9</sup>. The diagnostic accuracy of FNAC is very high with sensitivity of 81-100% and specificity of 94-100%<sup>6,7,10</sup>. After definitive diagnosis parotid TB is completely curable with ATT<sup>5,6,9</sup>. As in our case, patient is recovered and enjoying happy healthy life. So, no need of unwanted parotidectomy to increase morbidity of patient.

#### Authors Contributions:

**Madeeha Shahid:** Research conception, data collection and Writing of final draft  
**Pirhay Fatma:** Research Concept, Data collection  
**Nazia Qamar:** Data Collection  
**Muhammad Salman Zafar:** Data Collection  
**Aun Ali:** Review of Final draft  
**Aamir Hussain:** Review of Final Draft

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**JN.1 Variant Alert: Pakistan's Precarious Healthcare System under Intense Scrutiny**

Kanza Mehmood, Maryam Moazzam, Minahil Fatima Sajid

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Dear Editor,

The recent COVID-19 variant, JN 1, identified by the World Health Organization, is considered a notable strain stemming from theOMICRON subvariant BA.2.86. Despite its unique spike protein mutation (S:L455S), JN.1 is anticipated to have minimal impact on global public health. The singular modification in the virus's spike protein, distinguishing JN.1 from BA.2.86, suggests that existing vaccines should effectively counter both variants. The World Health Organization emphasizes the continued efficacy of current vaccines in protecting against diseases and deaths caused by JN.1, urging individuals, especially those at high risk, to maintain updated vaccinations<sup>1</sup>.

Nonetheless, JN.1 exhibits substantial resistance to monovalent XBB.1.5 vaccine sera, highlighting its potential as a highly immune-evading variant<sup>2</sup>. The JN.1 strain initially surfaced in Pakistan in early January, and cases have steadily increased, reaching 15 by the second week of the month. Early on, the National Institute of Health (NIH) ordered increased covid testing at airports for the passengers inbound from international flights<sup>3</sup>.

The initial waves of COVID-19 were managed better than expected in Pakistan, thanks to early and effective measures, including travel restrictions, contact tracing, quarantine facilities, and lockdowns<sup>4</sup>.

However, concerns arise with the enhanced immune-evasion of the JN.1 variant; as previously implemented measures may no longer be as practical in curbing its spread.

The COVID-19 pandemic in Pakistan led to widespread economic challenges, including unemployment and increased poverty, affecting the standard of living for many. The fear

of another lockdown is heightened as these economic difficulties make public cooperation less likely. Furthermore, Pakistan appears to have the ideal combination of variables for the spread of JN.1. The living conditions, exacerbated by rising poverty, contribute to challenges in isolating and quarantining individuals, potentially facilitating the spread of the JN.1 variant<sup>5</sup>.

The medical infrastructure in the country is inadequate, and rural populations are unable to access quality and timely healthcare facilities leading to underreported cases and hindered contact tracing. Despite the government's acquisition of 500,000 additional COVID-19 vaccines in response to the new variant, vaccine hesitancy persists due to low literacy rates which can lead to misunderstandings about long-term vaccination consequences<sup>3</sup>.

In summary, the emergence of the JN.1 COVID-19 variant in Karachi, Pakistan, raises concerns due to its enhanced immune evasion and resistance to specific vaccines. Existing economic challenges, potential lockdown fears, and the country's healthcare limitations contribute to the complexity of managing the variant. Urgent and coordinated efforts are needed to address these issues and safeguard public health in Pakistan.

**Authors Contributions:**

**Kanza Mehmood:** Idea conception, proof reading, final approval

**Maryam Moazzam:** Write up and editing

**Minahil Fatima Sajid:** Write up

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- 1) Objective, 2) Study design and setting, 3) Methodology, 4) Result and 5) Conclusion.

[state the purpose of the study (objective), basic procedures (methodology with study design, subjects/animals, place & duration of study, drug/chemical/equipment, procedure or protocol), main findings (results) and conclusion (It should emphasize new and important aspects of the study.)]

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### 2. Introduction

State the purpose of the article and summarize the rationale for the study. Give only strictly pertinent references and do not include data or conclusions from the work being reported. At least 10 to 12 references should be included in the introduction. International and national literature review indicating the rational and objective of the study.

### 3. Methodology:

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Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the Introduction or the Results section. Include in the Discussion section the implications of the findings and their limitations, including implications for future research. Relate the observations to other relevant studies. Link the conclusions with the goals of the study.

#### **6. Acknowledgment**

List all contributors who do not meet the criteria for authorship, such as a person who provided purely technical help, writing assistance, or a department chair who provided only general support. Financial and material support should also be acknowledged.

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The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. *Med J Aust* 1996; 164: 282-4

#### **c) No author given**

Cancer in South Africa [editorial]. *S Afr Med J* 1994;84:15

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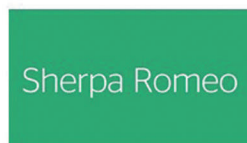
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