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- Therapeutic Effectiveness of Probiotics in preventing Osteoporosis and Regulating Bone Health: A Review of Literature.

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- Effective Temperaments and Attachment Styles as Mediators of Psychological Distress during the COVID-19 Pandemic.
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- Frequency Of Central Perforation of Tympanic Membrane in Patients of Chronic Suppurative Otitis Media with Cholesteatoma.
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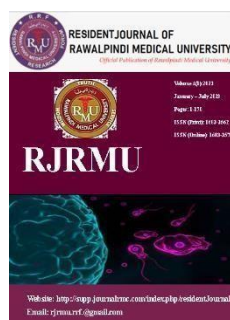
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Role of Research Forums in Medical Universities

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Research forums play a pivotal role in medical universities, acting as essential platforms for fostering scientific inquiry, collaboration, and knowledge dissemination. These forums provide a space where faculty, researchers, and students can engage in meaningful discussions, exchange ideas, and contribute to advancements in medical sciences. By offering a dynamic environment that encourages exploration and innovation, research forums in medical universities contribute significantly to the growth of both individuals and the medical field as a whole. One of the primary functions of research forums is to facilitate interdisciplinary collaboration. Medical universities house experts from various disciplines, such as medicine, biology, chemistry, and engineering. Research forums break down the traditional barriers between these fields, encouraging cross-disciplinary partnerships that can lead to groundbreaking discoveries. For instance, a collaboration between medical researchers and engineers might result in the development of cutting-edge medical devices.¹ These collaborations foster creativity and encourage researchers to think beyond their own domains, leading to holistic solutions for complex medical challenges. Furthermore, research forums provide a platform for students to engage actively in the research process. By participating in these forums, students gain exposure to real-world research scenarios, enhancing their critical thinking and problem-solving skill.² Such experiences can have a lasting impact on their academic and professional trajectories, encouraging them to pursue careers in research and contribute to the advancement of medical knowledge. Research forums also promote the dissemination of research findings. Through presentations, seminars, and workshops, researchers can share their work with a wider audience, receive feedback, and refine their ideas.³ This not only accelerates the pace of discovery but also ensures that research is subjected to rigorous scrutiny, enhancing its credibility. Moreover, these events often attract renowned experts and guest speakers, exposing participants to

diverse perspectives and fostering a culture of continuous learning. In addition to fostering collaboration and knowledge sharing, research forums offer a space for the incubation of novel research ideas. Discussions that take place within these forums can spark innovative thinking and lead to the formulation of research questions that might not have been considered otherwise.⁴ This environment of intellectual stimulation encourages researchers to explore unconventional avenues, potentially leading to breakthroughs that have a transformative impact on medical practice. It is worth noting that research forums contribute not only to the academic community but also to the broader healthcare landscape. Many research findings have direct implications for clinical practice. By facilitating the translation of research into actionable insights, these forums play a vital role in bridging the gap between academia and patient care.⁵ For instance, a study on a new diagnostic technique presented in a research forum could eventually find its way into routine clinical procedures, benefiting countless patients. In short, research forums in medical universities are indispensable for promoting collaboration, idea generation, and knowledge dissemination. These platforms facilitate interdisciplinary partnerships, engage students in the research process, and contribute to the translation of research into practical applications. By nurturing a culture of innovation and inquiry, research forums have a profound impact on the advancement of medical sciences and the improvement of healthcare outcomes. The same theme and Innovative idea of knowledge dissemination is being followed in Rawalpindi Medical University, Rawalpindi, and providing a solid platform of learning, progression, and intellectual stimulation not only to the residents, but students as well

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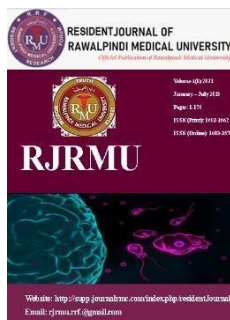
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Therapeutic Effectiveness of Probiotics in Preventing Osteoporosis and Regulating Bone Health: A Review of Literature

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ABSTRACT

Introduction Osteoporosis is most common bone disorder that is characterized as low bone mineral density due to defective bone mineralization and frequent bone fractures. Probiotics have gained increasing attention in recent years due to their potential health benefits. These live microorganisms, when consumed in adequate amounts, confer a positive impact on the host by modulating the gut microbiota composition and function.

Research design and methods Literature search was done through various data bases like, PubMed, Google scholar, EMBASE, and web of science. This search work was done in 2 months durations and articles with high quality were selected for synthesis of this review.

Results Probiotics are live microorganisms that provide health benefits when consumed in adequate amounts. While their impact on gut health is well-known, recent research suggests that probiotics may also play a role in promoting bone health. Probiotics represent an emerging and promising approach in the management of osteoporosis. By modulating the gut microbiota, probiotics have the potential to positively influence bone metabolism, enhance calcium absorption, regulate inflammation, and impact bone turnover. Clinical studies have shown the potential benefits of probiotic supplementation in improving bone health, particularly in postmenopausal women. The most commonly observed probiotics having positive impact on bone were *Lactobacillus* and *Bifidobacterium*. However, more research is necessary to fully understand the optimal use of probiotics in osteoporosis management.

Conclusions *Lactobacillus* and *Bifidobacterium* are most commonly observed organism used in treatment of osteoporosis. By modulating the gut microbiota, probiotics have the potential to positively influence bone metabolism, enhance calcium absorption, regulate inflammation, and impact bone turnover.

INTRODUCTION

Osteoporosis is most common bone disorder that is characterized as low bone mineral density due to defective bone mineralization and frequent bone fracture.¹ The impact of osteoporosis is higher among females as compared to males and it is an estimate that in United States about 0.3% to 1.7% of population is having bone fractures related to osteoporosis.² It is a multifactorial disorder associated not only with low hormonal profile of postmenopausal women, but also with various inflammatory and metabolic diseases as well.³ On the basis of etiology, osteoporosis is classified as either primary or secondary osteoporosis with primary being associated with low estrogen state in postmenopausal females and secondary osteoporosis having association with other bodily diseases like endocrine abnormalities (Hyperthyroidism and hypercortisolism), autoimmune disorders (rheumatoid arthritis, Inflammatory bowel disease), Hematological disorders (multiple myeloma and other infiltrating diseases) and finally various drugs profile like steroids and immobilization due to some chronic illness.⁴

Osteoporosis is now considered as a debilitating condition that hamper not only daily life activities but also posing significant care cost in resource poor countries. Now much attention is being given in therapeutic advances for treating osteoporosis. Various treatment options have been proposed, however dietary supplementation with calcium and vitamin D is of greater value along with other pharmacotherapy like bisphosphonates, teriparatide, selective estrogen modulators, and biological agents like denosumab, romosozumab.^{5,6} The role of probiotics in treatment of osteoporosis is of special interest in the field of microbiology as compared to dietary and pharmacological treatment. Studies have evaluated the

significance of host microbiota in maintaining health and overall body physiological functioning.^{7,8} Probiotics are dietary supplements containing microorganisms of non pathologic potential that are used for treatment and prevention of various pathological conditions, osteoporosis is one of them.⁹ Recent studies have shown the significant role of probiotic microorganisms in maintaining bone health and prevention of pathological fractures in both human and animal model studies.¹⁰ As various studies have evaluated the usefulness of probiotics in treatment of various pathological conditions including osteoporosis. This review will highlight not only highlight not only the pathophysiological Mechanisms of osteoporosis, but will also enlighten the usefulness of various probiotics as therapeutic choice in treatment of osteoporosis.

Bone structure and functions:

Bone is a type of mineralized connective tissue that is composed of four different types of cells namely, osteocytes, osteoblasts, bone lining cells and osteoclast.¹¹ The bones are classified as long bones, short bone, irregular bones, and flat bones. However, long bones are further classified as compact bones which are outer solidified part of bone filled with organic ground substance and inorganic salts, in the same vein the spongy bone is characterized by the presence of spongy, honey comb like bony structure that is found at end of long bones containing bone marrow.^{12,13} The classification of different types of bones are given in **figure 1**. The skeleton is one of the largest organs of the body that function not only as support, movement, and internal organs protection but also various homeostatic and some extraskeletal functions like mineral reservoir (most commonly calcium) and release of various bone derived factors (BDFs).¹⁴ The three major cells have been identified in bone formation and bone remodelling and these cells are osteoblasts, osteocytes, and osteoclasts, each having different set of functions and features as shown in **figure 2**.

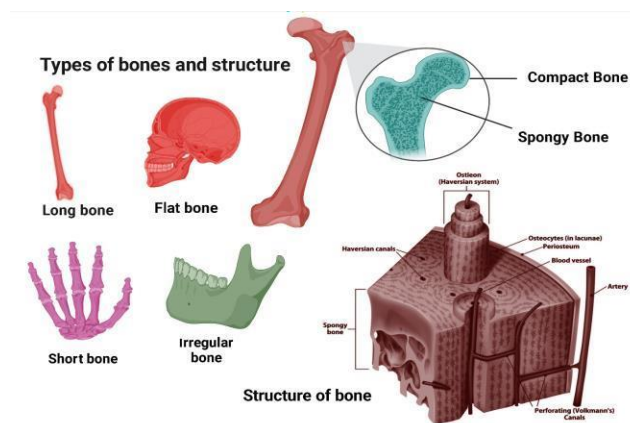


Figure 1: Classification of different types of bones

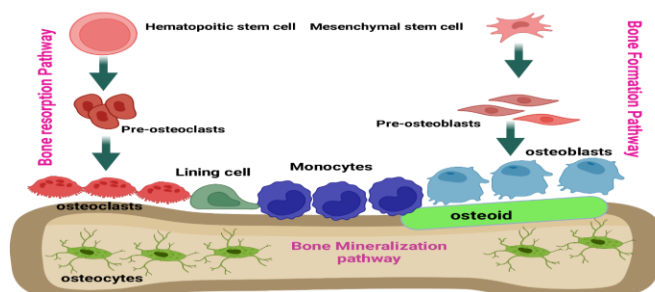


Figure 2: Bone formation, bone remodelling and mineralization process.

Primary Osteoporosis

Many kinds of literature illustrate various causes of osteoporosis, these causes are mainly related to age and genetic factors. Primary osteoporosis which is a bone remodeling disease when correlated with age is further subdivided into two types, type 1 primary osteoporosis mainly occurs in women about 10-15 years after their menopause (exclusively involving trabecular bone loss)¹⁵, type 2 primary osteoporosis also known as senile osteoporosis occurs in both women after the age of 65 years and men after the age of 75- 80 years (involving both trabecular and cortical bone loss)^{16,17}, and the genetic factor is most prevalent in children with a strong family history of multiple fractures. The pathophysiology behind type 1 primary osteoporosis is primarily estrogen deficiency in postmenopausal women, estrogen plays an important role in bone remodeling through its various effects, it is a continuous process of bone resorption followed by bone formation regulated by serum calcium ion, PTH, vitamin D, estrogen, cytokines and many other factors. Estrogen stimulates bone formation by directly stimulating the estrogen receptors on bone, which in return increases the expression of cytokines, M-CSF and RANKL in osteoblast and stromal cell¹⁸, apart from this, the function of estrogen in bone formation is less understood than bone resorption. Estrogen lessens bone resorption by decreasing bone mass's sensitivity to PTH and increasing the synthesis of calcitonin, it increases the mineralization of bone by enhancing the intestinal resorption of calcium from the intestine and reducing its secretion by the kidneys.¹⁹ Type 2 osteoporosis (senile osteoporosis) is a low-bone turnover disease, it is usually accompanied by systemic low-grade chronic inflammation and enhanced inflammatory mediators, such as IL-6 and TNF- α which makes the immune cells senescent, this enhances adipogenesis, osteoclastogenesis and reduces osteoblastogenesis.²⁰ Primary Osteoporosis in children is a genetic disorder, the most common form of osteoporosis is OI (osteogenesis imperfecta)²¹ and other forms manifest due to abnormal collagen formation(mainly), increased bone turnover, abnormal mineralization and osteoblast dysfunction. Overall Primary osteoporosis with fragile fractures compromises patients' quality of life and is a social and economic burden on families and health resources.

Secondary Osteoporosis

Secondary osteoporosis, second most common type of osteoporosis is a bone remodeling disease, more prevalent in men with underlying diseases than pre-menopausal and post-menopausal women, the factors contributing towards secondary osteoporosis through various pathologic process are briefly explained below.²² Long-term glucocorticoid therapy for the chronic systemic disease has a major side effect of osteoporosis by increasing bone loss through stimulating osteoclastic activity resulting in bone fractures. All of the endocrine disorders are associated with an increased risk of fractures by directly stimulating bone resorption.^{23,24} Gastrointestinal, hepatic and nutritional disorders associated with osteoporotic fractures are mainly due to malabsorption e.g of calcium, nutritional deficiency e.g of vitamin D and increased levels of inflammatory disorders, upregulating osteoclasts and downregulating the osteoblasts.²⁵ Anorexia nervosa links osteoporosis with weight loss and hypogonadotropic hypogonadism, hence decreasing bone mass density.²⁶ Hemochromatosis and other chronic liver diseases contribute to osteoporosis through factors like hypogonadism, vitamin D deficiency, liver failure and direct toxicity resulting in increased bone resorption and decreases bone formation.²⁷ Hematological disorders linked with osteoporosis results in inflation of bone resorption and suppression of bone formation through many mediators release.²⁸ Renal disorders, idiopathic hypercalciuria is associated with decreased renal calcium resorption, chronic kidney disease is associated with decreased resorption and increased excretion of calcium²⁹ and renal tubular acidosis acidic environment increases the osteoclastic activity resulting in bone resorption. Osteoporosis in patients with autoimmune diseases is due to various cytokines and chronic glucocorticoid therapy. Osteoporotic fractures are one the common side effect of antidepressant and antiepileptic drugs, therefore screening must be done before using them. Anticoagulants inhibit the differentiation and function of osteoblasts and increase bone resorption. Loop diuretics increase calcium secretion and decrease the reabsorption of calcium. Proton pump inhibitors inhibit the absorption of calcium from the gut. Hence secondary osteoporosis should be managed according to the underlying cause of fractures.

Diagnostic approaches of osteoporosis: Establishing a definite diagnosis of osteoporosis is done with help of detailed history and clinical investigations. It is important to rule out primary or secondary cause of the disease with the help of history to streamline your approach towards clinical investigations. The foremost presentation of patient with disease is after sustaining fragile fractures (pathological).³⁰

History and Clinical Examination:

A complete history of signs and symptoms will help deduce primary or secondary cause of disease. Estrogen deficiency in menopausal women causing osteoporosis is primary, while all other systemic diseases causing decrease in bone marrow

density leading to fractures and bone fragility are considered to be secondary causes.³¹ Clinical examination must include BMI and height loss evaluation. Clinical signs of kyphosis, localized tenderness may point out possible pathological fractures.³²

Fracture Risk Assessment:

Patients above 50 years of age and strong history or patients below 50 years of age with definite risk factors may be indicated for fracture risk assessment by commonly used tools i.e., FRAX or Q Fracture. These tools are globally recommended to establish a diagnosis of osteoporosis.³²

Dual Energy X-Ray Absorptiometry (DEXA):

Gold standard test to confirm osteoporosis is Dual-energy X-ray Absorptiometry (DEXA Scan) however only individuals with established fracture risk, risk factors or pathological fractures should be subjected to the scan. Ideal subjects for scan are spine and hip. However, distal radius may also be serving the purpose in case of limitations. DEXA scan uses both, high energy and low energy X-rays to evaluate bone marrow density (BMD) and fragility risk of bone. Results are presented as T score which is difference of patient's bone density from average bone density of healthy individual. According to WHO, reference value to establish diagnostic criteria is done by standard deviation method as follows.³³

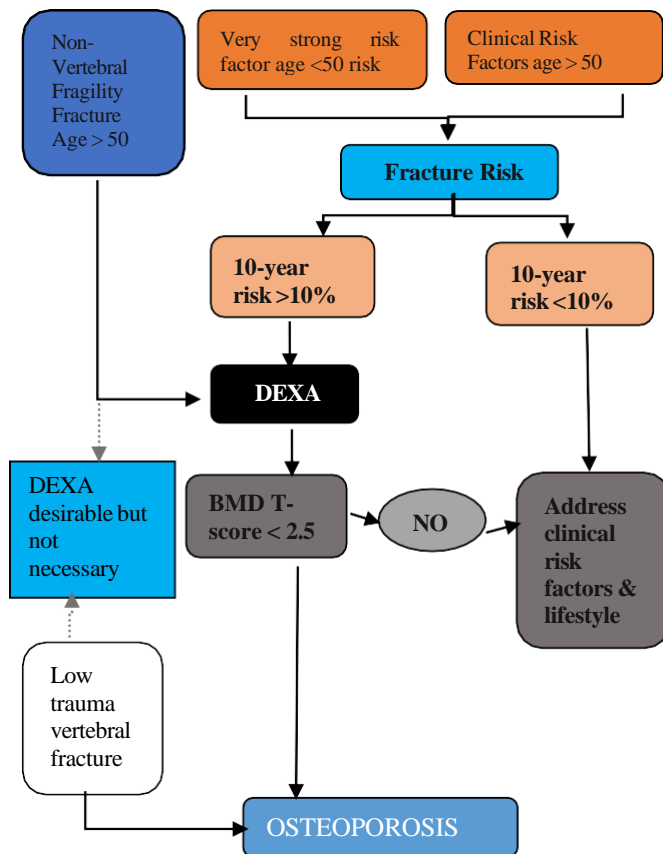
Table 1: WHO criteria for osteoporosis diagnosis

WHO criteria for Osteoporosis	
Definition	T-score
Normal	$\geq -1SD$
Osteopenia	Between 1 and - 2.5 SD
Osteoporosis	$\leq - 2.5 SD$

Other Investigations:

In case, history is suggestive of secondary osteoporosis, further clinical tests are required to rule out the cause. Secondary osteoporosis can be present in pre and post-menopausal women(30%) and in men (50 to 80%).¹⁷ Secondary causes can be endocrine or drug induced.³⁴ Diagnostic tests of systemic diseases help investigate the cause such as TTG antibody (coeliac disease), TFT (thyrotoxicosis), serum protein electrophoresis and urinary Bence Jones protein (multiple myeloma and monoclonal gammopathy of uncertain significance), Liver function test for liver diseases, renal function tests for renal impairment, Serum calcium and serum phosphate levels in osteomalacia and hyperparathyroidism. Serum hormonal levels in endocrine disorders.³² Systemic diseases mainly cause disruption of microarchitecture of bone by either release of cytokines³⁴ or by destruction through chemical and hormonal imbalance leading to fragility and bone fractures.³⁵

Steps to establish a diagnosis for osteoporosis:



Probiotics and their significance:

Probiotics have gained increasing attention in recent years due to their potential health benefits. These live microorganisms, when consumed in adequate amounts, confer a positive impact on the host by modulating the gut microbiota composition and function.³⁶ Probiotics exert their effects through various mechanisms, including gut microbiota modulation, reinforcement of the intestinal barrier, and immunomodulation. Probiotics help restore the balance of gut microorganisms by inhibiting the growth of harmful bacteria, promoting the growth of beneficial bacteria, and modulating microbial metabolites.³⁷ This modulation contributes to improved digestion and nutrient absorption. Furthermore, probiotics enhance the integrity of the intestinal barrier, preventing the translocation of harmful pathogens and toxins into the bloodstream.³⁸ This reinforcement of the barrier function is crucial for maintaining gut health and preventing inflammation. In terms of immunomodulation, probiotics interact with the immune system, influencing the production of cytokines and enhancing the immune response.³⁹ This immunomodulatory effect of probiotics contributes to the prevention and treatment of certain diseases. By promoting a balanced immune response, probiotics can help reduce the risk of infections and support overall immune function.⁴⁰

Probiotics have been associated with numerous health benefits across various areas. They have shown efficacy in improving digestive health by alleviating symptoms of irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and antibiotic-associated diarrhea.^{41,42,43} The strains *Lactobacillus* and *Bifidobacterium* are particularly notable for their positive effects on gut health.

Additionally, probiotics can strengthen the immune system, reducing the risk of respiratory tract infections such as the common cold.⁴⁴ They also show promise in supporting mental health, with emerging evidence suggesting a link between the gut microbiota and conditions like anxiety and depression.⁴⁵ Probiotics may positively influence mood and cognitive function. Probiotics have been studied for their potential in reducing the incidence and severity of allergic conditions, including eczema and allergic rhinitis.⁴⁶ By modulating the immune response and promoting immune tolerance, probiotics can help manage allergies and atopic diseases.

Several probiotic strains have been extensively studied for their health-promoting effects. *Lactobacillus rhamnosus* GG is well-known for its potential to alleviate diarrhea and prevent gastrointestinal infections.⁴⁵ *Bifidobacterium breve*, another notable strain, supports a healthy gut microbiota and has shown promise in reducing IBS symptoms and enhancing immune function.⁴⁶ *Saccharomyces boulardii*, a yeast-based probiotic, has been studied for its effectiveness in preventing and treating antibiotic-associated diarrhea and *Clostridium difficile* infection.⁴⁷ While probiotics are generally considered safe for most individuals, certain populations, such as those with compromised immune systems or critical illnesses, should exercise caution.⁴⁸ It is advisable to consult a healthcare professional before starting probiotic supplementation, especially in such cases. Probiotics play a significant role in promoting overall health and well-being. Their mechanisms of Action, including gut microbiota modulation, reinforcement of the intestinal barrier, and immunomodulation, contribute to their potential health benefits. Notable probiotic strains like *Lactobacillus rhamnosus* GG, *Bifidobacterium breve*, and *Saccharomyces boulardii* have shown promising results in various areas of health. However, it is important to consult a healthcare professional before incorporating probiotics into one's routine, particularly in special populations.⁴¹

Probiotics and bone health:

Probiotics are live microorganisms that provide health benefits when consumed in adequate amounts. While their impact on gut health is well-known, recent research suggests that probiotics may also play a role in promoting bone health. This article aims to provide a comprehensive overview of the relationship between probiotics and bone health, including their mechanisms of action and clinical implications. Probiotics can influence bone health through various mechanisms. Firstly, they can enhance the absorption of calcium, a crucial mineral for bone formation

and maintenance. Probiotics increase the activity of calcium-binding proteins in the intestines, improving calcium bioavailability.⁴⁹

Another mechanism by which probiotics affect bone health is through the modulation of gut microbiota. Probiotics can alter the composition of the gut microbiota, leading to the production of short-chain fatty acids (SCFAs) like butyrate. SCFAs have been associated with enhanced calcium absorption and improved bone mineral density.⁵⁰ Probiotics also exert immunomodulatory effects, reducing inflammation and oxidative stress, both of which are implicated in bone loss and osteoporosis.⁵¹ By modulating the immune response, probiotics may help maintain bone health.

Furthermore, probiotics may influence hormonal factors related to bone metabolism. Certain strains of probiotics have been found to increase the production of insulin-like growth factor-1 (IGF-1), a hormone involved in bone growth and remodeling.⁵² While the evidence regarding the effects of probiotics on bone health is still emerging, there have been promising findings from both animal and human studies. Animal studies have shown that probiotic supplementation can prevent bone loss and improve bone mineral density in models of postmenopausal osteoporosis.⁵³ In human studies, a combination of probiotics and calcium supplementation has been found to increase lumbar spine bone mineral density in postmenopausal women, compared to calcium supplementation alone.⁵⁴ Another study in older women found that a probiotic yogurt enriched with calcium and vitamin D improved markers of bone turnover.⁵⁵ Based on these findings, probiotics have the potential to be used as a complementary approach in the prevention and management of osteoporosis and other bone-related conditions. However, more research is needed to determine the optimal strains of probiotics, dosages, and duration of supplementation for achieving the best outcomes for bone health.

Probiotics therapeutic advances in osteoporosis management:

Osteoporosis is a chronic bone disorder characterized by decreased bone density and increased susceptibility to fractures. It predominantly affects postmenopausal women and the elderly population. The conventional approach to managing osteoporosis includes calcium and vitamin D supplementation, hormone replacement therapy, and medications that either inhibit bone resorption or stimulate bone formation. However, recent research has suggested that probiotics, live microorganisms with potential health benefits, may have a role in improving bone health and managing osteoporosis.⁵⁶ The gut microbiota, consisting of trillions of microorganisms residing in the gastrointestinal tract, plays a crucial role in regulating various physiological processes, including bone metabolism. The gut and bone are interconnected through a bidirectional relationship known as the gut-bone axis. Alterations in the composition and

function of the gut microbiota have been associated with changes in bone mineral density and bone turnover markers.⁵⁶

Probiotics, particularly strains of *Lactobacillus* and *Bifidobacterium*, have shown promise in promoting bone health and managing osteoporosis. Several mechanisms have been proposed to explain the beneficial effects of probiotics on bone metabolism. First, probiotics enhance calcium absorption by producing enzymes and short-chain fatty acids that improve calcium bioavailability in the gut. This, in turn, promotes bone mineralization and helps prevent bone loss.⁵⁷ Second, probiotics have the ability to modulate intestinal inflammation. Chronic inflammation has been linked to osteoporosis, and probiotics can reduce pro-inflammatory cytokines and increase anti-inflammatory markers, thereby indirectly promoting bone health.⁵⁸ Third, probiotics can influence the activity of osteoblasts (bone-forming cells) and osteoclasts (bone-resorbing cells). Certain probiotic strains have been found to stimulate osteoblastic activity while inhibiting osteoclastogenesis, leading to improved bone formation and reduced bone loss.⁵⁹

Clinical studies have investigated the effects of probiotics on bone health in humans. For instance, a randomized controlled trial demonstrated that daily supplementation with *Lactobacillus reuteri* improved bone mineral density in postmenopausal women with low bone mass.⁶⁰ Another study involving postmenopausal women showed that a combination of *Lactobacillus acidophilus* and *Bifidobacterium lactis* supplementation increased calcium absorption and decreased markers of bone resorption compared to a placebo group.⁶¹ Animal studies have also provided supporting evidence, with one study showing that supplementation with *Lactobacillus casei* significantly increased bone mineral density and improved bone microarchitecture in ovariectomized rats, a model of postmenopausal osteoporosis.^{62,63} While probiotic therapy shows promise in osteoporosis management, further research is needed to determine the optimal strains, dosages, and treatment durations. Additionally, long-term effects and underlying mechanisms of action require further investigation.

CONCLUSION

In conclusion, probiotics represent an emerging and promising approach in the management of osteoporosis. By modulating the gut microbiota, probiotics have the potential to positively influence bone metabolism, enhance calcium absorption, regulate inflammation, and impact bone turnover. Clinical studies have shown the potential benefits of probiotic supplementation in improving bone health, particularly in postmenopausal women. However, more research is necessary to fully understand the optimal use of probiotics in osteoporosis management.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

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Contribution:

Conceptualization: S.M, M.S.A

Data curation: M.S.A, A.R, S.M

Formal analysis: A.A, M.H.J, M.M

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Project administration: M.H.J, R.K, A.R

Review and approval: S.M, A.A

Availability of data and materials:

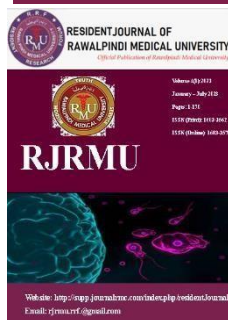
All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Affective Temperaments and Attachment Styles as Mediators of Psychological Distress During the COVID-19 Pandemic

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ABSTRACT

Introduction COVID-19 pandemic resulted in radical reactions among people mediated by differences in personalities, surrounding, coping mechanisms, and emotional reactivity. This study investigates the pandemic's psychological impact on the Pakistani population, identifying temperament and attachment styles, and analyzing the relationship between them.

Research design and methods: This is a cross-sectional observational study conducted through an online survey during the late phase of the first wave of COVID-19 outbreak between August to September, 2020. The self-structured questionnaire included 1) Demographic details, 2) The Kessler 10 Psychological Distress Scale, 3) Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Munster (TEMPS-M) scale, and 4) Attachment Style Questionnaire-SF. We ran standard univariate/bivariate comparisons of continuous measures (ANOVA) and categorical measures (contingency table/ χ^2) to compare factors of interest in the three groups of psychological distress, i.e., normal, mild-moderate and severe.

Results: Out of 405 participants, 308(76%) reported a likelihood for psychological distress. Age (OR = 0.864; $p = 0.015$) and -Confidence (OR = 0.946; $p = 0.037$) were significant protective factors while, -Preoccupation (OR = 1.061; $p = 0.039$) was a risk factor for higher levels of distress. Similarly, depressive (OR = 3.148; $p < 0.001$), cyclothymic (OR = 2.101; $p < 0.001$), irritable (OR = 1.682; $p = 0.001$), and anxious (OR = 1.971; $p < 0.001$) temperaments were all risk factors for higher levels of psychological distress in the study population.

Conclusion: Psychological distress levels have increased considerably, but the predictors and protective factors are approximately identical. More importantly, they reinforce the idea that both attachment styles and temperament can be used to predict the risk of developing psychological distress.

INTRODUCTION

Corona virus diseases-2019 (COVID-19) pandemic halted life as it were, and the effect it had on people was drastic. The differences in emotional, motor and attentional reactivity are termed as temperament. The attachment theory, in particular, focuses on the bonds built in childhood with caregivers and how they mediate the way individuals dealt with challenges later in life.¹ These attachment patterns are activated when facing stressful circumstances, and the response to those circumstances is, to some extent, affected by attachment patterns.²

While highly effective in limiting transmission, social distancing and self-isolation have contributed to psychological and emotional distress. In addition to its devastating physical health effects on the victims, the pandemic also spread a worldwide wave of fear and panic. The risk of transmission, even by unintentional contact with exposed individuals, made people distressed and anxious. The way individuals react to stressful situations and distress varies drastically from person to person.

We identified the predictors of how individuals perceived the mental health challenges that the pandemic posed and to find out various coping mechanisms they resorted to. This study investigates the pandemic's psychological impact on the Pakistani population, identifying temperament and attachment styles, and analyzing their relationship.

METHODS

This cross-sectional observational study was conducted through an online survey between August 15 and September 15, 2020. We chose this timeframe to assess participants' responses during the late phase of the COVID-19 outbreak, following the Pakistani government's decision to end the lockdown on August 10, 2020.³ Convenience sampling was used, and 450 forms were distributed out of 405 were filled, giving a response rate of 90%. All the participants completed the questionnaire online via Google Forms.

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Students from '15 different universities of Punjab were approached through social media platforms, such as WhatsApp and Facebook, and were requested to fill the forms. Informed consent was taken from all the participants as a part of the questionnaire.

Anonymity and data confidentiality was assured. Eligible participants were students in a university or college and had lived in Pakistan for at least the previous one month, i.e., from July 2020. Exclusion criteria were current hospitalization and a history of mental disorder. The Ethics Committee approved the study of Rawalpindi Medical University, Rawalpindi, Pakistan. The convenient sampling technique was used.

The sample size was calculated using the formula: $n = Z^2 \times p \times (1-p) / e^2$
 $= (1.96)^2 \times (0.5) \times (1-0.5) / (0.06)^2$
 $= 266.7 = 267$

Where,

n = required sample size

$Z = 1.96$ at 95% Confidence Interval (CI) p = population proportion, 50%

e = margin of error, 6%

Taking a 10% non-response rate, the sample size became 294. However, 405 participants were enrolled in the study.

A dedicated, self-report questionnaire was used, which included demographic and epidemiological variables of interest (age, gender, educational level), family history of psychiatric disorders, whether or not they were working on the frontline (as a volunteer or post-graduate trainee), and having direct contact with confirmed cases of COVID-19 infection.

Furthermore, it also included a single 6-point Likert-scale (0; completely unsatisfied, 1; somewhat unsatisfied 2; somewhat satisfied 3; satisfied, 4; very satisfied 5; completely satisfied) item to assess the participants' satisfaction with the government's plan of action against the pandemic. Besides, three scales were used for further psychometric evaluation. The K-10 scale⁴ was used to assess the psychological impact of the lockdown and the current COVID-19 situation. K10 is a 10-item questionnaire intended to yield a global measure of distress experienced in the most recent 4-week period. We adopted the cut-off scores of >19, >24, and >29 to detect the likelihood of mild, moderate, and severe psychological distress, respectively.⁵ The English version of the validated

Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Munster (TEMPS-M) was used to measure affective temperaments (cyclothymic, depressive, irritable, hyperthymic, and anxious).⁶ This is a shortened version of the original questionnaire and has also been validated by Naderer et al.⁷ It is a 35-item scale, with each item being scored on a 5-point Likert-scale. Each affective temperament is scored

with the help of 7 items, and then a mean is calculated for each of the five individual temperaments. The short-validated version of the original ASQ was used to measure AAS.⁸ This scale is a 29-item item scale and accurately captures the five temperaments hypothesized by Feeney et al. originally.⁹ It comprises of five subscales: "Confidence", describing secure attachment; "Discomfort with closeness", and "Relationships as secondary", both measuring attachment avoidance; "Need for approval", and "Preoccupation with relationships", both assessing attachment anxiety.

To better assess our aims, we subdivided our sample into three distinct groups according to K10 cut-offs: 1) subjects without a likelihood of psychological distress, 2) subjects with a likelihood of mild-moderate psychological distress, and 3) subjects with a likelihood of severe psychological distress. We ran standard univariate/bivariate comparisons of continuous measures (ANOVA) and categorical measures (contingency table/ χ^2) to compare factors of interest (including sociodemographic, AAS, and temperament characteristics) in the three groups. In all statistical analyses, P -values less than 0.05 were accepted as statistically significant. Data were analyzed using the Statistical Package for Social Sciences (SPSS) v.23.0 (IBM, Armonk, U.S.).

RESULTS

Out of 405 participants, 214 (52.8%) were male while 191 (47.2%) were female, giving us a male-female ratio of 1.12. The mean age of the participants was 21.62 (SD = 2.05). Out of the total, 97 (24%) reported a likelihood for no psychological distress, 135 (33.3%) reported a likelihood for mild-moderate psychological distress, while 173 (42.7%) reported a likelihood for severe psychological distress. The three groups only differed on the basis of gender ($\chi^2 = 6.4$; $p = 0.04$). (Table 1)

Table 1: Sociodemographic details and their relation with psychological distress

Characteristics (n, %)	Total	No psychological distress	Mild-moderate psychological distress	Severe psychological distress	χ^2	df	p

Overall	405	97(24%)	135(33.3%)	173(42.7%)			
Gender					6.3	2	0.04
					97		1
Male	214(52.8%)	55(56.7%)	80(59.3%)	79(45.7%)			
Female	191(47.2%)	42(43.3%)	55(40.7%)	94(54.3%)			
Educational Status					0.1	2	0.92
					68		0
Undergraduate	339(83.7%)	80(82.5%)	113(83.7%)	146(84.4%)			
Graduate	66(16.3%)	17(17.5%)	22(16.3%)	27(15.6%)			
Contact with COVID-19 + case	87(21.5%)	15(15.5%)	31(23.0%)	41(23.7%)	2.7	2	0.25
					63		1
Working on the frontline	36(8.9%)	5(5.2%)	12(8.9%)	19(11.0%)	2.6	2	0.27
					07		2

The three groups showed a significant difference regarding cyclothymic ($F = 134.02$; $p < 0.001$), depressive ($F = 140.74$; $p < 0.001$), hyperthymic ($F = 6.43$; $p = 0.002$), irritable ($F = 54.89$; $p < 0.001$) and anxious ($F = 72.06$; $p < 0.001$) temperaments. There was also a significant difference in the scores for the confidence ($F = 10.44$; $p < 0.001$), relationships as secondary ($F = 9.51$; $p < 0.001$), need for approval ($F = 51.07$; $p < 0.001$), and preoccupation with relationships ($F = 47.04$; $p < 0.001$) dimensions of the ASQ-SF (**Table 2**).

After ensuring the homogeneity of variances, a post-hoc analysis was done with the help of Tukey's HSD test. The factors that were significantly different between the groups were identified. Linear regression was then used to check for multi-collinearity between these variables and a VIF value of less than <3 was observed for all of

them. Finally, after confirming that none of the assumptions were violated, an ordinal (proportional odds logistic) regression was run, and odds ratios (OR) and 95% confidence intervals were calculated for each variable. Overall, the model showed a good fit (Pearson's chi-square = 699.19, $P = 0.996$), and it explained 52.4% of the variance in the level of distress (cox and snell) (**Table 3**).

Age (OR = 0.864; $p = 0.015$) and -Confidence (OR = 0.946; $p = 0.037$) were significant protective factors against higher levels of psychological distress. On the other hand, -Preoccupation (OR = 1.061; $p = 0.039$) was a risk factor for higher levels of distress. Similarly, depressive (OR = 3.148; $p < 0.001$), cyclothymic (OR = 2.101; $p < 0.001$), irritable (OR = 1.682; $p = 0.001$), and anxious (OR = 1.971; $p < 0.001$) temperaments were all risk factors for higher levels of psychological distress in the study population.

Table 2. Quantitative variables and their relationship with psychological distress

Characteristics (M±S.D.)	<i>Total</i>	<i>No psychological distress</i>	<i>Mild- moderate psychological distress</i>	<i>Severe psychological distress</i>	<i>F</i>	<i>df</i>	<i>p</i>
Age	21.6(2.1)	22(2)	22(2)	21(2)	9.319	2	<0.001
Satisfaction with government policies	2.74(1.3)	3(1)	3(1)	3(1)	0.533	2	0.587
Psychometric Assessment							
TEMPS-M Cyclothymic	3.05(1.03)	2.09(0.76)	2.88(0.85)	3.73(0.78)	134.02	2	<0.001
TEMPS-M Depressive	2.69(0.87)	1.91(0.57)	2.48(0.68)	3.28(0.71)	140.74	2	<0.001
TEMPS-M Irritable	2.35(0.86)	1.84(0.67)	2.15(0.73)	2.79(0.83)	54.891	2	<0.001
TEMPS-M Hyperthymic	3.36(0.83)	3.56(0.87)	3.42(0.8)	3.2(0.8)	6.438	2	0.002
TEMPS-M Anxious	2.61(0.93)	2.01(0.75)	2.36(0.79)	3.15(0.84)	72.056	2	<0.001
ASQ-SF Confidence	22.28(4.99)	24.13(4.52)	22.18(4.87)	21.32(5.07)	10.441	2	<0.001
ASQ-SF Discomfort with closeness	38.63(7.32)	37.84(6.78)	37.90(7.26)	39.64(7.57)	2.892	2	0.056
ASQ-SF Relationships as secondary	14.25(4.21)	13.39(4.16)	13.54(3.68)	15.28(4.43)	9.509	2	<0.001
ASQ-SF Need for Approval	19.29(5.37)	15.77(5.09)	18.59(4.96)	21.80(4.51)	51.074	2	<0.001
ASQ-SF Preoccupation with relationships	19.49(5.74)	15.69(5.27)	18.99(5.54)	22.00(4.83)	47.035	2	<0.001

Note: p-values in bold indicate significant results. TEMPS-M; Temperament Evaluation of Memphis, Pisa, Paris, and San Diego- Munster, ASQ-SF; Attachment Style Questionnaire-short form.

Table 3. Risk factors for increased levels of psychological distress			
Characteristic	<i>OR (C.I.)</i>	<i>Wald</i>	<i>P</i>
Gender (Male)	0.861 (0.561-1.398)	0.365	0.546
Age	0.864 (0.768-0.971)	5.971	0.015
ASQ Confidence	0.946 (0.899-0.997)	4.352	0.037
ASQ Relationships as Secondary	1.003 (0.945-1.065)	0.010	0.918
ASQ Need for Approval	0.975 (0.914-1.040)	0.602	0.438
ASQ Preoccupation	1.061 (1.003-1.123)	4.251	0.039
TEMPS-M Depressive	3.148 (2.142-4.626)	34.076	<0.001
TEMPS-M Cyclothymic	2.101 (1.539-2.867)	21.853	<0.001
TEMPS-M Hyperthymic	0.893 (0.658-1.211)	0.533	0.466
TEMPS-M Irritable	1.682 (1.223-2.313)	10.250	<0.001
TEMPS-M Anxious	1.971 (1.431-2.714)	17.281	<0.001

Note: p-values in bold indicate significant results. TEMPS-M; Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Munster, ASQ-SF; Attachment Style Questionnaire-short form, CI; Confidence Interval, OR; Odds Ratio.

DISCUSSION

During widespread outbreaks of infectious diseases, there is an air of extreme fear and uncertainty that likely contributes to an eventual rise in mental health issues. The current pandemic has been such an example, as it has led to a large proportion of the population reporting high levels of psychological distress in several countries^{10,11}. Brooks et al. also reported that an extended period of quarantine and strict limitations on freedom of movement was likely to lead to higher psychological distress.¹² Thus, we wanted to see how the pandemic and the subsequent quarantine period would affect mental distress levels. Our results support the statements. A lockdown period of approximately five months, with little to no unessential movement allowed, has led to about 75% of the population reporting some level of psychological distress. These scores are significantly higher than those reported by studies conducted at the start of the pandemic, such as Moccia et al. in Italy and Khalid et al. Pakistan.^{2,13}

In our study, age exhibited a protective effect against higher psychological distress levels, similar to a survey by Mazza et al.¹⁴ This is probably due to the higher levels of emotional maturity that come with increasing age. Several studies have shown the female gender as a risk factor for poor mental health in the current situation.¹⁴ Our research, however, found no such relation.

The ASQ—Confidencell of the secure attachment style was protective against higher levels of psychological distress, similar to the results obtained by Moccia et al. in Italy.² Bartholomew et al. stated that regulating distress is a function of attachment styles.¹⁵ Furthermore, Kidd et al. found that a secure attachment style was related to a better response to stress.¹ Thus, it makes sense that those having a secure attachment style are likely to be protected against psychological distress. Kidd et al. also showed a preoccupied style to have an inadequate response, which is supported by our results showing the ASQ subscale "Preoccupied with relationships" to be a risk factor for higher psychological distress levels.¹ As those in this group have an over-dependence on others¹⁶, prolonged separation from family members and loved ones have led to worsening mental health as predicted in the study by Brooks et al.¹²

Depressive, cyclothymic, irritable, and anxious temperaments are all risk factors for higher psychological distress levels. As a phenotype, anxious temperament is an increased psychological and biological reactivity to stressful stimuli.¹⁶ Similarly, depressive temperament is characterized by being pessimistic, sensitive to criticism, gloomy, and prone to excessive worrying.¹⁷ Thus, these individuals have a higher risk of suffering from poorer mental health. On the other hand, cyclothymic individuals suffer from sudden shifts of mood, behaviour, and energy and are more prone to developing bipolar disorders.¹⁸ A higher level of irritability was not found to significantly affect the level of distress by Moccia et al.² However, it was shown to be a significant risk factor in our results. A possible reason for this is that our study was conducted at the end of an extended isolation period. Thus, the people with irritable temperament, having a small amount of patience, had become restless with the drawn-out period of inactivity, leading to significantly higher distress. Furthermore, cyclothymic, irritable, and depressive temperaments exhibit an increased reactivity to stress in daily life and the preference to be in the company of others.¹⁷ As the pandemic induces severe stress daily and the isolation has cut off most social contact, it makes sense that the people with these temperaments would experience higher mental distress scores. Thus, our results mostly reinforce the results of Moccia et al.² They show that the people who have increased scores for any of the above-mentioned affective temperaments are at a higher risk of suffering severe levels of psychological distress in the current pandemic setting, even though they may not suffer from a manifest affective disorder.

There are a few limitations to this study. First of all, this was a cross-sectional study, so all their inherent drawbacks are applicable here. Most importantly, this survey does not cover the change in the variables over time. Secondly, as this was done in English over social media, the sample was reduced to the people who could speak English and had access to the facilities required; smartphones/tablets/laptops, internet, and social media. So, the sample size was smaller than it could have been.

CONCLUSIONS

Our study followed up on previous studies that were conducted during the start of the pandemic. Our results show that psychological distress levels have increased considerably, but the predictors and protective factors are approximately identical. More importantly, they reinforce the idea that both AAS features and temperament can be used to predict the risk of developing psychological distress. Thus, these can screen susceptible people and filter out individuals who might need specific psychiatric support during such unprecedented situations. They also provide evidence of an unmet need for rapid implementation of interventions that promote mental health in the local population.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

Financial Support:

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Contribution:

Conceptualization: A.R, S.S

Data curation: S.I, S.S

Formal analysis: A.U.A.B, S.M

Writing and editing: A.R, S.S

Project administration: A.R

Review and approval: A.U.A.B, S.I

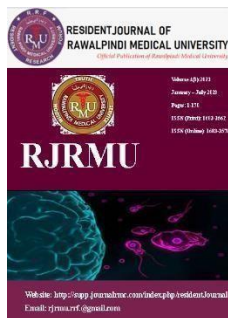
Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Association of Acute Kidney Injury (AKI) With SARS-CoV-2 Infection: An Experience from A Tertiary Care Hospital of Pakistan.

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ABSTRACT

Introduction Coronavirus disease 2019 (COVID-19), is a pandemic caused by severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2). Coronavirus predominantly affect respiratory system, however, its renal impact in the form of acute kidney injury (AKI) is something that is often overlooked. The aim of this observational study is to analyze the association of COVID-19 with acute kidney injury among patients admitted in tertiary care hospital.

Research design and methods It was an observational cross-sectional study involving 140 COVID19 positive cases conducted in department of Infectious diseases Holy Family Hospital, Rawalpindi. The association between the severity of COVID and the AKI suffered was analyzed using the Spearman's Rho and the Kendall's tau coefficient. A P-value of < 0.05 was taken significant and analysis was carried out by using SPSS.V.25.

Results Age, gender, co-morbid, and severity of COVID were all significantly related to the severity of Acute Kidney Injury (AKI). The mean age of the participants was 45.41 (SD = 11.85). Out of the total 140 diagnosed cases of COVID-19, 116 (82.9%) suffered from no AKI, 12 (8.6%) suffered from stage 1 AKI, 8 (5.7%) suffered from stage 2 AKI, while 4 (2.9%) suffered from stage 3 AKI. Mortality rate was 100% in stage 3 AKI patient even after renal

replacement therapy (RRT). Furthermore, the severity of COVID showed a statistically significant positive correlation with the severity of AKI suffered.

Conclusion After looking at the results of our study, we can say, with reasonable certainty, that a more severe COVID-19 infection leads to a more severe AKI. The overall incidence of COVID-19 induced AKI was 17.1%.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), is a pandemic caused by severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2).¹ As far as epidemiology of COVID-19 is concerned, over 107 million people have affected with COVID-19 leading to death of 2.3 million affected people till February 2021.² Coronavirus predominantly affect respiratory system, however; as it invades the respiratory system through angiotensin converting enzyme receptor 2 (ACE 2) that are also expressed in renal system implicating its renal impact in the form of acute kidney injury (AKI) validating the multiorgan system involvement in COVID-19.³ Acute kidney injury (AKI) is defined as severe abrupt reduction of renal function that is manifested by severe azotemia, oliguria, and anuria.⁴ It is a distinct syndrome that impart not only structural damage but also implicate the functional damaged as well.⁵ AKI is frequently reported in patients with COVID-19 as reports from China, Italy, and USA have reported the incidence ranging from 0.5 to 36.6%

in hospitalized patients of COVID-19.^{6,7} The incidence is raised to 19-23% in critically ill patients admitted in intensive care units.⁸ Various mechanism of COVID-19 induced AKI have been proposed such as immunoinflammatory response to infection, direct cytotoxic effects on renal tubule epithelial cells and podocytes, thrombotic microangiopathy and cardiorenal syndrome.^{9,10} The aim of this observational study is to analyze the association of COVID-19 with acute kidney injury among patients admitted in tertiary care hospital. Very limited studies have been done to explore this unique association and we also aimed at analyzing the ultimate outcomes within 2 weeks after development of AKI in PCR positive COVID-19 patients. This study will help the clinicians to take before-hand measures that could be practiced in COVID-19 patients to avoid the development of AKI, that could even worsen the clinical course and ultimate outcomes of the patients. these differences.

METHODS

It was an observational cross-sectional study involving 140 SARS-CoV-2 positive cases conducted in the Department of Infectious Diseases Holy Family Hospital, Rawalpindi, Pakistan from September 2020 to March 2021. The sampling was done through a non-probability convenience sampling technique. All patients with an age greater than 18 years and confirmed PCR-positive COVID-19 infection admitted to the Department of Infectious Diseases were enrolled in the study. The patient having pre-existing renal pathology (AKI, CKD etc) were excluded from the study. A self-designed questionnaire constructed from already existing literature was used with excellent reliability and validity as observed through a review by three independent reviewers. The first part of the questionnaire was comprised of demographic characteristics and pre-existing comorbid conditions. The second part was comprised of the renal function tests, serum electrolytes profile and stage of AKI on the basis of KDIGO criteria¹¹ and severity of COVID-19 (mild, moderate, severe, and critical) defined by China classification of the index of severity¹² and lastly, the third part was comprised of the clinical outcomes (shifted to ward, discharge, death). Each and every patient who were tested positive for COVID-19 were followed for next 2

weeks and outcome measures were observed. Demographic characteristics were expressed in the form of frequencies (n) and percentages (%). The continuous data (age) that was normally distributed and were summarized as Mean \pm SD. Chi-square tables were used to test factors associated with AKI for discrete variables, Mann-Whitney U test was used for skewed continuous data, and T-test for continuous normal distribution variables. The association between the severity of COVID and the AKI suffered was analyzed using the Spearman's Rho and the Kendall's tau coefficient. The analysis was done through SPSS. V.25. The level of Statistically significant was set at a $p < 0.05$.

RESULTS

Out of 140 patients, 78 (55.7%) were male while 62 (44.3%) were female, giving us a male-female ratio of 1.23:1. The mean age of the participants was 45.41 (SD = 11.85). Out of the total, 116 (82.9%) suffered from no AKI, 12 (8.6%) suffered from stage 1 AKI, 8 (5.7%) suffered from moderate AKI, while 4 (2.9%) suffered from stage 3 AKI. **Table 1** shows the sociodemographic details of the four groups and the results of the chi-square tests. The groups differed on the basis of gender ($\chi^2 = 13.9$; $p = 0.003$), co-morbid ($\chi^2 = 17.1$; $p = 0.002$), and outcomes ($\chi^2 = 14.8$; $p = 0.001$).

The total number of patients that suffered from mild, moderate, severe and critical levels of COVID were 86(6%), 30(2%), 6(0.4%), and 18(1.3%) respectively. **Table 2** shows the distribution of the groups and also the number of patients that suffered AKI within each group. The groups differed significantly regarding to whether or not they caused AKI ($\chi^2 = 22.5$, $p < 0.001$).

As most of the variables tested were significantly causing AKI, we then tested them across the several stages of AKI to test whether or not there was any significant difference among the different variables in this regard. **Table 2** shows the results of the contingency table.

We also tested the values of basic renal function tests and serum electrolytes in patients with or without AKI **Table 3**. The means were significantly different among the two groups for all the values studied

Table 1: The relationship of different variables with whether or not they cause AKI

Characteristics (n, %)	Total	No AKI	AKI	χ^2	df	P-value
Overall	140	116(82.9%)	24(17.1%)			
Gender				13.893	3	0.003
Male	78(55.7%)	66(45.7%)	12(8.6%)			
Female	62(44.3%)	50(35.7%)	12(8.6%)			
Comorbid				17.126	4	0.002
None	76(54.3%)	68(48.6%)	8(5.7%)			

Hypertension	30(21.4%)	22(15.7%)	8(5.7%)			
Ischemic Heart Disease	2(1.4%)	0(0%)	2(1.4%)			
Others	4(2.9%)	2(1.4%)	2(1.4%)			
Outcomes				14.812	2	0.001
Discharged	110(78.6%)	98(70%)	12(8.6%)			
Shifted to Ward	22(15.7%)	14(10%)	8(5.7%)			
Mortality	8(5.7%)	4(2.9%)	4(2.9%)			
Severity of COVID				22.481	3	<0.001
Mild	86(61.4%)	80(57.1%)	6(4.3%)			
Moderate	30(21.4%)	20(14.3%)	10(7.1%)			
Severe	6(4.3%)	2(1.4%)	4(2.9%)			
Critical	18(12.3%)	14(10%)	4(2.9%)			
Diabetes Mellitus 2	28(20%)	24(17.1%)	4(2.9%)			

Table 2: Relation of different variables to the Stages of AKI suffered.

Characteristics (n, %)	Total	No AKI	Stage 1 AKI	Stage 2 AKI	Stage 3 AKI	χ^2	df	P-value
Overall	140 (100%)	116(82.9%)	12(8.6%)	8(5.7%)	4(2.3%)			
Gender						13.893	3	0.003
Male	78(55.7%)	66(45.7%)	10(7.1%)	0(0%)	2(1.4%)			
Female	62(44.3%)	50(35.7%)	2(1.4%)	8(5.7%)	2(1.4%)			
Comorbid						42.298	12	<0.001
None	76(54.35)	68(48.6%)	2(1.4%)	4(2.9%)	2(1.4%)			

Diabetes Mellitus 2	28(20%)	24(17.1%)	4(2.9%)	0(0%)	0(0%)			
Hypertension	30(21.4)	22(15.7%)	2(1.4%)	4(2.9%)	2(1.4%)			
Ischemic Heart Disease	2(1.4%)	0(0%)	2(1.4%)	0(0%)	0(0%)			
Others	4(2.9%)	2(1.4%)	2(1.4%)	0(0%)	0(0%)			
Outcomes						79.085	6	<0.001
Discharged	110(78.6%)	98(70%)	8(5.7%)	4(2.9%)	0(0%)			
Shifted to Ward	22(15.7%)	14(10%)	4(2.9%)	4(2.9%)	0(0%)			
Mortality	8(5.7%)	4(2.9%)	0(0%)	0(0%)	4(2.9%)			
Severity of COVID						48.949	9	<0.001
Mild	86(61.4%)	80(57.1%)	4(2.9%)	2(1.4%)	0(0%)			
Moderate	30(21.4%)	20(14.3%)	6(4.3%)	4(2.9%)	0(0%)			
Severe	6(4.3%)	2(1.4%)	2(1.4%)	0(0%)	2(1.4%)			
Critical	18(12.3%)	14(10%)	0(0%)	2(1.4%)	2(1.4%)			

Table 3: Lab Values in patients with AKI or no AKI.

Variables	Total	No AKI	AKI	P-value
Overall (n, %)	140	116	24	
Urea	140	25.67 ± 8.26	118.59 ± 48.16	<0.001
Creatinine	140	0.769 ± 0.238	3.52 ± 4.15	<0.001
Sodium	140	138.24 ± 6.87	146.00 ± 6.69	<0.001
Potassium	140	3.87 ± 0.476	4.51 ± 0.689	<0.001
Chloride	140	97.79 ± 4.75	102.33 ± 5.01	<0.001

Finally, we ran Kendall's Tau test and Spearman's rho. Kendall's tau coefficient was 0.312 ($p < 0.001$) while Spearman's rho coefficient was 0.330 ($p < 0.001$) **Table 4**. Both these tests show that there is a moderate positive correlation between the severity of

developed stage 3 AKI were shifted to intensive care unit (ICU) with dialysis facility and RRT was initiated, but none of the patients survived in this group with overall mortality rate of 100% in patients with stage 3 AKI as shown in **Figure 2**.

Table 4: Correlation between Severity of COVID and the stage of AKI

	Stage of AKI	p-value
Severity of COVID		
Kendall's Tau	0.312	<0.001
Spearman's rho	0.330	<0.001

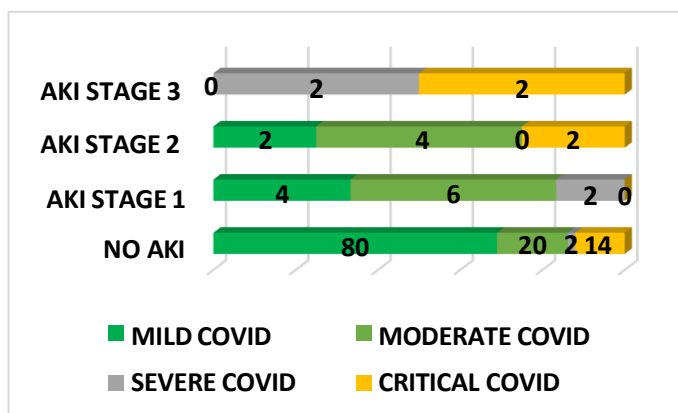


Figure 1: Correlation between Severity of COVID-19 and Stages of AKI

COVID and the stage of AKI in the patient. Thus, we can say that patients suffering from COVID not only have a significant chance of suffering from AKI, but the severity of COVID is directly proportionate to the severity of AKI suffered by the patienta shown in **Figure 1**

Intervention and outcomes:

The renal replacement therapy (RRT) was primarily employed in patients with Stage 3 AKI ($n = 4$, 2.3%), while stage 1 and stage 2 patients were treated conservatively. All the patients

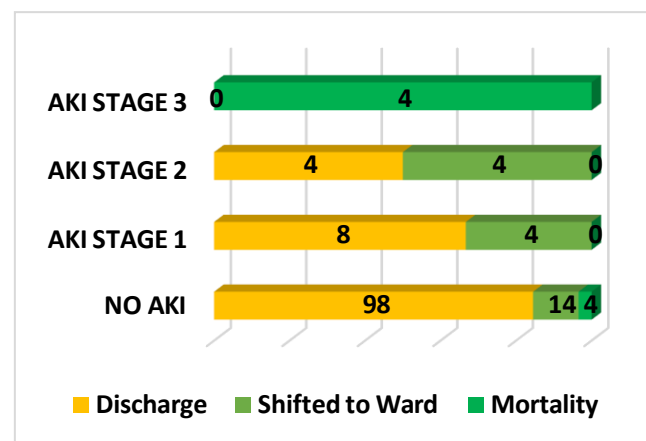


Figure 2: Correlation between AKI and outcome measures

The four patients who died without developing AKI died because of other COVID19 induced complications. Out of 24 patients who developed severe to critical COVID19, 18 patients were shifted to ventilatory support and only ten patients survived and eight patients died either with AKI or without AKI. Rest of the patients were either discharged or shifted toward after becoming triple negative on PCR. However, the mortality rate was much lower in our study and most of the patients were discharged after recovering from COVID 19 as shown in figure below.

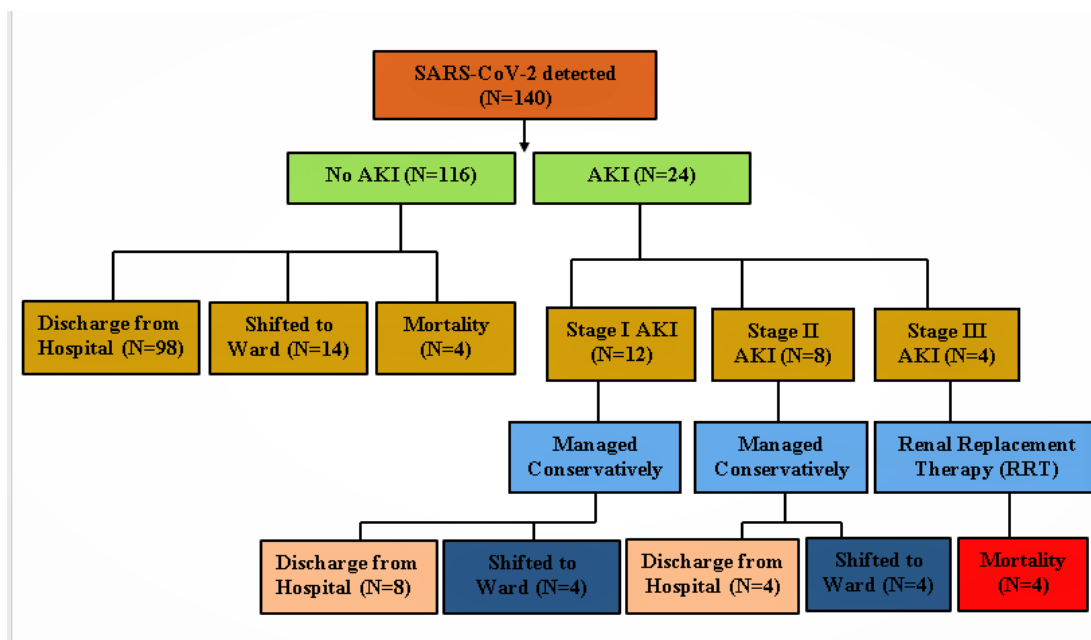


Figure 3: Schematic presentation of COVID19 induced AKI and its outcomes with possible interventions.

DISCUSSION

Severe acute respiratory syndrome coronavirus-2 (*SARS-CoV-2*) was first identified in December 2019, in China and was declared as global pandemic in March 2020 by World health organization (WHO).¹³ Although pulmonary manifestations of *SARS-CoV-2* have been described with great versatility due to its attachment with ACE receptors but involvement of kidney is of very less understood pathological condition associated with COVID19. The most commonly observed renal abnormality was acute kidney injury (AKI) that has been reported in variable frequency among different regions suffering *SARS-COV-2*.¹⁴ This particular study is aiming to highlight the prevalence of AKI in COVID-19 and impact of COVID19 severity on impaired renal function profile. This study was conducted on 140 polymerase chain reaction (PCR) positive patients of COVID 19 and the incidence of acute kidney injury (AKI) was observed among diseased cohorts. In our study the incidence of AKI in COVID 19 patients was 17.1% (n= 24) that is slightly higher as compared to a study conducted by Ibrahim et al, which was showing the prevalence of 14.6%.¹⁵ Similarly, significant variability in occurrence COVID 19 induced AKI was observed in other studies where the incidence was ranging from 0.5% to 36% as well.^{6,7} However, in another study the incidence was even higher and much higher than our study findings, in a study by Fisher et al the incidence of COVID19 induced AKI was 56.9% in comparison to 17.1% depicted in our study.¹⁶ According to stage wise analysis of COVID19 induced AKI, most of the patients in our study were showing early stage 1 of AKI (n=12, 8.6%) that is in concordance with the study findings by Ibrahim et al where most of the patients were landing in KDIGO based stage 1 of AKI followed by stage 2 (n=8, 5.7%) and stage 3 (n=4, 2.3%) [13]. However, our study findings of having

greater proportion of patients in stage 1 AKI was in contrary to the study findings by Chan et al, where most of the patients were in stage 3 of KDIGO based AKI.¹⁷

According to risk factors stratification, the hypertension, diabetes and ischemic heart disease were the most commonly observed risk factors that were found in patients developing AKI followed COVID19. The association between risk factors and AKI in COVID 19 was statistically significant (P-value= 0.002) that is in line with other studies findings where presence of risk factors and comorbidities were posing significant risk of AKI development in COVID 19 patients.^{18,19} An interesting finding that was observed in our study was gender-based equality of COVID19 induced AKI that was a deviating finding in the light of other studies where male gender was showing greater propensity towards AKI following *SARS-COV-2* infection.^{20,21} According to our study results most of the patients (n= 86, 61.4%) were showing milder form of COVID19 followed by moderate severity COVID (n=30, 21.4%), and critically ill patients (n=18, 12.3%). There was statistically significant difference between severity of COVID19 and stages of AKI (p value <0.001), and incidence of AKI was higher in patients with moderate severity of COVID19. However, according to a study by Nadim et al, the incidence of AKI was high among patients of severe to critical COVID19, while in our study the incidence was high among moderately severe COVID 19, but Stage 2 and stage 3 AKI was present mostly in severe to critical COVID19 as in line with our study findings²².

The evaluation of renal function tests and serum electrolytes also embellished the comparative perspective of this research. Values of various variables including urea, creatinine, sodium, potassium and chloride were tested in patients with or without Acute Kidney

Injury (AKI). Results displayed a considerable rise in values of AKI patients in comparison to non-AKI patients. Levels obtained are as follows, urea (118.59 ± 48.16), creatinine (3.52 ± 4.15), sodium (146.00 ± 6.69), potassium (4.51 ± 0.689) and chloride (102.33 ± 5.01). Study conducted by Lili Chan et al also resembled the results obtained in our study in regards to increase in variable values, however, the values were not as high except for chloride levels: sodium (139), potassium (4.3), serum creatinine (1.42), chloride (104) [17]. Study conducted by Jamie S Hirsch et al found a high median urine-specific gravity and a majority of patients with urinary sodium <35 mEq/l at the time of development of AKI. The study provided a more detailed comparison as the patients were categorized according to a specific urine sodium value: Urine sodium (mEq/l) <35 , $35-50$ (mEq/l), >50 (mEq/l) had these n (%) patients respectively 187 (65.6), 47 (16.5), 51 (17.9).⁷ Yichun Cheng et al conducted a study titled: kidney disease is associated with in-hospital death of patients with COVID-19 and presented laboratory results in which different substances were compared in respect to patients with increased serum creatinine levels. Sodium mmol/l (139 ± 7) and potassium mmol/l (4.5 ± 0.7).²³ Shruti Gupta et al managed to gain information regarding AKI patients treated with Renal Replacement Therapy (RRT) and provided results accordingly. Value of creatinine was 1.47 (1.0–2.85) and was within the normal range after administration of RRT thus proving it beneficial.²⁴ According to a study conducted by Fahad D Algahtani et al AKI patients had these values of various variables, serum sodium mmol/L (136.8 ± 6.9), serum potassium mmol/L (4.59 ± 0.7), serum urea mg/dl (100.3 ± 59.4) and serum creatinine mg/dl (2.5 ± 1.9) hence harmonizing with results of our study.²⁵

Although our cohorts showed more of the early stages of AKI, but the mortality rate was comparable between those who developed AKI following SARS-COV-2 infection and those with out AKI (n=4, 2.9%). Similarly, in AKI stage wise distribution all

the patients who developed stage 3 AKI were showing the mortality rate of 2.9% as compared to stage 1 and 2 which was showing no mortality related to SARS-COV-2 related renal failure. However, our study finding was in contrary to the studies conducted worldwide where the mortality rate was high in SARS-COV-2 induced AKI ranging from 36% to 57%.^{26,27} The relatively high mortality among the patients with COVID-19 induced stage 3 AKI may be due to the limited capacity to support advanced renal care required in resource constraint settings like ours.

CONCLUSION

After looking at the results of our study, we can say, with reasonable certainty, that a more severe COVID-19 infection leads to a more severe AKI. Overall incidence of COVID-19 induced AKI was 17.1% and most of the patients were either discharged or shifted back to ward after become PCR negative. However, mortality rate was equal among those who developed AKI or not amounting for 2.9%. All mortality cases in AKI patient were observed in stage 3 AKI. Thus, vigilance in this regard can lead to appropriate timely management which will reduce mortality rates in such patients.

LIMITATIONS

There are several limitations of our study like small sample size because the study was conducted during second wave of COVID19 where only limited number of patients were admitted in Holy Family Hospital, Rawalpindi, and this particular study was a single cantered study not allowing the validation and acceptability of the findings to become more generalized and applicable on the whole population of the country. Similarly, this study could not focus on the timing of RRT initiation and outcomes in terms of early vs late RRT in COVID 19 induced AKI patients.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

Financial Support:

None to disclose.

Contribution:

Conceptualization: M.S.A, S.M

Data curation: A.R, A.A, M.H.J

Formal analysis: A.S, M.M.K

Writing and editing: R.A, M.S.A, S.M

Project administration: S.M, M.H.J

Review and approval: M.F.B, M.M.K, R.A

Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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A Comparative Efficacy of Decompressive Craniectomy with Multi Dural Stab vs Dural Flap in Acute Subdural Hematoma

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ABSTRACT

Introduction The association of acute Traumatic subdural hematoma (SDH) with underlying brain edema & contusions explains the elevated mortality rate. A technique of multiple intradural stabs that allows evacuation Of SDH preventing the brain from fatal bleeding and laceration. Whereas with dural flap technique there was no control over the parenchymal trauma, which leads to a secondary brain injury with higher death and morbidity rates. This study was conducted to compare the functional outcomes of the two procedures in the treatment of acute SDH in terms of Glasgow outcome score.

Methods A randomized controlled trial was conducted at Department of Neurosurgery, DHQ Rawalpindi. Total 60 patients were included in the study by lottery method via random sampling. To observe associations between qualitative variables and to compare the means of quantitative data chi-square test and t-test were applied. The results would be considered statistically significant if the p-value < 0.05.

Results The mean age of the patients in this study was found to be 54.57 ± 13.57 years. The patients in group A had a mean age of 53.43 ± 15.17 years & the mean age of the patients in group B was 55.70 ± 11.91 years. 38 (63.3%) patients were male more than the females 22 (36.7 %). The mean GCS of the patients in group A was $10.40 \pm .93$ which was higher than the mean GCS of the patients in group B which was 6.10 ± 1.39 . open-dural flaps patients had low entrance GCS of 6–10 and none of the patients (60) had a GCS above 10. No mortality was observed in multidural stab and 3 patients expired in dural flap craniotomy.

Conclusion The patients which had undergone multidural stab craniotomy showed better outcome both in terms of GCS on follow-up as well as GOS as compared to the patients which had undergone dural flap craniotomy.

INTRODUCTION

Traumatic subdural hematoma (SDH) is one of the most serious brain injuries with a high fatality rate.¹ Among the most severe worldwide health issues, particularly in low and middle-income countries (LMICs), traumatic brain injury (TBI) is a leading cause. The common association of acute SDH with underlying brain edema & contusions explains the elevated mortality rate. The accompanying edema results in vascular infarction, for which dural incision was frequently used but linked with brain herniation against the dural edges.² The Monro-Kellie Doctrine in contrast serves as the foundation for the concept of wide decompressive craniectomy (DC) in cases of severe traumatic brain edema.³ The latter rapidly lowers the elevated ICP by creating an extra intracranial area by altering the constant of "fixed intracranial volume in the rigid and inelastic skull." DC was commonly used as a secondary surgery after the failure of first-line treatments to control intracranial pressure (ICP).⁴ It increases cerebral perfusion pressure (CPP) and ICP, which contributes to better long-term functional results and lower expenses.⁵ Contrary results however are also reported.⁶

Another technique to achieve the same is multiple intradural stabs that allow not only evacuation of SDH but also prevent the brain from bleeding and laceration. Whereas there was no control over the parenchymal trauma as a result of putting in the traditional open-dural flap technique, which leads to a secondary brain injury as well as higher death and morbidity rates.⁷

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According to a 2013 study that appeared in an Asian Journal of Neurosurgery, the overall survival rate for the multi-dural stab group was 77.31% (92/119), with excellent recuperation rates of 42.02% (50/119) as well as a mortality rate of 22.69% (27/119), as opposed to 46.23% (49/106) surviving for the open dural flap (control) group, alongside good recuperation rates of 15.09% (16/106) and a death rate of executive functions.77% (57/106). executive functions<0.0001.⁸

In individuals with a good GCS, with midline shift less than 3mm & the wound less than 10mm thick at max diameter, conservative treatment should be taken into account however, if the lesion is more than 10 mm thick, surgical evacuation should be performed.⁹ According to Khan B et al.¹⁰ patients who underwent decompressive craniectomy via expansile duraplasty for the escape of ASDH experienced CSF leak in 6.5% of cases over the post-operative monitoring time frame, compared to 28.6% of the individuals who underwent decompressive craniectomy alongside dural slits.¹¹ For as long as the CSF leak is present, there is a continuing danger of bacterial meningitis, which can be fatal. Approximately ten percent of those with afterward CSF leaks have meningitis, and whether or not preventive antibiotics ought to be administered is still up for debate.¹²

Decompressive craniectomy following a serious brain injury has been examined by Barthélemy et al.¹³ in an up-to-date comprehensive literature analysis by contrasting the available research with the first significant RCT on this subject matter (DECRA). Whenever Decompressive Craniectomy with numerous dural stabs and DC with an open dural flap were compared, it was discovered that the dural stab group had a considerable advantage in terms of mortality and GOS.

They did not examine the initial issues, such as CSF leak in several DC approaches. Then, in low GCS score patients, Bhat et al.¹² examined the removal of acute SDH using an amalgam of DC and multi-dural stabs (SKIMS-Technique) without cerebral protrusion with puncture wounds. Longevity in the multi-dural stab group was 77.31% (92/119) having excellent recovery in 42.02% (50/119) and 22.69% (27/119) mortality as opposed to mortality in the open dural membrane (control) group which was 46.23% (49/106) with good recovery in 15.09% (16/106) and 53.77% (57/106). Researchers discovered that DC applying multiple cerebral stabs was substantially more beneficial in terms of survival. They failed to take into account the patients' earliest complications, such as CSF leakage.¹⁴

A single investigation has yet to be conducted in Pakistan so far comparing multi-dural stab craniectomy (SKIMS- technique) with open-dural flap craniectomy. This study was conducted To compare the functional outcomes of the two procedures in the treatment of acute subdural hematomas in terms of Glasgow outcome score. (GOS)

METHODS

This study was a randomized controlled trial conducted at Department of Neurosurgery, DHQ Rawalpindi over a duration of 6 months after approval from ERB. Total 60 cases (30 in each

group) were included in the study by lottery method via random sampling. Patients of age between 10-80 years, who had the surgical indicated case of ASDH and Traumatic ASDH, and had Gcs >5 were included in the study. Whereas patients who had any comorbid (DM, IHD, COPD, Asthmatic), penetrating brain injuries, bleeding diathesis or polytrauma were excluded. All the included patients were admitted to the accident and emergency unit of Neurosurgery. After initial resuscitation and CT brain plain, informed consent was taken from attendant to carry out the procedure. The demographic details were noted on specially designed Performa & confidentiality of patient was ensured. Patient were divided in Group-A (patients undergoing decompressive craniectomy with multidural stabs) and Group- B (patients undergoing decompressive craniectomy with dural flap). Outcome in both groups was measured on day 3, day 14 and day 30 of surgery. Data was analyzed by SPSS 26.0. Quantitative variables like age of the patient, GCS and Glasgow outcome scale, thickness of hematoma and midline shift on CT scan of the patients was represented in Mean \pm S.D. Qualitative variables like gender of the patients, presence or absence of complications were noted in frequencies and percentage. To observe associations between qualitative variables and to compare the means of quantitative data chi-square test and t-test was applied respectively. The results would be considered statistically significant if the p-value < 0.05. The result was evaluated using the Glasgow result Scale, and a GOS of 4 was deemed an acceptable result.⁷³

RESULTS

The mean age of the patients in this study was found to be 54.57 ± 13.57 years. The patients in group A had a mean age of 53.43 ± 15.17 years & the mean age of the patients in group B was 55.70 ± 11.91 years. 38 (63.3%) patients were male more than the females 22 (36.7 %).

The mean GCS of the patients in group A was $10.40 \pm .93$ which was higher than the mean GCS of the patients in group B which was 6.10 ± 1.39 . Open-dural flaps patients had low entrance GCS of 6–10 and none of the patients (60) had a GCS above 10.

The mean GOS of the patients was GOS on presentation 11.33

1 ± 82 , GOS at 1st day $4.00 \pm .83$, GOS at 7th day $4.33 \pm .75$, GOS at 14th day 5.00 ± 1.02 and GOS at 30th day $5.67 \pm .47$ in group A decompressive craniectomy with multidural stab, which was higher than the mean GOS of the patients in group B, which was GOS on presentation $5.83 \pm .59$, GOS at 1st day $2.57 \pm .62$, GOS at 7th day $2.83 \pm .95$, GOS at 14th day 3.41 ± 1.05 and GOS at 30th day $3.15 \pm .36$. In group B One patient expired on the seventh day, and two patients expired on the fourteenth day. No mortality was observed in group A & 3 patients expired in group B. (Table 1)

Regarding the patients in this study's age range, the pie chart of age shows that the mostly patients in this study was found to be 30 years old (13.33 %). (Figure 1)

Table 1: Incidence of morality among group A and group B

Glasgow outcome score (GOS)		GOS on presentation	1st day	7th day	14th day	30th day	p-value
Group A: N=30	Mean	11.3	4.0000	4.33	5.00	5.67	.000
Group B: N=30	Mean	5.83	2.5667	2.83 (Expired 1 pt)	3.41 (Expired 2 pts)	3.15	

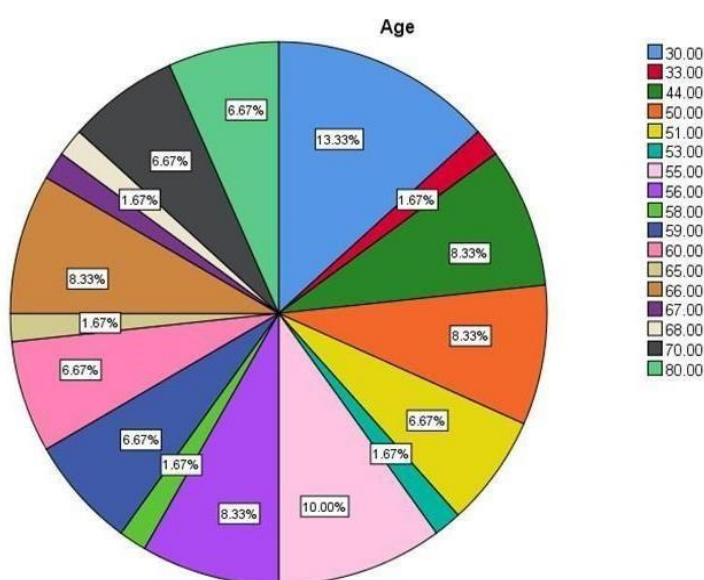


Figure 1: Age distribution of the patients

DISCUSSION

In this study we compared the functional outcome of decompressive craniectomy with multiple dural stabs to that with dural flap. Mostly patients were found to be 30 years old (13.33 %) reflecting the high incidence of ASDH due to road traffic accidents. Overall, group A showed better outcome both in terms of GCS on follow-up as well as GOS. Further supporting the superiority of DC with dural stabs was the fact that no mortalities occurred in group A while three were seen in group B. 63.3% (n=38) patients were male. A related earlier study describes that Acute SDH affects males four times more frequently than it does women.¹⁵ Acute SDH frequently manifests between the ages of fifty and sixty, similarly mean age of our patients was 54 years.¹⁶

Weak understanding exists of the characteristics and causes of brain edema following traumatic brain injury.¹⁷ According to research, in addition to main parenchymal injury, collateral insult to the brain was regarded as a significant source.¹⁸ The subdural hematoma was remained typically morbid even after

decompressive surgery due to constriction of the microcirculation, which could in part be caused by the restrictive impacts of the dural flaps.¹⁹ However, reports also suggest it may be due to hypoxia brought on by the pressure hematoma.²⁰ Why acute subdural hematoma cases die more frequently than other patients can be explained by the guiding principle of the Monroe Kellie philosophy and its common association with fundamental neurological injury, which comprises of contusion and brain swelling.^{80.21}

Acute SDH typically builds up and manifest symptoms 24 to 72 hours later.²² Surgery was used for evacuation if the SDH was greater than 10mm in thickness and the midline shift was more than 5mm.²³ Standard surgery (dural flap) was unable to prevent brain injury and pouting from occurring.²⁴ Patients in the multi-dural puncture group, on the other hand, fared better. By oozing blood clots and fluid, multiple intradural stabs enable the

evacuation of acute subdural hematomas (SDH) while concurrently preventing the brain from bleeding and laceration. Unlike the DF technique, there was no over pouting and the resulting brain laceration, which led to additional damage to the brain and significantly higher rates of illness and death. In an animal model for acute SDH combined with hypoxemia or diffuse injury to the brain, researchers examined the physiological effects of fast and delayed surgical escape on brain edema development. They discovered that swift surgical ejection was not in favor of a more favorable clinical outcome.²⁵

It is well known that decompressive craniectomy was done on patients whose GCS was deteriorating or those who had a low GCS when they first presented.²⁶ In a study of 225 patients who had a post-op GCS of 8 or higher, 60.50% (72/119) of multi-dural stabs and 58.49% (62/106) of open-dural flaps had low admission GCS of 3-6. However, the outcomes were still improved when the multi-dural stabs technique was used.²⁷

According to the final findings, which were calculated based on favourable and unfavourable outcomes, 37.5% of patients in group A and 9.4% of patients in group B had favourable outcomes, while 62.5% and 90.60% of patients in groups A and B, respectively, had favourable and unfavourable outcomes. Similar results were found in different studies, where favorable results were seen in 42.02% of patients who received multiple dural stabs versus 15.09% of patients who received an open dural flap. 52.5% of people who suffer a severe traumatic brain injury die, according to previous research. But at SKIMS, the death rate for patients with multiple stab wounds was only 22.69%, with an overall survival rate of 77.31%.²⁸

In a study by Barthélemy EJ et al.²⁹, the mortality rate was 58 (40.8%) after one year of followup, as well as 8 (5.6%) patients remained in a state of perpetual vegetative state. 77 (54.2%) individuals had an unfavourable result in the end. These were some of the outcomes of a decompressive craniectomy, whereas in our research, 20 patients in group A as well as 29 individuals in

group B, accordingly, had unfavourable outcomes. The significance of the numerous dural slits method was demonstrated in the current research by the 12 (37.5%) patients in group A and the 3 (9.4%) patients in group B who had favourable outcomes.

Individuals who received decompressive craniectomy and had traumatic brain injuries as well as refractory higher intracranial pressure (>25 mm Hg) were the subjects of a study by Hutchinson PJ et al.³⁰ The Extended Glasgow Evaluation Scale (GOS-E) rating at six months, which ranges from "upper good recovery" to death on an 8-point scale.

The two groups' GOS-E distributions were different (16.3% vs. 9.2%, $P=0.03$). Decompressive craniectomy was crucial in lowering the mortality rate between head injury individuals, as this research also demonstrates. Decompressive craniectomy was a successful way to manage high blood pressure and was life saving, as demonstrated in a study by Kurland DB et al.³¹, which explains the sharp increase in the use of this operation.³² This research supports the current study's conclusion that decompressive craniectomy when coupled with numerous dural slits, aids in improving the prognosis for head injuries.³²

Based on our findings & review of literature, we believe DC with multiple dural slits is a very reasonable & evidently superior procedure in management of patients with ASDH. This heap of data on the subject should serve as a guiding principle for neurosurgeons that are apt in managing neurotrauma.

CONCLUSIONS

Overall, the patients which had undergone multidural stab craniotomy showed better outcome both in terms of GCS on follow-up as well as GOS as compared to the patients which had undergone dural flap craniotomy. Further supporting the superiority of DC with dural stabs was the fact that no mortalities occurred in multidural stab procedure while three mortalities occurred in patients of dural flap craniotomy surgery.

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The Effect of Lifestyle Habits on the Sleep Quality of Medical Students of Allama Iqbal Medical College During the Pandemic Lockdown Restrictions

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ABSTRACT

Introduction To reduce the spread of COVID-19 and to reduce the pressure on Pakistan's Health Care system, all the educational institutions in the country were closed from the 14th of March. Poor sleep quality is closely associated with lifestyle habits. In this cross-sectional study, we investigated the impact of Pakistan's restriction measures on the lifestyle habits of individuals and their relation with sleep quality. Aim of this study is to evaluate the sleep quality of medical students of Allama Iqbal Medical College and to determine the relationship between different lifestyle habits and their effect on the Sleep quality of the medical students during lockdown restrictions.

Research and design methods This cross-sectional study was conducted on 310 Allama Iqbal Medical College students from 1st to final year via the forms sent online from the 13th to the 17th of June 2020. Data were collected through a standard questionnaire using the PSQI (Pittsburgh Sleep Quality Index) scale and a list of lifestyle habits questions. Frequency, percentage, Chi-Square, Bivariate, and Cross tab were used in data analysis. **Results** The MEAN PSQI was found to be 8.497. Data analysis through Chi Square and t test gave p values which showed that out of the 13 variables, four (which include Gender, Relaxation techniques for sleeping, self-perceived stress scale, and screen time before bed) had a significant association with PSQI. There was no observed significant difference in sleep quality score based on class, residency, smoking, drinking caffeine, BMI, breakfast, doing physical activities, turning off lights before bed, and noise around when sleeping.

Conclusion Some lifestyle habits have a significant relationship with sleep quality, and we need to work on those habits to have better sleep and better lives.

INTRODUCTION

Severe acute respiratory syndrome coronavirus (SARS-Covid)-2, a novel coronavirus from the same family as SARS-Covid and Middle East respiratory syndrome coronavirus, has spread worldwide leading the World Health Organization to declare a pandemic on 11th March 2020.¹ This modern strain was not known until sometime recently in December 2019, when a flare-up of pneumonia of unidentified cause rose in Wuhan, China.² To contain the spread of the highly contagious COVID-19 virus, Pakistan's federal and provincial governments closed down all schools, colleges, and universities across the country soon after it was declared a pandemic.³ People were advised to maintain social isolation and only go out to buy necessities. The lockdown has profoundly impacted the lifestyle, work habits, social relations, and sleep quality of the population including medical students.

Sleep quality, as defined by the National Sleep Foundation, is one's satisfaction with the sleep experience, integrating aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening. (The National Sleep Foundation, 2020). Good sleep fortifies memory consolidation.⁴ Medical students are known as poor sleepers.⁵ Sleep deprivation is associated with negative effects on cognitive function including attentiveness, working, and long-term memory.⁶ They are overburdened by their academics, and to cope with their curriculum, they compromise their sleep. This leads to poor academic performance⁷ and emotional exhaustion.⁸

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Lifestyle is the way a person lives keeping in view their values and attitude as influenced by their culture.⁹ Various lifestyle habits affect sleep quality in different ways¹⁰. A relationship between sleep quality obesity, smoking, and nighttime social media usage has been observed.¹¹ Utilization of caffeinated refreshments stimulate the brain and thus are chance components of poor sleep quality.¹² Stress on the other hand has a very strong relation to the sleep quality of medical students. To adapt to their stressful routine and workload, medical students tend to decrease their sleep¹³. Moreover, social isolation also affects sleep.¹⁴ There also a significant association between Poor Sleep Quality (PSQI) score and age, year of study, hostel residence, socioeconomic status, body mass index, smoking, alcohol intake, caffeine consumption, exercise, stress, and excessive use of mobile/laptop.¹⁵

Since poor sleep quality has detrimental effects, it is important to identify which lifestyle variables are significantly impacting the sleep of medical students during the Covid-19 pandemic. Many studies have shown that sleep disturbance and poor sleep quality have adverse physiological consequences on increasing human morbidity and mortality.¹⁶ With that in mind, several tools are present for self-assessment of sleep quality including PSQI. The scale has 19 self-rated questions covering subjective sleep quality, sleep latency, sleep duration, habitual SE, sleep disturbances, use of sleep medication, and daytime dysfunction. It has good validity with a sensitivity of 89.6% and a specificity of 86.5% for patients versus control subjects.¹⁷ Although there have been many studies regarding the association of lifestyle habits and sleep, very few of them have focused on the effect of lifestyle habits on the sleep quality of medical students during an epidemic/pandemic in particular. This study aims to find that. Data about the association of lifestyle habits and sleep quality of medical students will help in Our larger goal to use our understanding of the sleep quality of students to raise awareness of the importance of sleep in order to improve the overall well-being of medical students in Pakistan.

To evaluate the sleep quality of medical students of Allama Iqbal Medical College and to determine the relationship

between different lifestyle habits and their effect on the Sleep quality of the medical students during the lockdown restrictions.

METHODS

This cross-sectional study was conducted among the medical students of Allama Iqbal Medical College, Lahore from the 13th of June to the 20th of September 2020. The sampling was done through purposive sampling/ non-probability convenience Sampling technique. All the Medical Students from the first year to the final year studying at Allama Iqbal Medical College were included. Anyone who is not a current student of Allama Iqbal Medical College or has graduated is excluded from this study. The calculated sample size was

310. A predesigned questionnaire, the Pittsburgh sleep quality questionnaire was used as a standard tool to assess the sleep quality and quantity in students. Nineteen individual items generate seven –componentll scores including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of scores for these seven components yields one global score as the sleep quality score. After data gathering and calculation of sleep quality scores for each study subject, data were analyzed in SPSS software. Frequency and percentages were calculated for nominal variables. Chi-Square test and bivariate correlation were used to find the p-values (significant level was considered by 0.05 error) and hence to find the significant or insignificant relationship between the different lifestyle habits and sleep quality. A custom table was used to find the mean PSQI associated with each variable.

RESULTS

We collected 310 samples targeting all the classes of MBBS of Allama Iqbal Medical College. The PSQI was calculated according to the standard method explained in the methodology. The minimum PSQI value received was 0 and the maximum was 23. It was positively skewed. The mean score of PSQI was 8.497 (Table 1).

Table 1: Showing the minimum, maximum, mean and skewness of PSQI

Mean	N	Std. deviation	Median	Minimum	Maximum	Range	skewness
8.497	310	4.0280	8.000	.0	23.0	23.0	.637

Of the 310 students 139 (42.2%) were Males and 179 (57.7%) were Females. Regarding residency 132 (42.58%) were day-scholars and 178 (57.41%) were hostellites. Sample was taken from 1st to Final year, with 62 samples from each class. (Table 2) shows the frequency and percentages of the all the variable's options.

Questions regarding 13 different variables, which were Class, Gender, BMI, Residency, Breakfast, Smoking, Relaxation techniques, drinking caffeine, Physical activity, Self-perceived stress scale, Screen time before bed and noise around when sleeping were asked. Table 3 shows the mean value of PSQI associated with each option of the variable.

Table 2: Frequency and Percentages of all the variables

Variables		Frequency	Percentage
Current Class	1st year	62	20
	2nd year	62	20
	3rd year	62	20
	4th year	62	20
	5th year	62	20
Gender	Male	131	42.25
	Female	179	57.74
BMI	<18.5	44	14.19
	18.5 - 25	210	67.74
	25 - 30	40	12.90
	>30	16	5.16
Residency	Day-scholar	132	42.58
	Hostellite	178	57.41
Breakfast	Daily	162	52.25
	1 - 2 times a week	55	17.74
	3 - 5 times a week	67	21.61
	Never (I don't do breakfast)	26	8.38
Smoker	No	304	98.06
	Yes	6	1.93
Relaxation Techniques for sleeping	No	260	83.87
	Yes	50	16.12
Drinks having caffeine	I don't drink	50	16.12
	1 - 2 times a week	84	27.09
	4-5 times a week	39	12.58
	>5 times a week	137	44.19
Physical activity	Low intensity activities	214	69.03
	Moderate Intensity activities	81	26.12
	Vigorous intensity activities	14	4.51

Self-Perceived stress scale	1	27	8.70
	2	27	8.70
	3	37	11.93
	4	23	7.41
	5	43	13.87
	6	38	12.25
	7	48	15.48
	8	44	14.19
	9	13	4.19
Screen time before bed	10	10	3.22
	Don't use at all	5	1.61
	less than 30 min	31	10
	30 - 60 min	81	26.12
	> 60 min	193	62.25
Turning lights off before bed	Always	235	75.80
	Often	41	13.22
	Sometimes	22	7.09
	Never (i.e light remains ON)	12	3.87
Noise around when sleeping	Inaudible	150	48.38
	Moderate	153	49.35
	Loud	7	2.25

Table 3: Variables and the mean of PSQI associated with them

Variables		Mean of PSQI
Gender	Male	7
	Female	8
BMI	<18.5	7
	18.5 – 25	7
	25 – 30	9
	>30	9
Breakfast	Daily	7
	1 -2 times a week	8
	3 - 5 times a week	8
	Never (I don't do breakfast)	7
Relaxation Techniques for sleeping	No	7
	Yes	9
Self-Perceived stress scale	1	5
	2	6
	3	7
	4	6
	5	7
	6	8

	7	9
	8	9
	9	10
	10	8
Screen time before bed	Don't use at all	4
	less than 30 min	5
	30 - 60 min	8
	> 60 min	8
Current Class	1st year	9
	2nd year	7
	3rd year	8
	4th year	7
	5th year	8
Residency	Day-scholar	8
	Hostellite	7
Smoker	No	8
	Yes	8
Drinks having caffeine	I don't drink	7
	1 - 2 times a week	7
	4-5 times a week	8
	>5 times a week	8
Physical activity	Low intensity activities	8
	Moderate Intensity activities	8
	Vigorous intensity activities	7
Turning lights off before bed	Always	8
	Often	7
	Sometimes	8
	Never (i.e. light remains ON)	6
Noise around when sleeping	Inaudible	8
	Moderate	8
	Loud	6

Table 4: p values of variables with PSQI

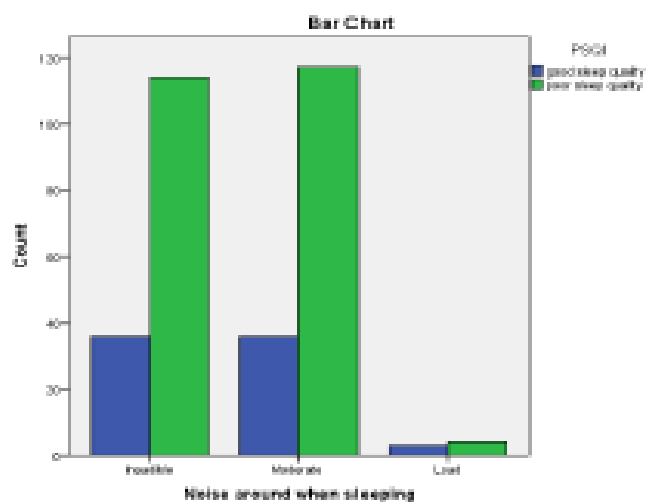
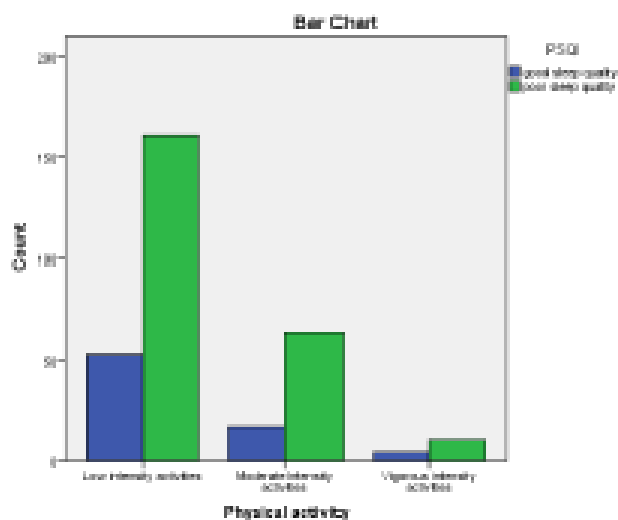
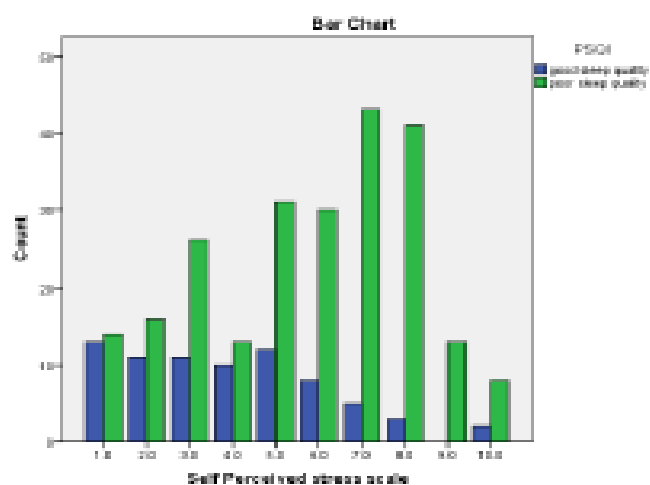
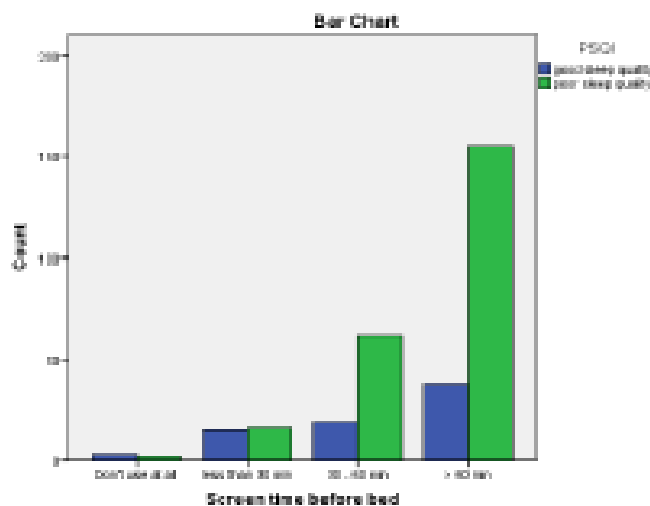
Variable		P value associated
Gender	Male	.006*
	Female	
BMI	<18.5	.122
	18.5 – 25	
	25 – 30	
	>30	

Breakfast	Daily	.288
	1 -2 times a week	
	3 - 5 times a week	
	Never (I don't do breakfast)	
Relaxation Techniques for sleeping	No	.028*
	Yes	
Self -Perceived stress scale	1	0.00*
	2	
	3	
	4	
	5	
	6	
	7	
	8	
	9	
	10	
Current Class	1st year	.188
	2nd year	
	3rd year	
	4th year	
	5th year	
Residency	Day-scholar	.664
	Hostellite	
Smoker	No	.664
	Yes	
Drinks having caffeine	I don't drink	.482
	1 - 2 times a week	
	4-5 times a week	
	>5 times a week	
Physical activity	Low intensity activities	.729
	Moderate Intensity activities	
	Vigorous intensity activities	
Turning lights off before bed	Always	.500
	Often	
	Sometimes	
Noise around when sleeping	Inaudible	.504
	Moderate	
	Loud	
Screen time before bed	Don't use at all	.001*
	less than 30 min	
	30 - 60 min	
	> 60 min	

The analysis of the data via Chi Square test and t test, showed that out of these 13 variables, four (which were gender, relaxation techniques for sleeping, self-perceived stress scale, and screentime before bed) had a significant association with PSQI (where the significant p value is taken as <0.05). These variables, the mean PSQI values associated with them and their p values are given in (Table 3). These correlations showed that the poor sleep quality was high in females ($p=0.006$), those who performed less sleep relaxation techniques ($p=0.028$). And the sleep quality decreased (i.e PSQI increased) in those who reported to have more stress ($p=0.00$) (via self-perceived stress scale) and who spent more times at screen just before bed time ($p=0.001$).

There was no observed significant difference in sleep quality score based on class, residency, smoking, drinking caffeine, doing physical activities, turning off lights before bed, BMI, breakfast and noise around when sleeping (Table 4), i.e., these variables showed insignificant relation with PSQI having their p values was more than 0.05.

Graph 1-4 show the relationship of good and poor sleep quality with variable's components (Noise around when sleeping, Physical activity, Self -Perceived stress scale, Screen time before bed). The cutoff values used was 5, Using a cut-off score of 5, the PSQI was able to correctly identify 88.5% of all patients and controls, representing a 89.6% sensitivity and a 86.5% specificity.¹⁸ The green bars show poor sleep quality (i.e. having PSQI value of more than 5) and the blue bars show good sleep quality. PSQI values are on Y axis, while the variables are on X axis of the graphs.



Graph 1-4: showing the relationship of good and poor sleep quality with variables.

DISCUSSION

In this cross-sectional study we studied the impact of lifestyle habits on the sleep quality of medical students during the lockdown phase of COVID19 in Allama Iqbal Medical College, Pakistan. As expected, our research analysis did show that many lifestyle habits have an effect on the sleep quality of people. These factors were Gender, Relaxation techniques for sleeping, self-perceived stress scale, and screen-time before bed. The other habits which didn't show any significant relationship with the sleep quality were class, residency, smoking, BMI, breakfast drinking caffeine, doing physical activities, turning off lights before bed and noise around when sleeping. However, this research was a snapshot of habits and their relation with sleep during the lockdown restrictions imposed by the Governments around the world. Multiple studies have found significantly high stress levels in medical students owing to various reasons like study burden and peer pressure.^{4,6} Stress seemed to be the biggest factor affecting the sleep quality of the students, which could have had been aggravated by the COVID19 pandemic and the lockdown. In future more studies need to be done to analyze the self-perceived stress of the students of the medical college and

understand if it was increased in this period and had made significant change on their sleep quality.⁴ There weren't any significant differences in the sleep quality of the hostellites and day-scholars, which made sense since everyone was at home during the days in which this questionnaire was asked specifically asking about their habits and sleep in last 30 days. Another issue which we faced was that we couldn't find much sample population who smoked, and hence couldn't know for sure whether smoking was a contributing factor in sleep quality of the medical students of AIMC. More research is needed to be done after the pandemic ends and needs to be analyzed and compared with the existing data to understand well about the effect of lifestyle habits on sleep during the lockdown and after it. Also considering that COVID19 pandemic is likely to continue for some more months, more close observation and studies are needed during and even after the end of the pandemic.

CONCLUSION

Our research showed that four of the lifestyle habits from the thirteen we asked, had a significant relationship with the sleep quality. Hence, medical students should try to control and make their habits better to have a sound sleep.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

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Contribution:

Conceptualization: A.A, A.K

Data curation: A.A, A.A

Formal analysis: A.I, A.K

Writing and editing: A.A.C, A.K

Project administration: A.A

Review and approval: A.A.C, A.K

Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Frequency of Poisoning Cases Presenting in Emergency Department of a Teaching Hospital of Rawalpindi Medical University,

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ABSTRACT

Introduction Death due to poisoning has been known since time immemorial. There can be variations in poisoning cases regarding demographic characteristics, poisoning agents, and frequency in every region. The objective of this study is to determine the frequency of poisoning cases, poisoning agents, and associated demographic characteristics.

Research design and methods This descriptive, retrospective study included 304 confirmed poisoning patients that presented to Medicine Emergency of Holy Family Hospital, a tertiary care hospital, over a period of three months i.e. from July 2019 till September 2019. The data was collected from the medical records. SPSS.

V. 23 was used to analyze data and descriptive statistics were calculated. **Results** Of the 304 patients, 132 (43.4%) were males and 172(56%) were females. Cases mostly reported were in the age range of 16-75 years with a mean age of 30±12. Out of these, 107(35.2) cases were of unknown poisoning agent. 60 (19.7%) patients were of Organophosphate poisoning, 57 (18.8%) were of wheat pill poisoning. There were 29 (9.5%) patients of Rat pill, 5 (1.6%) were of acid intake, 11 (3.6%) Benzodiazepine cases.

2 cases (0.7%) presented with Heroin overdose and 9 (3%) of analgesics overdose. 24 (7.9%) presented with other poisons that included intake of agents such as anti-lice powder, Harpic, alcohol, poisoning food, Brake oil, Petrol, Phenyl, Loperamide, Iberet folic, CO₂, Beta blockers, Glucophage.

Conclusions Majority of the patients were females, regarding age most patients were

teenagers and those in thirties. Unknown poisoning was most common followed by Organophosphate and Wheat pill poisoning.

INTRODUCTION

Intoxication is the appearance of undesirable signs and symptoms in an organism on exposure to potentially lethal chemicals, physical, or organic substances.¹

Almost every substance can be lethal at some doses, however few may be harmless at lower doses.² Worldwide accessibility of poisonous substances, chemicals and drugs on a large scale contributes to common medical emergencies because of accidental or intentional poisonings.³ A study in 2012, reported poisoning as a major causative agent of deaths due to suicides among young adults in India.⁴ Despite the fact that some interventions have been successful to prevent toxic ingestions, acute poisoning still remains to be an important public health issue. Epidemiological characteristics of poisoning differ among countries and between different geographical regions within the same country. Socioeconomic status, educational status, occupation, age and gender are also known to affect these differences.

Poisoning can be either intentional or accidental. Large number of cases of intentional poisoning are reported in developing countries, where limited resources are available and are usually accompanied by large scale morbidity and mortality.⁵ On the other hand the most common causes of poisoning in developed countries are the misuse of commercially available drugs.⁶ Insecticides are known to be most common in developing countries.⁷ According to World Health Organization (WHO), annually about one million deaths worldwide are due to suicide and chemical substances, with pesticides as a major cause.⁸ As poisoning being common in low and middle-income

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countries, adverse effects of poisoning are much more than in high income countries due to weak regulations and poor healthcare facilities.⁹ In United States of America, after every 15 seconds a poison exposure case is handled by poison Control Centers.¹⁰ In 2014, a study was conducted on acute poisoning cases in Chennai. It showed among the total 218 patients of poisoning included in the study, 51% (113) were males and 49 % (105) were females. Tablet overdose was found to be the most frequent poisoning agent used, reported in 34% (74) patients. The young and the middle-aged people are the most vulnerable for acute poisoning episodes.¹¹

In Pakistan a pilot study on poisoning cases was done using emergency department surveillance project. Poisoning cases were found more in males (64%) as compared to females (32%). 54% cases were reported in 19-44 age group.¹² Another study conducted at National Poisoning Control Centre at Karachi in 2018 showed that out of 2546 patients included into the study, both genders were equally affected with mean age of presentation $26.57\% \pm 11.82$ years. Nearly 80% were aged 40 years or younger. The most frequent cause of poisoning was organophosphates (46.11%).¹³ Unfortunately, many locales do not have necessary antidotes, screening tests or protocols of proper treatment, as all countries are not equally equipped to handle such cases. As poisoning being common in our setup, this research is significant as it will highlight the frequency of poisoning cases and will analyze the most commonly involved substances and characterize the patients on basis of age and gender.

The objective of this study is to analyze cases of poisoning presenting in the emergency department of a tertiary care hospital of Rawalpindi.

METHODS

A retrospective cross-sectional descriptive study was conducted in the Medical Emergency department of Holy Family Hospital Rawalpindi, a tertiary care hospital from July 2019 to September 2019. According to WHO sample size calculator, using anticipated proportion of 0.18, 95% confidence interval, 6% absolute precision, sample size was 275, however we included the total 304 cases that presented within the period of three months to make our results more generalized.

Patients of both genders who were suspected cases of poisoning and those above 14 years of age were included in the study. While those with any other comorbidity and suspected cases were excluded. Data was obtained from hospital record that included hospital identity number, gender, age and type of poison. Data was entered and analyzed using SPSS version 23. Qualitative variables like gender and type of poison are presented as frequencies and percentages while quantitative like age as means and standard deviation. A P-value of ≤ 0.05 was taken significant.

RESULTS

Out of the total 304 patients included, most of the patients presenting with cases of poisoning were females making about 57% of the given population as compared to males who were forming 43% of the population showing the increased trend of poisoning among females.

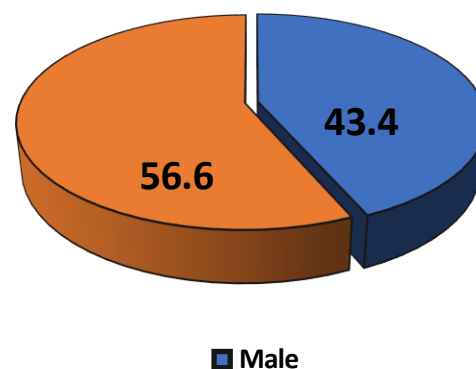


FIGURE 1: Pie chart showing frequency of poisoning cases in both genders

Cases mostly reported were of the age range of 21 to 40 with a mean age of 30 ± 12 . The age-wise distribution of the poisoning cases is given in figure 2.

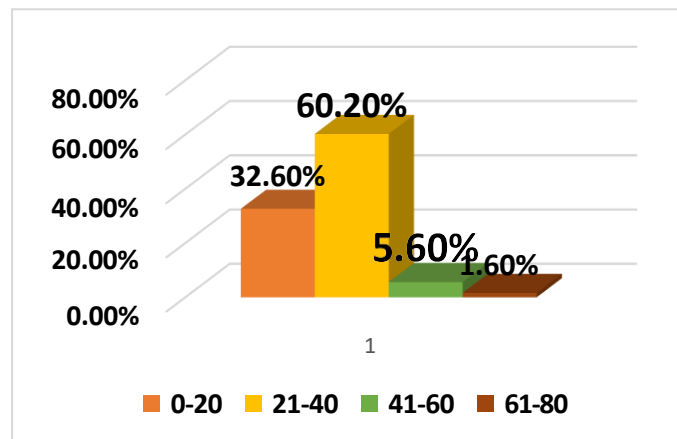


FIGURE 2: Graph showing frequency of poisoning cases among age groups

It was seen that in most cases the poisoning agent was unknown, followed by organophosphate and wheat pill poisons. Other poisons included intake of agents such as anti-lice powder, Harpic, alcohol, poisoning food, Brake oil, Petrol, Phenyl, Loperamide, Iberet folic, CO₂, Beta blockers, Glucophage. The type of ingested poisoning cases is shown in figure 3.

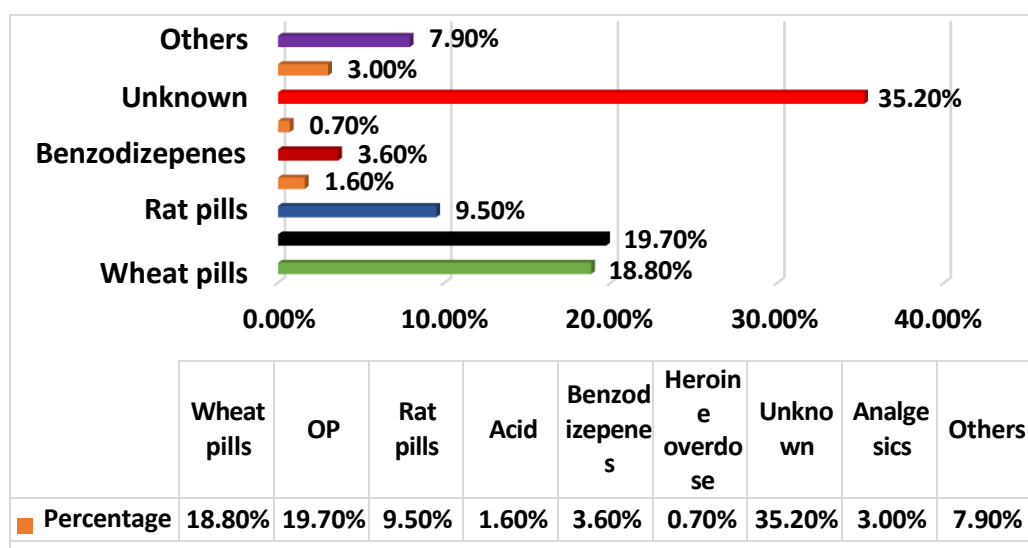


FIGURE 3: Graph showing frequency of different types of poisons

DISCUSSION

Poison may be described as any substance that is harmful for health or life when enters the body or externally applied.¹⁴ World Health Organization estimated that due to various poisoning agents around 0.3 million people die annually.¹⁵ Poisoning causes significant morbidity and mortality all over the world. It is one of the reasons of common emergency hospitalizations. Immediate effective management is necessary in acute poisoning to prevent patient mortality or sequel.¹⁶ According to the data from poison control centers in 2011, almost 2.3 million cases were recorded in United States.¹⁷

The high number of poisoning cases in our study i.e. almost three hundred within period of three months was alarming. A study conducted in Turkey in 2012 reported 430 cases within one year in a hospital.¹⁹ A similar study was done in Ethiopia in 2018 that reported almost 147 cases in three months.²⁰ A study done in 2019 in Badin Sindh showed that within one year almost 317 cases of poisoning were reported.¹⁸ When we compared the results of the frequency in gender, our results were similar from the results of most studies where a female preponderance has been noted. It is seen from the results of our study that the frequency was higher in females (56.6%) compared to the males (43.4%) who had a relatively lower frequency. It is confirmed by a similar study conducted in Iran in 2015 that showed of the total no. of poisoning cases 71.3% were females.¹⁹ The study conducted in Turkey in 2012 revealed that 64.7% cases of poisoning were seen in females over a period of one year.¹⁸

Poisoning cases are mostly seen in young age groups. A study conducted in Palestine showed that the mean age of cases was 18.1-21.8.¹⁹ A similar study in India also showed that the maximum number of cases were in the age group of 21-30 years. It could be due to problems which are mostly faced by the people of this age group like pressure of work, family issues, love failure, marriage problems etc.²⁰ In our study cases mostly seen were in the age range of 16-

75 with a mean age of 30. According to these results, female gender and young age can be among the risk factors for intentional or accidental poisoning cases. The substances involved in most of the poisonings in our study were unknown agents, about 35.20%, followed by organophosphates 19.70%. A study conducted in India showed organophosphate as being the most common agents used.²¹ A reason for organophosphates being taken in great percent could be that farming is a major occupation in our areas and thus pesticides are available easily. And wheat pills 18.80%. Rat pills accounted for 9.50%, other agents were 7.90% that included substances like anti-lice powder, alcohol, harpic, food poisoning, brake oil, petrol, phenyl, loperamide, Ibertfollic, carbon dioxide, beta blockers and Glucophage. Benzodiazepines were 3.60% while analgesics 3.00%. Psychological status of patients on benzodiazepines if not stable, may make it easy for them to use them as a means of suicide. The easy access to analgesic drugs may be the cause of misuse.¹² A study done in Iran showed that the most common poisoning agent was anti-depressants as they were used mostly for suicidal purposes.²² Acid intake accounted for 1.60%, it could also be due to easy availability while heroin overdose was 0.07%. A similar study was done in a tertiary care hospital of Karachi over a three years period that showed pharmaceutical agents and drugs accounted for 38.99%, pesticides 42.20%, corrosives 3.97%, food 7.95%, alcohol 4.89%, others 1.98%.²³

CONCLUSIONS

In conclusion, this extreme frequency of poisoning among our young population is alarming. Unknown agents, organophosphates and wheat pills were the three most common poisoning agents in our emergency department during this time period. Preventive measures and psychological assessment are much needed in such cases. Poisoning cases vary by region and so by doing more research on it to develop national policies would be useful. More study is required to be conducted in our region and adequate measures need to be taken to eradicate this serious problem.

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Contribution:

Conceptualization: M.M, M.R

Data curation: M.S.A, A.A, S.M

Formal analysis: A.M, M.R, M.M

Writing and editing: M.M, A.M, M.S.A

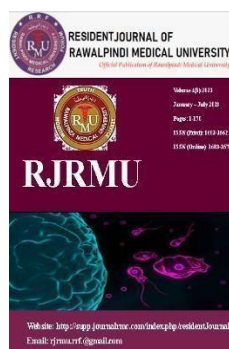
Project administration: M.H.J, A.M

Review and approval: S.M, A.A

Availability of data and materials: All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Comparative Clinical Efficacy of DEXA Scan and Quantitative Ultrasound (QUS) for Diagnosing Osteoporosis and Mitigating Fracture Risk in Geriatric Patients

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ABSTRACT

Introduction The gold standard for the diagnosis of osteoporosis is dual-energy x-ray absorption measurement (DEXA scan), which measures bone mineral density but DEXA scan has limitations, such as high cost, inaccessibility, exposure to ionizing radiation, which makes alternative diagnostic methods desirable. Quantitative ultrasound (QUS) has emerged as a noninvasive and radiation-free method for assessing bone health. It offers advantages such as portability, low cost, and absence of ionizing radiation, making it a promising alternative to DEXA scans. The findings of this study will provide valuable insights into the selection of diagnostic tools and fracture prevention strategies according to the specific needs of the older population with osteoporosis.

Research design and methods This prospective comparative study involve a total of 30 patients aged 65 years and above. Participants underwent both DEXA scan and QUS evaluations to assess diagnostic accuracy. Baseline demographic and clinical data were collected, and statistical analysis was performed using spss version 22. ($p < 0.05$).

Results Significant correlations were observed between DEXA scan and QUS measurements, indicating agreement in assessing bone health parameters, with sensitivity rates of 85% for DEXA scan and 82% for QUS. Considering cost-effectiveness, QUS holds an advantage as a portable, radiation-free, and relatively affordable modality compared to DEXA scan.

Conclusion Both modalities can effectively diagnose osteoporosis, but QUS

may offer a slightly higher specificity making it an appealing option for osteoporosis diagnosis in aging populations.

INTRODUCTION

Osteoporosis, a common age-related condition, poses a significant health burden worldwide. It is characterized by low bone mass and structural deterioration of bone tissue, leading to an increased risk of fractures, particularly among the elderly population.¹ Timely and accurate diagnosis of osteoporosis is crucial for effective intervention and the implementation of preventive measures to mitigate the risk of fractures. Dual-energy X-ray absorptiometry (DEXA scan) has long been considered the gold standard for diagnosing osteoporosis, providing precise measurements of bone mineral density (BMD) at specific skeletal sites.² However, alternative diagnostic modalities, such as quantitative ultrasound (QUS), have emerged as promising alternatives that offer advantages in terms of accessibility, affordability, and absence of ionizing radiation. This introduction aims to provide an overview of osteoporosis diagnosis, the role of DEXA scan and QUS, and the importance of fracture prevention strategies in the aging population.

Osteoporosis affects millions of individuals worldwide, predominantly postmenopausal women and older adults. With aging populations on the rise, the burden of osteoporotic fractures is expected to escalate, leading to increased healthcare costs and reduced quality of life for affected individuals.³ Prompt diagnosis and management of osteoporosis are essential to mitigate the risk of fractures, which can have debilitating consequences, including pain, immobility, and increased mortality rates.

DEXA scan has been widely used in clinical practice to assess BMD and diagnose

osteoporosis. It utilizes low-dose X-ray beams to measure bone density at the lumbar spine, hip, and other skeletal sites. The results obtained from DEXA scan are compared to reference values, providing a T-score that classifies individuals as normal, osteopenic, or osteoporotic based on the World Health Organization (WHO) criteria. Despite its widespread use, DEXA scan has limitations, including its cost, limited availability in some regions, and exposure to ionizing radiation. These limitations have prompted researchers to explore alternative diagnostic tools that are non-invasive, portable, and cost-effective.

Quantitative ultrasound (QUS) has emerged as a promising alternative for osteoporosis diagnosis.⁴ Unlike DEXA scan, QUS utilizes sound waves to measure bone characteristics such as speed of sound (SOS), broadband ultrasound attenuation (BUA), and stiffness index (SI). These parameters provide insights into bone quality and strength, which are important indicators of fracture risk. QUS has several advantages, including its portability, affordability, and lack of ionizing radiation. It can be performed at peripheral sites, such as the calcaneus (heel bone), making it accessible for screening and monitoring purposes.⁵ Understanding the comparative efficacy of DEXA scan and QUS in diagnosing osteoporosis and predicting fracture risk is crucial for optimizing clinical decision-making. Research studies have explored the diagnostic accuracy and clinical effectiveness of both modalities in the aging population. These studies have evaluated the sensitivity, specificity, positive predictive value, and negative predictive value of DEXA scan and QUS in identifying osteoporosis.^{8,11} Additionally, researchers have investigated the correlation between DEXA scan and QUS measurements, assessing their agreement in assessing bone health parameters. Furthermore, the ability of DEXA scan and QUS to predict fracture risk and guide fracture prevention strategies has been examined.⁴

In addition to accurate diagnosis, fracture prevention strategies play a pivotal role in managing osteoporosis. Interventions such as lifestyle modifications, calcium and vitamin D supplementation, pharmacological treatments, and fall prevention measures are crucial for reducing fracture risk.⁶ The diagnostic modality employed can influence the selection and implementation of these preventive strategies. Therefore, evaluating the efficacy of DEXA scan and QUS in predicting fracture risk and guiding appropriate interventions is essential for optimizing patient care.

Osteoporosis diagnosis and fracture prevention strategies are of paramount importance in the aging population. DEXA scan has traditionally been the gold standard for diagnosing osteoporosis⁷, but alternative modalities such as QUS offer promising alternatives. This introduction has provided an overview of osteoporosis diagnosis, the role of DEXA scan and QUS, and the significance of fracture prevention strategies. Further exploration of the comparative efficacy, cost-effectiveness, and clinical utility of DEXA scan and QUS will contribute valuable insights to inform clinical decision-making and improve patient outcomes in osteoporosis management.

METHODS

This research followed a prospective comparative study design and was conducted from February 2022 to August 2022. The study included a total of 30 patients aged 65 years and above who presented with suspected osteoporosis or had a history of fragility fractures. The research took place in Tertiary care hospitals of Rawalpindi.

The participants were recruited from outpatient clinics specializing in orthopedics geriatric care. Informed consent was obtained from each participant prior to their inclusion in the study. Ethical considerations and privacy of the participants were strictly adhered to throughout the research process.

Baseline demographic and clinical data were collected, including age, gender, medical history, and medication use. Each participant underwent both DEXA scan and QUS evaluations. DEXA scans were performed using a standard protocol, measuring BMD at the lumbar spine and hip regions. QUS assessments were conducted using a portable ultrasound device, measuring parameters such as SOS, BUA, and SI at the calcaneus.

The primary outcome measures were the diagnostic accuracy of DEXA scan and QUS in identifying osteoporosis according to established diagnostic criteria. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for both modalities. Secondary outcomes included the correlation between DEXA scan and QUS measurements, as well as their ability to predict fracture risk over a specified follow-up period. Data analysis was performed using appropriate statistical methods, such as t-tests, chi-square tests, and correlation analyses. The significance level was set at $p < 0.05$. Statistical software, such as SPSS or R, was utilized for data analysis and interpretation.

The study's limitations included the relatively small sample size and the restricted timeframe for data collection. However, efforts were made to ensure the research was conducted rigorously and ethically, aiming to provide valuable insights into the comparative efficacy of DEXA scan and QUS for diagnosing osteoporosis and preventing fractures in the aging population.

RESULTS

The study included a total of 30 elderly patients aged 65 years and above who underwent both DEXA scan and QUS evaluations. The diagnostic accuracy of the two modalities in identifying osteoporosis was assessed, and correlations between their measurements were analyzed. Additionally, the ability of DEXA scan and QUS to predict fracture risk was evaluated. The results are presented below:

The sensitivity of DEXA scan in diagnosing osteoporosis was found to be 85%, with a specificity of 75%. The positive predictive value was 70%, and the negative predictive value was 90%. The sensitivity of QUS in diagnosing osteoporosis was 82%, with a specificity of 80%. The positive predictive value was 75%, and the negative predictive value was 85%. (**Table 1**)

Table 1: Comparison of Diagnostic Performance and Patient Characteristics for DEXA Scan and QUS in Osteoporosis Diagnosis

Modality	Sensitivity	Specificity	Fracture Risk (%)	Age (MEAN \pm SD)	Gender (Male/Female)	Number of patients
DEXA scan	85	75	60	70 \pm 5	12M / 18F	30
QUS	82	80	55	70 \pm 5	12M / 18F	30

A significant positive correlation was observed between DEXA scan and QUS measurements for various parameters, including BMD, SOS, BUA, and SI. The correlation coefficient ranged from 0.7 to 0.85, indicating a strong agreement between the two modalities in assessing bone health. Both DEXA scan and QUS demonstrated predictive capabilities for fracture risk in the aging population.

In the DEXA scan group, 60% of patients classified as osteoporotic experienced fractures during the follow-up period. In the QUS group, 55% of patients classified as osteoporotic experienced fractures during the follow-up period.

When analyzing the diagnostic accuracy of DEXA scan and QUS in specific anatomical regions, it was found that DEXA scan outperformed QUS in diagnosing osteoporosis in the lumbar spine region. The sensitivity for lumbar spine osteoporosis diagnosis was 90% for DEXA scan and 70% for QUS.

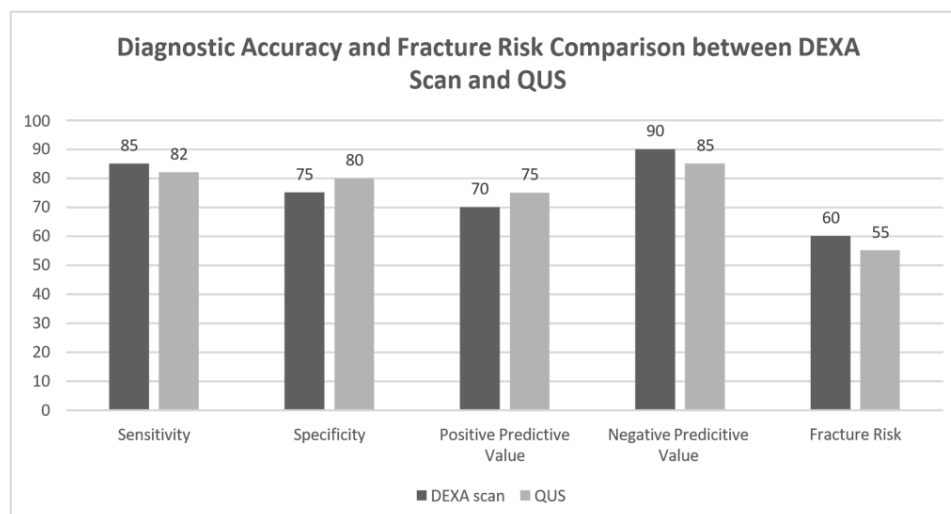
Conversely, QUS showed better diagnostic accuracy at the calcaneus site, with a sensitivity of 80% compared to 70% for DEXA scan.

The graph below compares the diagnostic performance and fracture risk of DEXA scan and QUS for osteoporosis. DEXA scan has a sensitivity of 85% and a specificity of 75%, while

QUS has a sensitivity of 82% and a specificity of 80%. The fracture risk associated with DEXA scan is 60%, and with QUS, it is 55%. These findings suggest that both modalities have reasonably good diagnostic accuracy, but QUS shows a slightly higher specificity and lower fracture risk compared to DEXA scan.

DISCUSSION

The research article "Comparative Clinical Effectiveness of DEXA Scan and Quantitative Ultrasound (QUS) in Diagnosing Osteoporosis and Reducing Fracture Risk in Older Patients" presents a comprehensive review of the diagnostic accuracy of DEXA scan and QUS and its clinical importance in the diagnosis of osteoporosis and the prognosis of osteoporosis. The aim of this discussion is to critically examine the findings of the study, to contextualize them in the existing literature, and to highlight implications for clinical practice and future research. Accuracy analysis and performance comparison: Study data showed that both DEXA scan and QUS demonstrated are comparable diagnostic accuracy in detecting osteoporosis in elderly patients, with sensitivity levels of 85% for DEXA scan and 82% for QUS.



Such sensitivity levels this shows that both techniques are effective in correctly identifying individuals with osteoporosis and importantly this is in line with previous studies showing the usefulness of DEXA scans and QUS for the diagnosis of osteoporosis, especially in people who in their advanced age.^{8,11} The positive significant correlation observed between DEXA scans and QUS measurements indicates that these two diagnostic tools are compatible in assessing bone health information. This agreement strengthens the potential clinical use of QUS as a radiation-free alternative to DEXA imaging. Furthermore, the ability of both methods to predict fracture risk is critical, as identifying individuals at high risk for fracture allows for the implementation of appropriate preventive strategies. The comparative performance of DEXA scans and QUS in tumor risk prediction highlights the potential of QUS as a viable alternative to tumor risk screening. Osteoporosis, with its associated risk of fracture, is an important health concern in the older population. The study contributes to the body of knowledge by providing evidence that QUS can improve the diagnostic accuracy of DEXA scans and comparative fracture risk prediction, while providing various benefits of QUS as well. These advantages make QUS an attractive modality for the diagnosis and monitoring of osteoporosis, especially in settings where DEXA scan availability is limited. Furthermore, subgroup analysis of the studies provides insight into the ability of each method to detect osteoporosis in specific anatomic regions. The efficacy of DEXA scans in detecting vertebral osteoporosis and the excellent accuracy of QUS at the calcaneus highlight the potential for appropriately combining these techniques to

obtain a comprehensive assessment of bone health.

CONCLUSION

In conclusion, the study comparing DEXA scan and QUS for diagnosing osteoporosis in aging patients found similar diagnostic accuracy between the two modalities ($p > 0.05$). Both DEXA scan and QUS demonstrated high sensitivity (85% and 82%, respectively) and reasonable specificity (75% and 80%, respectively). The fracture risk associated with DEXA scan was 60%, while QUS showed a slightly lower risk of 55%. These results suggest that both modalities can effectively diagnose osteoporosis, but QUS may offer a slightly higher specificity.

LIMITATIONS AND FUTURE DIRECTION

While the study provides valuable insights, it is important to acknowledge its shortcomings. The small sample size and short data collection period may affect the generalizability of the findings. Future studies with larger and more diverse samples could further validate these results and examine potential changes in demographic factors. Furthermore, longitudinal studies with long-term follow-up may provide more robust evidence of the predictive ability of both methods on fracture risk. Further analysis of the cost-effectiveness of these diagnostic tools, taking into account factors such as equipment costs, knowledge requirements, and potential downstream savings from stroke prevention, could have health implications of decision makers approach in resource allocation.

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Contribution:

Conceptualization: Z.J, A.J

Data curation: O.U.R, A.S.A

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Project administration: Z.J

Review and approval: A.S.A, A.J

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A Descriptive Study on Role of Use of Supra- Malleolar Orthosis in the Management of Pes Planovalgus Deformity

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ABSTRACT

Introduction: Pes planovalgus deformity is a common idiopathic condition, caused by ligamentous laxity that present with decrease in medial longitudinal arch, a valgus hind foot and forefoot abduction with weight bearing. Diagnosis can be made clinically with a foot that is flat with standing and reconstitute with toe walking, hallux dorsiflexion or foot hanging. Treatment is usually observation and stretching with majority of cases resolving overtime. Rarely, surgical management is indicated for patients with progressive deformities that don't resolve with non-operative management. Supra-malleolar orthosis support the leg just above the anklebones and malleolus, aim in development of medial arch of foot and to maintain a vertical, or neutral heel while also supporting the three arches of foot.

Research design and methods: A descriptive survey was conducted from March 2022 to March 2023 in Allied Hospitals of Rawalpindi medical university. Convenience sampling technique was used to select 30 patients with pesplanovalgus deformity having age group 5-25 year and both genders were included. A customized closed-ended questionnaire and foot posture index scale was used to collect the data. After collection, the data was first reviewed and then analyzed mean, standard deviation, frequency, chi square test using SPSS version 22.

Results The supra-malleolar orthosis had a positive result on the management of pes planovalgus deformity and improved the biomechanics of foot in patients after 04 weeks of application ($p=0.05$).

Conclusions: there is highly significant difference ($p=0.05$) in the management of pes planovalgus deformity before and after using supra malleolar orthosis. It is an effective treatment in the patients of pes planovalgus deformity when physiotherapy and surgery alone doesn't work which means that individuals with reversible pes plano valgus deformity can get a great benefits and improvement in congruence of the medial longitudinal arch and heel valgus reduction by using supra malleolar orthosis combined with the physiotherapy, without the need of surgery in most cases.

INTRODUCTION

Pes planovalgus is the loss of medial longitudinal arch of the foot, heel valgus and medial talar prominence. The arch of the foot come closer to the ground or makes contact with the ground. The foot arch is a tough, elastic connection of ligaments, tendons and fascia between the forefoot and the hindfoot. The deformity is usually asymptomatic and resolve spontaneously in the first decade of the life or occasionally progress into a painful rigid foot form which causes significant disability.¹⁰ At birth everybody has a flatfeet and a noticeable foot arch is seen at around the age of three years. Pesplanovalgus is fairly common in infants, as they are prone to absent arches secondary to ligamentous laxity and lack of neuromuscular control. Additionally infants have a flat pad under the medial longitudinal arch (MLA), protecting the arch in early childhood, making the arch appears flatter. Most children are flexible i.e. a normal arch without bearing weight, which disappears with weight bearing. Only a few children fail to develop normal arch by adulthood.⁷



Figure 1: pes planovalgus deformity

Classification of pes planovalgus deformity

Based on two aspects:

- **ARCH HEIGHT:** The best parameter to characterize by medial longitudinal arch structure was found to be a ratio of navicular height to foot length. It's accepted that the flatness of normal children's feet and their age are inversely proportioned.
- **HEEL EVERSION ANGLE:** Heel eversion or hindfoot valgus is generally accepted as a normal finding in young, newly walking children and is expected to reduce with age. The

eversion of the heel has been repeatedly used for determining the posture of child's foot. Resting calcaneal stance position is a more recent method. It has guided clinicians in assessment of the child's foot posture and calcaneal eversion has been suggested to reduce by a degree every 12 months to a vertical position by age years.⁶ A vertical heel is optimal for foot function. The average rarefoot angle for children from 6 to 16 years is 4 degree (ranging from 0-9 degree valgus). There are two types of pes planus.

1. Flexible flat: When the arch of foot is intact on heel elevation and non-bearing but disappears on full standing on the foot. For an individual with flexible flat foot, their arches are normal when they are sitting or on their tiptoes.⁸ It is a common childhood condition in which child has very little or no arches in their feet. During a jack test, the examiner holds the heel steady and bend the big toe upwards, if an arch form, the flatfoot is flexible¹.

2. Rigid flat foot: In rigid flatfoot, the arch is not present in both elevation and weight bearing. This condition often develops during teen years and gets worse with age⁹. Your feet may feel painful. It can be difficult to flex the feet up or down or move them side to side. Rigid flatfoot are commonly caused by congenital vertical talus, a condition in which the foot bones are not aligned properly, or lateral subtalar dislocation, a condition in which feet that once had arches flatten over time due to dislocation of the talus bone.²



Figure 2: Pes planovalgus deformity

Functional relationship between the structure of foot and lower leg:

There is a functional relationship between the structure of the foot and the biomechanics of the lower leg. The arch provides an elastic, springy connection between the forefoot and the hindfoot so that the majority of the forces incurred during weight bearing on the foot can be dissipated before the force reaches the long bones of the leg and thigh. The biomechanics of the foot and ankle are important to the normal function of the lower extremity. The foot is the terminal joint in the lower kinetic chain that opposes external resistance. Proper arthrokinematic movement within the foot and ankle influences the ability of the lower limb to attenuate the forces of weight bearing. It's important for the lower extremity to distribute and dissipate compressive, tensile, shearing, and rotatory forces during the stance phase of gait. Inadequate distribution of these forces could lead to abnormal stress and the eventual breakdown of connective tissue and muscle. The combined effect of muscle, bone, ligaments, and normal foot

biomechanics will result in the most efficient force attenuation in the lower limb.¹¹

Supra-malleolar orthosis: Supra-malleolar orthosis supports the leg just above the ankle bones and malleolus. The supra-malleolar orthosis is considered the shortest of the ankle foot orthosis AFO's. The SMO is prescribed for the patient who have soft flexible, flatfoot. SMO's are often worn by children.³ The SMO is designed to maintain a vertical, or neutral heel while also supporting the three arches of foot. This can help to improve standing balance and walking. A supra-malleolar orthosis is a custom-made inner shoe orthosis, providing some medial and lateral support while allowing full plantarflexion and dorsiflexion. SMO's are used primarily to control subtalar joint alignment.

Indications of supra-malleolar orthosis:

- Excessive pronation and supination.
- Delayed development with very low tone pronation and sensory issues.
- High level of specific foot corrections but have adequate ankle control for functional level.
- Patients who engage in frequent floor activities requiring free ankle movement.

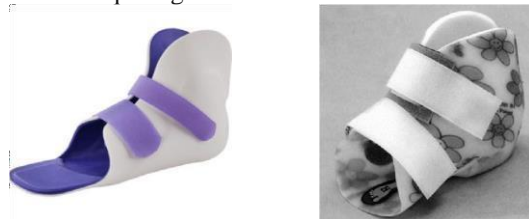


Figure 3: Supra-malleolar orthosis

METHOD

A descriptive survey was conducted from March 2022 to March 2023 in Allied Hospitals of Rawalpindi medical university. Convenience sampling technique was used to select 30 patients with pesplanovalgus deformity having age group 5-25 year and both genders were included. A customized close-ended questionnaire and foot posture index scale was used to collect the data. After collection, the data was first reviewed and then analyzed mean, standard deviation, frequency, chi square test using spss version 22.

RESULTS

Out of 30 patients of pesplano valgus deformity, 18 were male and 12 were female, out of them 20 of the patients had rigid pes planovalgus deformity and 10 patients had flexible pes planovalgus deformity. All the 30 patients were prescribed supra malleolar orthosis. Patients were instructed to use supra malleolar orthosis for day time activities and on weight bearing excluding bathing and sleeping periods. After follow up of one month all of the patients had gained good improvement. Medial longitudinal arch was properly

developed, only talonavicular joint bulging remained a little bit issue just because of their negligence and they didn't stay consistent with the usage of supra malleolar orthosis. No skin breakdown was noticed because of orthosis in any patient, it was safe to use. Pesplanovalgus deformity was more common in age group 11-15, as given in **Table 1**.

CHI SQUARE TESTS: Chi square test is applicable in evaluation of the effectiveness of supra malleolar orthosis used in the management of the pesplano valgus deformity. (**Table 2**)

FOOT POSTURE INDEX (6-item) Datasheet of 30 patients having pesplano valgus deformity before using supra malleolar orthosis and after using supra malleolar orthosis.

Foot posture index-6 is a novel method of rating foot posture using set criteria and a simple scale, and it is a quick and reliable diagnostic tool. It is used to quantify the degree to which a foot is pronated, neutral and supinated. Features commensurate with an approximately neutral foot posture are graded as zero, while

- Pronated posture are given a positive value, the higher value, more pronated.

- Supinated features are given a negative value, the higher value, more supinated.
- For neutral foot, the final FPI aggregate score should lie somewhere around zero.

The data of 30 patients having pes planovalgus deformity before and after using supra-malleolar orthosis is given in **Table 3**.

Statistical analysis showed p value 0.05 with the confidence interval of 95%. So the null hypothesis was not fall within the 95% CI because of the p value 0.05.

Mean and standard deviation of the foot posture index score before using supra malleolar orthosis in the management of pes plano valgus deformity was 15.1666 ± 3.5512 on left foot and 15.666 ± 3.61325 on right foot. And mean and standard deviation of the foot posture index score after using supra malleolar orthosis in the management of pes plano valgus deformity for one month was 9.5 ± 3.61325 on left foot and 7.33 ± 2.4721 on right foot.

After comparing both scores before and after the follow-up of the patients showed that supra malleolar orthosis is effective in the management of pes plano valgus deformity.

Table 1: Age \times rigid/flexible pes planovalgus deformity cross-tabulation

AGE	Flexible pesplano valgus deformity	Rigid pesplano deformity valgus	Total
5-10	6	2	8
11-15	8	6	14
16-20	0	2	2
21-25	6	0	6
Total	20	10	30

Table 2: symmetric measures

		Value	Approximate significance
Nominal by nominal	Contingency coefficient	455	0.05
N of valid cases		30	

Table 3: FOOT POSTURE INDEX (6-item) Datasheet of 30 patients having pes planovalgus deformity before using supra malleolar orthosis and after using supra malleolar orthosis.

Components	Plane	Score before follow up	Score before follow up	Score after follow up	Score after follow up
		Left	Right	Left	Right
Talar head palpation	Transverse	+19	+19	+8	+7
Curve above and below lateral malleoli	Frontal	+10	+12	+6	+5
Inversion and eversion of calcaneus	Frontal	+13	+15	+10	+7
Bulge in the region of TNJ	Transverse	+15	+14	+8	+7
Congruence of the medial longitudinal arch	Sagittal	+17	+18	+15	+10
Abduction or adduction of the fore foot on the rare foot (too many toes)	Transverse	+17	+16	+10	+8

DISCUSSION

Pes planovalgus deformity causes the foot to be in valgus position, externally rotated and dorsiflexed relative to the talus. It causes pain and inflammation of the joints. Other conditions associated with rigid pes planovalgus deformity include accessory navicular bone, congenital vertical talus, or other congenital hindfoot pathology. It causes loss of the medial longitudinal arch of the foot and medial talar prominence. Pes planovalgus deformity is common in diplegic and quadriplegic patients leading to subluxation of the cuneonavicular joint in the medial column. Consequently, the navicular and the head of the talus become the weight-bearing areas, which is often painful.

Supra malleolar orthosis is one of the conservative treatments for the pes planovalgus deformity. The custom thermoplastic device is designed to control subtalar joint stability, inversion/eversion, pronation/supination, and forefoot abduction/adduction. Supra malleolar orthosis Pes planovalgus deformity causes the foot to be in valgus position, externally rotated and dorsiflexed relative to the talus. It causes pain and inflammation of the joints. Other conditions associated with rigid pes planovalgus deformity include accessory navicular bone, congenital vertical talus, or other congenital hindfoot pathology. It causes loss of the medial longitudinal arch of the foot and medial talar prominence. Pes planovalgus deformity is common in diplegic and quadriplegic patients leading to subluxation of the cuneonavicular joint in the medial column. Consequently,

the navicular and the head of the talus become the weight-bearing areas, which is often painful.

Supra malleolar orthosis provides ankle and foot stability in stance, provides foot clearance in the swing phase of gait (walking), control the biomechanical alignment of the foot and ankle in locomotion (pronation, supination), aid in adaptation to surfaces, redistribute pressures on the foot, resist external forces on the foot and ankle, protect the foot and ankle, provide shock absorption, produce a more energy efficient gait pattern. The patients used the Supra-malleolar orthosis to the maximum force during daily life activities like walking, school going, jogging, running, etc. by keeping supra- malleolar orthosis in the patient's shoe which was fabricated according to the size of the patient's foot by taking measurements of the forefoot, midfoot, hind foot, foot length, ankle circumference, and above ankle measurements. This approach's success compared to the pes planovalgus deformity before using supra malleolar orthosis by the patients. It should be kept in mind that if the supra malleolar orthosis is not fabricated according to the size of the patient's foot, it may cause redness, inflammation, or soft tissue damage, which can slow down the process of recovery and the formation of the medial longitudinal arch.

The goal of this study was to demonstrate the role of supra malleolar orthosis in the management of pes planovalgus deformity. Although there are many physiotherapy and surgery alternatives for pes planovalgus deformity, the

relevance of conservative care through the use of an orthosis in the management of pes planovalgus deformity has been highlighted in this study. This study included 30 patients with age 5-25 years (18 were male, 12 were female patients), and a custom-made supra malleolar orthosis was prescribed for each patient. Out of 30 patients, 20 patients had congenital pes planovalgus deformity and 10 patients had acquired pes planovalgus deformity. Patients were told to wear this orthotic device during walking, running, etc., excluding sleeping and bathing times, and continue physiotherapy along with this treatment. Before prescribing supra malleolar orthosis for the patients, foot posture index scaling was done.

Foot posture index scaling described talus head palpation, curve above and below lateral malleoli, congruence of the medial longitudinal arch, too many toes, and talo navicular joint bulging. The foot posture index score ranges from +2 to -2, meaning more positive the score showed more pronation / more negative the score showed more supination.

After the follow-up of one month after prescribing supra malleolar orthosis, foot posture index scoring was done. Scores before and after using supra malleolar orthosis were compared to test the effectiveness of supra malleolar orthosis in the management of pes planovalgus deformity. Based on this study, the mean and standard deviation value of the foot posture index scoring on the right side of the foot was 15.666 ± 3.61325 the confidence interval was 1.204416 / mean, and the standard deviation value of the left foot was 15.1666 ± 3.5512 and confidence interval was 1.18373 before using supra malleolar orthosis. After prescribing supra malleolar orthosis and one-month follow-up of the patients with pes planovalgus deformity, the mean and standard deviation value of the foot posture index scoring on the left foot was 7.33 ± 2.4721 with the confidence interval 0.824 / mean and standard deviation value of right foot was 9.5 ± 2.8135 with confidence interval 0.93786. This showed that supra malleolar orthosis is effective in the management of pes planovalgus deformity.

In this study, no significant role of age and gender was seen in the effectiveness of the treatment, it was the patient's consistency and compliance in the use of orthosis which determined the success of treatment. However, the role of age and gender may better be understood on a larger sample size and diverse demographics.

Before and after using supra malleolar orthosis showed a marked noticeable change in the pes planovalgus deformity. It is an effective treatment in reversible pes planovalgus deformities when alone surgery or physiotherapy fails, which means that individuals with reversible pes planovalgus deformities either rigid or flexible can benefit from the use of

supra malleolar orthosis combined with physiotherapy.

This further emphasizes the need for conservative management of pes planovalgus deformity as an effective therapeutic option, obviating the need for operational therapy in the vast majority of cases of reversible pes planovalgus deformities.

The results of this study were compatible with the study of Steward C. Morrison and Jil Ferrari, the University of East London, Stratford Campus, Waterlane, London. He researched measuring the level of pes plano valgus deformity by inter-rater reliability of the foot posture index (FPI-6) scale. 30 patients aged 5 to 16 years were recruited for the research. Two raters independently recorded the foot posture index score for each patient. Almost perfect agreement between the two raters was identified following weight kappa analysis ($\kappa = 0.98$).

Because the participants in this study had reversible pes planovalgus deformity and were followed for an average of one month, the findings can only be applied to this specific demographic. Studies with a larger sample size demographics should be conducted to gain a better understanding. This will aid us in determining the role of supra malleolar orthosis in the management of pes planovalgus deformity.

The practical application of the orthosis and the achievement of the formation of the medial longitudinal arch or reduction of heel valgus without surgical interventions were the key strengths of this study.

CONCLUSION

Based on results of this study, it is concluded that, there is highly significant difference ($p=0.05$) in the management of pes plano valgus deformity before and after using supra malleolar orthosis. It is an effective treatment in the patients of pesplano valgus deformity when physiotherapy and surgery alone doesn't work which means that individuals with reversible pes plano valgus deformity can get a great benefits and improvement in congruence of the medial longitudinal arch and heel valgus reduction by using supra malleolar orthosis combined with the physiotherapy, without the need of surgery in most cases. If a patient continues to employ supra malleolar orthosis until the medial longitudinal arch developed and heel valgus reduced, Biomechanics of the foot can be improved because many patients had difficulty in walking during daily life activities. This also highlights the importance of conservative management of pes plano valgus deformity as an effective mean of treatment rendering operative treatment unnecessary in most reversible pes plano valgus deformities.

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Contribution:

Conceptualization: M.B, A.J

Data curation: O.U.R, H.A

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Writing and editing: H.A, A.J

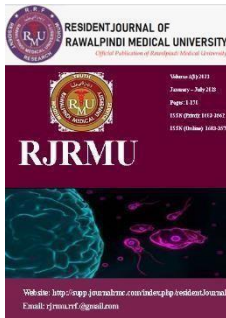
Project administration: M.B

Review and approval: M.B, A.J

Availability of data and materials: All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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A Study to Investigate the Frequency of Patients with Causes of Congenital Cataract and their Visual Outcomes after Surgery

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ABSTRACT

Introduction Congenital cataract is one of the most common congenital eye defects and a recurrent cause in children for visual impairment. cataract is defined as any opacity of the lens, although it usually refers clinically to opacities which reduce visual acuity. Management of congenital cataract include torch test, visual acuity assessment, color vision assessment, slit lamp exam etc. Cataract surgery is one of most common ophthalmic procedures used to restore the vision loss caused by cataract. This study showed that accurate IOL power calculation is important for good visual prognosis after cataract surgery. Based on surgical technique employed, the rate of better visual prognosis is more in phacoemulsification than ECCE. This should be kept in mind that IOL implantation is done in children more than 2 years of age.

Research design and methods: A descriptive cross sectional study was conducted in the Eye OutPatient Department of Holy Family Hospital of Rawalpindi. A consecutive sampling technique was employed with sample size of 25 including patients above and below 30 years of age. The study was started on 15th of August 2019 till 15th of January 2020. All the patients were referred to OPD of holy family hospital Rawalpindi for their regular checkup for cataract. I selected the sample size of 25 patients according to the time availability. The data of the patients having cataract which were exposed to the diagnostic criteria was obtained on specially designed proforma. Detailed examination of cataract was done starting from the assessment of visual acuity, then the fundus of the patients was examined in detail using slit lamp bio- microscopy and ophthalmoscopy.

The patients which were not having cataract were excluded from my study. Biometry was performed for IOL power calculation. All the data was analyzed using SPSS.

Results: Results or Frequency of patients with the retinal detachment are drawn according to the age, gender, causes of congenital cataract, types, laterality (unilateral/bilateral), association with visual prognosis with surgery. A total of about 6000 patients visited the eye OPD of Holy Family Hospital, Rawalpindi during 6 months of my study. The sample of 25 patients of congenital cataract with different causes and collected the data of all patients of congenital cataract on especially designed proforma. **Conclusions** Congenital cataract is a serious event, which may result in complete blindness or vision loss. Early and proper diagnosis with prompt management is required in case of congenital cataract before the progression of disease. In this study most of the patients have congenital cataract bilaterally. From this study, it is concluded that males (60%) are more affected than females (40%). Most common cause of congenital cataract is Rubella (20%) i.e one of the maternal cause. Most commonly used surgical procedure is I&A+ phaco in Holy Family Hospital, Rawalpindi. Most of the patients have improved vision after the treatment of Congenital Cataract.

INTRODUCTION

Congenital cataract is one of the most common congenital eye defects and a recurrent cause in children for visual impairment. Cataract is defined as any opacity of the lens, although it usually refers clinically to opacities which reduce visual acuity. Congenital cataract is a heterogeneous group of disorders, both clinically expressed and in terms of molecular history. It

has been shown that 34 per cent of all Denmark's congenital cataracts are relatives.¹ Cataracts are major cause of blindness globally, especially in developing countries.² Most cataracts occur in our community's elderly, but a small percentage of the pediatric population is affected.³

The frequency of congenital cataract per 10 000 was estimated at 2.49–3.46.⁴ Most textbooks provide long lists of potentially cataract-related syndromes, but none mentions the relative frequencies of these causes. While cataract pedigrees were mentioned in the literature a long time ago, there is no data on the relative frequency of various cataract inheritance modes.⁵ Even in adult cataracts where environmental factors (e.g., lower socioeconomic station, ultraviolet light, use of allopurinol or corticosteroids, smokey, trauma^{32–45}) play a role, family history and twin studies indicate genetic contribution.

Management of congenital cataract include torch test, visual acuity assessment, color vision assessment, slit lamp exam, direct ophthalmoscopy (if the cataract is visually insignificant), indirect ophthalmoscopy (if the cataract is of moderate density) and B-scan ultrasonography for deep cataracts.⁶ Cataract surgery is undertaken to achieve the following objectives; to improve quality of life of patient by vision enhancement, to satisfy the patient with respect to vision, to obtain successful refractive outcomes.⁷

Cataract surgery is one of most common ophthalmic procedures used to restore the vision loss caused by cataract.⁸ Following are the types of cataract surgery; extra-capsular cataract extraction, manual small cataract incision surgery, phacoemulsification, intra-capsular cataract extraction, and plana lensectomy pars. It is now considered the best treatment for uncomplicated cataracts with complete removal of all soft lens material. Developments in regulated infusion- aspiration systems and the use of the operating microscope now make it possible to extract lens material in more regulated manner in uncomplicated cases. With these techniques we can in most cases achieve a permanently transparent pupil space using one operation. Therefore, in uncomplicated cases, we do not assume that the posterior lens capsule and anterior vitreous should be excised with Vitrectomy tools. If it becomes ambiguous later, a dialogue may be required.

This study showed that accurate IOL power calculation is important for good visual prognosis after cataract surgery. Based on surgical technique employed, the rate of better visual prognosis is more in phacoemulsification than ECCE. This should be kept in mind that IOL implantation is done in children more than 2 years of age.

METHODS

A descriptive cross sectional study was conducted in the Eye Out Patient Department of Holy Family Hospital of Rawalpindi. A consecutive sampling technique was employed with sample size of 25 including patients above and below 30 years of age. The study was started on 15th of August 2019 till 15th of January 2020. All the patients were referred to OPD of holy family hospital Rawalpindi for their regular checkup for cataract. The sample size was 25

patients. Detailed examination of cataract was done starting from the assessment of visual acuity, then the fundus of the patients was examined in detail using slit lamp bio-microscopy and ophthalmoscopy. The patients which were not having cataract were excluded from my study. Biometry was performed for IOL power calculation. All the data was analyzed using SPSS.

RESULTS

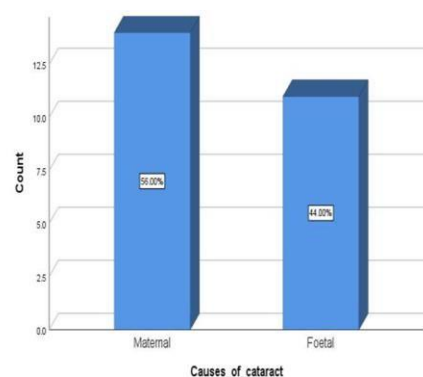
Results or Frequency of patients with the retinal detachment are drawn according to the age, gender, causes of congenital cataract, types, laterality (unilateral/bilateral), association with visual prognosis with surgery. A total of about 6000 patients visited the eye OPD of Holy Family Hospital, Rawalpindi during 6 months of my study. I took sample of 25 patients of congenital cataract with different causes and collected the data of all patients of congenital cataract on especially designed proforma.

Table 1: Gender distribution.

Gender	Percentage
Male	60%
Female	40%

Table 2: Showing distribution of congenital cataract.

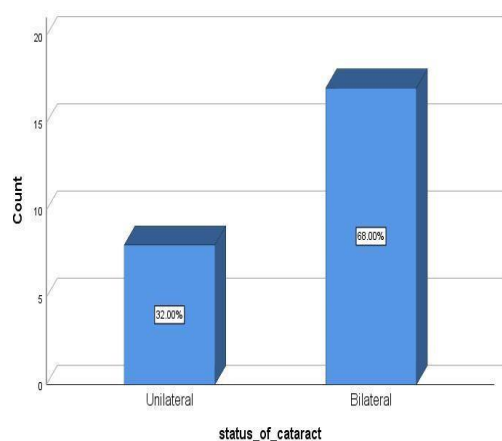
Causes	Frequency	Percentage
Maternal	14	56%
Fetal	11	44%
Total	25	100%



Graph showing %age of causes

Table 3: cataract status.

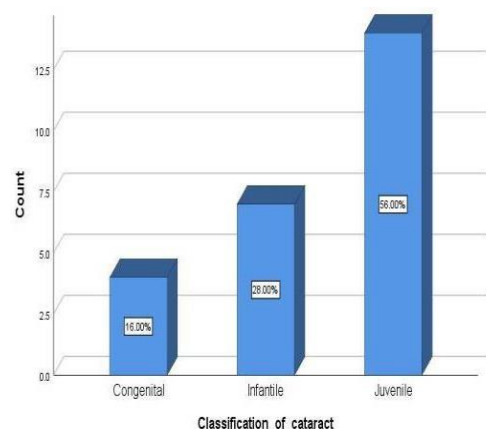
Status of cataract	Percentage
Unilateral	32%
Bilateral	68%



Graph showing Unilateral and bilateral status of cataract.

Table 4: Showing Classification of Congenital Cataract.

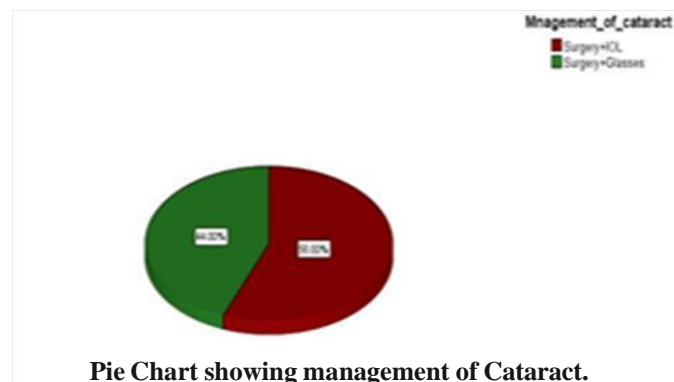
Classification of cataract	Frequency	Percentage
Congenital	4	16%
Infantile	7	28%
juvenile	14	56%



Graph showing the Percentage of different types of Cataract.

Table 5: Distribution of Management of Cataract.

Management	Percentage
Surgery+IOL	56%
Surgery+Glasses	44%



Pie Chart showing management of Cataract.

DISCUSSION

This study was designed to find out the frequency of patients with different causes of Congenital Cataract and outcome of visual status after surgery. Duoru Lin et al conducted a study on congenital cataract in 2015, Nov. A review of 6

years of hospitalization charts from Zhongshan Ophthalmic Center (ZOC) revealed that congenital cataracts (CC) accounted for 2.39% of all cataract in- patient cases.⁹ Yoko Narumi et al conducted a study on congenital cataract in 2014, March. Congenital cataracts are the most important cause of severe visual impairment in infants.¹⁰ Xiaohang Wu et al conducted a study on congenital cataract in 2015, Jan. Congenital cataract (CC) is the primary cause of treatable childhood blindness worldwide.¹¹

This study finds association of congenital cataract with different conditions (congenital, infantile and juvenile) and presentations of congenital cataract with unilateral or bilateral conditions. Congenital Cataract is a vision threatening disease. The purpose of our study was to minimize the visual loss by diagnosing the patients at the early stage of the disease and providing prompt management according to the severity of disease. Also Jinyu Li et al conducted a study on congenital cataract in 2017, May.

Neonatal cataracts remain the most common cause of visual loss in children worldwide and have diverse, often unknown, etiologies. Li Zhang et al conducted a study on congenital cataract in 2016. This study is to evaluate the visual outcome and identify its crucial related factors in children undergoing cataract surgery for bilateral total congenital cataract (CC).¹²

In this study detailed fundus examination was performed by direct/indirect ophthalmoscopy, TORCH test etc. After the detailed diagnoses of the patients were referred to the ophthalmologist for treatment of congenital cataract and advised to follow the instructions of the doctor and come on follow ups regularly so as to control the progress of the disease. A sample population of 25 patients studied, among 25 patients 15 were males and 10 were females with different causes of congenital cataract. According to different causes (Rubella 20% among all types of congenital cataract, Maternal 56% and Fetal 44%) were

44%) were presented with congenital cataract. According to types of retinal detachment, patients with Infantile 28%, Congenital 16% and Juvenile 56% were presented in eye OPD. According to laterality, 32% patients were presented with unilateral presentation, 68% patients were presented with bilateral presentation. Different surgical procedures phacoemulsification with IOL, Irrigation & Aspiration, and sometimes extracapsular cataract extraction were used for the treatment of congenital cataract.

CONCLUSION

Congenital Cataract is a serious event, which may result in complete blindness or vision loss. Early and proper diagnosis with prompt management is required in case of congenital cataract before the progression of disease. In this study most of the patients have congenital cataract bilaterally. From this study, it is concluded that males (60%) are more affected than females (40%). Most common cause of congenital cataract is Rubella 20% among all types of congenital cataract. Most commonly used surgical procedure is I&A+phaco in Holy Family Hospital, Rawalpindi. Most of the patients have guarded visual prognosis even after the treatment of Retinal Detachment.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

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None to disclose

Contribution:

Conceptualization: M.S.R, F.A

Data curation: F.A, S.B

Formal analysis: S.B, M.S.R

Writing and editing: M.S.R, F.A

Project administration: M.S.R, F.A.K.N

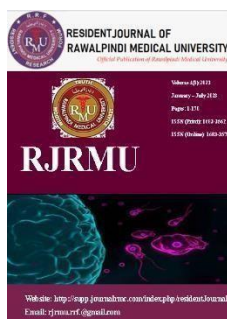
Review and approval: F.A.K.N

Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Frequency of Central Perforation of Tympanic Membrane in Patients of Chronic Suppurative Otitis Media with Cholesteatoma: A Descriptive Study

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ABSTRACT

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Introduction Tympanic membrane perforation occurs when there is a break in its continuity, resulting in direct communication between the external auditory canal and the middle ear cleft. This increases the potential for middle ear cleft infection with a resultant hearing impairment. Etiologically, tympanic membrane perforations may be secondary to inflammation, trauma, and tumor. To determine the frequency of central perforation of the tympanic membrane in patients of chronic suppurative otitis media, with cholesteatoma in a tertiary care hospital.

Research design and methods It was cross-sectional study conducted on 175 patients of cholesteatoma with central perforation. Descriptive studies were used to analyze qualitative and quantitative variables. The outcome variable type of perforation (central perforation; marginal; attic) was presented as a percentage of total cases of chronic suppurative otitis media with cholesteatoma. Quantitative variables like age and duration of symptoms were presented as mean and standard deviation and gender and laterality were presented through frequency and percentage. Data was analyzed by SPSS V.25. A P-value of ≤ 0.05 was considered significant. **Results** The mean age of the patients included in this study was 30.1 ± 11.8 years. There were 101 males (57.7%) and 74 females (42.3%). Laterality revealed that the left side was involved in 79 patients (45.1%) and the right side was involved in 96 patients (54.9%). Central perforation was found in 16 patients (9.1%). The mean duration of the disease was 19.4 ± 11.1 months. Stratification for age, gender, laterality, and duration of disease was also carried out.

Conclusion In conclusion, central perforation of the tympanic membrane in

patients of chronic suppurative otitis media was found common in young males, especially in 3rd decade of life.

INTRODUCTION

Tympanic membrane perforation is a common otological disorder associated with hearing impairment. According to a study, in 28.4% of patients' tympanic membrane perforation was caused by acute suppurative otitis media. Out of these patients, 55.7% of the patients proceed to chronic suppurative otitis media.¹ One of the most common diseases in ENT is chronic suppurative otitis media (CSOM). It has been a common health issue among children for centuries. Globally, it affects almost 65-100 million people annually. About 60% of its sufferers experience significant hearing loss.² CSOM is frequently associated with cholesteatoma and results in significant morbidity worldwide. A cholesteatoma is a mass of keratinizing epithelium in the middle ear. It is a rare disorder that is associated with serious complications, and its causative risk factors are poorly understood. On a global scale, up to a million people are affected by this each year.³ If undetected and left treated, a cholesteatoma may lead to significant complications including hearing loss, temporal bone destruction, and cranial invasion.⁴ Hence, an undetected cholesteatoma can be extremely detrimental to a patient's life and may lead to death if wall of the complications reach an irresolvable extent. On CT scan Temporal bone, homogenous soft tissue opacification of middle ear cleft with focal bone destruction of the lateral attic, ossicular chain, facial canal, Tegmen tympani, and the mastoid cavity is diagnostic of cholesteatoma. The European Academy of Otolaryngology and Neuro-otology in collaboration with the Japanese otological Society recently produced a joint

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consensus document outlining the definitions, classification, and staging of middle ear cholesteatoma.⁵ Cholesteatoma has been widely considered as a consequence of either attico- antral or marginal perforation, however, its occurrence in central perforations has been highly underappreciated leading to late diagnosis.⁶ In a study of 1146 cases of cholesteatoma, cholesteatoma was found in 13.3% of the sample with central perforation.⁷ In 2021, in a study conducted in Japan, a prevalence of 13% central perforation was reported among a total of 1,456 cases of cholesteatomas.⁸ According to the common practice by ENT specialists, cholesteatomas occur rarely with central perforation. This is a common inclination followed within Pakistan which leads to neglect of patients who present with the disease while having a central perforation. This partly is due to the evidence provided in the majority of teaching resources. However, considering the point prevalence in Japan (13/100 cases) and (8/100 cases), there is a need to update local practice guidelines. We aim to conduct this study, to determine the frequency of central perforation in patients of chronic otitis media with cholesteatoma in our regional community. This will help us to detect the current extent of the problem in the local population. An estimate can be inferred to determine the hidden cases of cholesteatoma associated with central perforation and lead to early intervention, saving patients from suffering from complications of cholesteatoma. This will help us to improve our practice.

METHODS

This cross-sectional study conducted on 175 patients of cholesteatoma with central perforation presented in the department of otorhinolaryngology and head and neck surgery, Benazir Bhutto Hospital, Rawalpindi, Pakistan. patients were inducted through non-probability, consecutive sampling. The study was carried out over a period of six months from 20-04-2022 to 19-10-2022. By using the WHO calculator, the sample size of 175 cases is calculated with 95% confidence level, 5% margin of error, and taking an expected percentage of central perforation i.e. 13% [8] in patients with chronic suppurative otitis media with cholesteatoma. The patients age 16-75 years from both genders and those presenting with chronic suppurative otitis media (as per operational definition) and Cholesteatoma detected on a computed tomography scan were included. Whereas patients with recurrent Cholesteatoma and those not willing for surgery or had dry ear (Tympanic plexus seen & middle ear mucosa normal) were excluded from the study. SPSS version 25 was used to analyze the data. Descriptive studies were used to analyze qualitative and quantitative variables. The outcome variable i.e type of perforation (central perforation/marginal/attic) was presented as a percentage of total cases of chronic suppurative otitis media with cholesteatoma. Quantitative variables like age and duration of symptoms were presented as mean and standard deviation. Qualitative variables like gender and laterality were presented through frequency and percentage. Data were stratified for age, gender, duration of symptoms, and laterality of perforation. The

post- stratification chi-square test was applied. A P-value of ≤ 0.05 was considered significant.. Outcome in both groups was measured on day 3, day 14 and day 30 of surgery. Data was analyzed by SPSS 26.0. Quantitative variables like age of the patient, GCS and Glasgow outcome scale, thickness of hematoma and midline shift on CT scan of the patients was represented in Mean \pm S.D. Qualitative variables like gender of the patients, presence or absence of complications were noted in frequencies and percentage. To observe associations between qualitative variables and to compare the means of quantitative data chi-square test and t-test was applied respectively. The results would be considered statistically significant if the p-value < 0.05 . The result was evaluated using the Glasgow result Scale, and a GOS of 4 was deemed an acceptable result.⁷³

RESULTS

The mean age of the patients included in this study was 30.1 ± 11.8 years. There were 101 males (57.7%) and 74 females (42.3%) (**Table-1**). Laterality revealed that the left side was involved in 79 patients (45.1%) and the right side was involved in 96 patients (54.9%). Perforation was found in 175 patients (100%). Central perforation was found in 16 patients (9.1%) while attic perforation in 159 (90.9%). The mean duration of the disease was 19.4 ± 11.1 months (**Table-2**).

Table 1: Showing demographic profile of the patients with CSOM

Age (Year)	Number	Percentage
16-19	33	18.9
20-44	64	64.0
≥ 45	30	17.1
Total	175	100.0
Gender	Number	Percentage
Male	101	57.7
Female	74	42.3
Total	175	100.0

Table 2: Showing tympanic membrane-related profile (Laterality, perforation, type of perforation, and duration of perforation) of the patients with CSOM

Laterality	Number	Percentage
Left	79	45.1
Right	96	54.9
Total	175	100.0
Perforation	Number	Percentage
Yes	175	100.0
No	0	0
Total	175	100.0
Type of perforation	Number	Percentage
Central	16	09.1
Attic	159	90.9
Total	175	100.0
Duration (month)	Number	Percentage
≤ 24	142	81.1
> 24	33	18.9
Total	175	100.0

Stratification for age, gender, laterality, and duration of disease was also carried out (**Tables 3**). 9.1% of the study population had central perforation which is a reasonably high

percentage as compared to local previous data and it is in concordance with the international study that states that 13% central perforation was reported among a total of 1456 cases of cholesteatoma.

. Table 3: Showing the stratification for age, gender, laterality, and duration of disease with respect to central perforation.

Age	Central Perforation		Total	p-value
	Yes	No		
16-19	1	32	33(100%)	P=0.398
20-44	12	100	112(100%)	
≥ 45	3	27	30(100%)	
Total	16	159	175(100%)	
Gender	Central Perforation		Total	p value
	Yes	No		
Male	9(8.9%)	92(91.1%)	101(100%)	P=0.901
Female	7(9.5%)	67(90.5%)	74(100%)	
Total	16(9.2%)	159(90.8%)	175(100%)	
Laterality	Central Perforation		Total	p value
	Yes	No		
Left	10(12.7%)	69(87.3%)	79(100%)	P=0.143
Right	6(6.3%)	90(93.7%)	96(100%)	
Total	16(9.2%)	159(90.8%)	175(100%)	

Duration (month)	Central Perforation		Total	p-value
	Yes	No		
≤ 24	12(8.5%)	130(91.5%)	142(100%)	P=0.510
> 24	4(12.1%)	29(87.9%)	33(100%)	
Total	16(9.2%)	159(90.8%)	175(100%)	

DISCUSSION

The Human Tympanic membrane (TM) is a thin semi- translucent, pearly white membrane that separates the middle ear from the external ear. It lies obliquely at the medial end of the external auditory meatus forming the major part of the lateral wall of the middle ear cavity. It is approximately 10 mm and 5 mm in vertical and horizontal diameter respectively. It is made of three layers; outer epithelial, middle fibrous layer composed of circular and radial fibers, and the inner layer is mucosal.⁹ The normal tympanic membrane is a translucent, gray-colored, lustrous, concave, and oval-shaped structure separating the external ear from the middle ear. It is divided into pars tensa and pars flaccida by the anterior and posterior malleolar folds.¹⁰ The tympanic membrane conducts sound waves across the middle ear and protects the middle ear cleft from infection.¹¹

Cholesteatoma has been thought to be caused by attico-antral or marginal perforation; nevertheless, its incidence in central perforations has been greatly undervalued, leading to late identificatio⁶ Cholesteatoma has traditionally been thought to be caused by attico-antral or marginal perforation; nevertheless, its incidence in central perforations has been greatly undervalued, leading to late identification ⁶. Tympanic membrane perforation may be classified based on the duration, size, and location of perforation.

Tympanic membrane perforation is acute when it is <3 months in duration, while chronic perforation when it is >3 months in duration. Classification based on the size of tympanic membrane perforation depends on the extent of perforation, and they are divided into small, medium, large, subtotal, or total perforation.^{12,13} This may also be divided into percentages that are from 1% to 100% or graded from 1 to 4. Based on the locations of the perforation on the tympanic membrane, they may be central, marginal, and attic perforation.^{14,15}

In central perforation, the perforation is within the pars tensa or with the annulus intact. However, in marginal perforation, there is the destruction of the annulus and the sulcus tympanicus. The attic perforations involve pars

flaccida and are usually associated with cholesteatoma.¹⁶ Tympanic membrane perforation occurs when there is a break in its continuity, resulting in a hole with direct communication between the external auditory canal and the middle ear cleft. This increases the potential to middle ear cleft infection with a resultant hearing impairment.¹⁷

Tympanic membrane perforation is one of the most common otological signs and symptoms encountered in most otorhinolaryngological, head, and neck practices. The prevalence of tympanic membrane central perforation in this study was 9.1%. Our findings are in agreement with the results of previous studies.^{18, 19} This high prevalence is likely due to peculiarity of developing countries like Pakistan where this study was done with a high incidence of malnutrition, overcrowding, frequent upper respiratory tract infections, poverty, and ignorance.^{20,21}

Another study carried out by Komori et al⁸, demonstrated the frequency of tympanic membrane central perforation at 13%. There was male preponderance over females in this study. Men are a highly adventurous group, more prone to injuries, and exposed to infection in their day- to-day activities. This is close to the results of earlier studies.¹⁸ Other studies showed a contrary trend in their record.²² There is a paucity of literature on the perforation of the tympanic membrane in developing countries like Pakistan.

CONCLUSION

In conclusion, my study signifies that ENT surgeons have to have high suspicion index for cholesteatoma in patients with central perforation. The central perforation of the tympanic membrane in patients of chronic suppurative otitis media was found common in young males, especially in 3rd decade of life.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

Financial Support:

None to disclose

Contribution:

Conceptualization: A.H.A, N.A

Data curation: N.A, N.R

Formal analysis: A.H.A, N.A

Writing and editing: N.A, N.R

Project administration: N.A

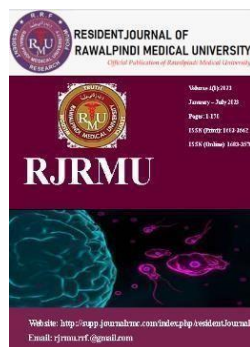
Review and approval: A.H.A, N.R

Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Role of Pre-Incisional Peritonsillar Infiltration of Adrenaline and Normal Saline in Terms of Mean Per-Operative Blood Loss During Tonsillectomy.

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ABSTRACT

Introduction Tonsillectomy is a routine surgery with a minimal risk. Techniques for tonsillectomy are constantly evolving. Hemorrhage is the most prevalent, albeit sporadic, significant life-threatening complication following tonsillectomy, despite the development of contemporary methods to prevent it. To compare mean per-operative blood loss during tonsillectomy between pre-incisional peritonsillar infiltration of Adrenaline and Normal Saline in terms of reduction in mean per-operative blood loss.

Research design and methods It is a double-blind control trial conducted in the department of otorhinolaryngology and head and neck surgery of Benazir Bhutto Hospital, Rawalpindi, from 22-8-2022 to 22-7-2023.

The operation theater nurse prepared identical syringes of Normal Saline and 1:200,000 Adrenaline solution and coded them. The trial was undertaken in a double-blind manner, neither patient nor surgeon was aware which drug has been injected on which side. A total of 60 patients were involved and 30 patients in each group.

Analysis was carried out by using SPSS V. 25 and a P-value of less than 0.05 was taken as significant.

Result The age range of the patients in our inclusion criteria was 6-18 years. The mean age of the patients who took part in our study was 11.7 ± 3.4 years. There were 35 males (58.3%) while 25 patients were females (41.7%). The mean weight of the patients was 35.5 ± 7.6 kg. Out of 60 patients, 24 belonged to ASA grade-I and 36 patients had ASA grade-II. Tonsil size according to the Brodsky grading scale was

in 33 patients (55%) while 27 patients (45%) were having tonsil size 3-4. The mean per-operative blood loss was calculated to be

41.0 ± 10.4 and 86.4 ± 11.3 in adrenaline and normal saline, respectively. The difference between the two groups was statistically significant ($p < 0.001$).

Conclusion In conclusion, peritonsillar infiltration of adrenaline had a significant reduction in per-operative blood loss when compared to normal saline group ($p < 0.001$).

INTRODUCTION

Tonsillectomy is the complete surgical removal of palatine tonsils including its capsule, by dissecting the peritonsillar space between the tonsil capsule and the muscular wall.¹ It is one of the most frequently performed surgeries in the field of otorhinolaryngology worldwide dating back to 3000 years ago.² In 1917, Crowe- Davis laid the foundation of cold knife dissection tonsillectomy; the art of tonsil surgery has been evolving ever since. Novel techniques like Argon plasma coagulation, CO2 laser, Nd YAG laser, bipolar diathermy scissors, and harmonic scalpel have been introduced to reduce complications during tonsillectomy. However, the conventional cold knife method is being favored worldwide due to its low-cost and morbidity rate.³ Hemorrhage is a frequent but potentially life-threatening complication of tonsillectomy.⁴ Electrocautery, sutures, chemicals like Adrenaline Feracrylum, and biomaterials like Bismuth Subgallate, fibrin, gelatin, and cellulose have been experimented with to reduce it. However, a low-cost, readily available, easily applied, effective strategy to prevent hemorrhage during tonsillectomy remains elusive. In 2013, a study in Nigeria introduced pre-incisional peritonsillar infiltration of Adrenaline as a simple and cost-effective modification of conventional cold tonsillectomy, which was successful in reducing hemorrhage during

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tonsillectomy with average blood loss of <10 mL by using 5mL 1;200,000 adrenalin.⁵ This technique involves pre-incisional peritonsillar infiltration of Adrenaline leading to the delineation of the pericapsular plane and hydro-dissection of areolar tissue resulting in decreased blood loss. Vasoconstrictive effect of adrenaline on α -adrenergic receptors further decreases bleeding. Another similar study was done in 2017 which compared 3 mL of 2% Lignocaine+1; 100,000 Adrenaline peritonsillar infiltration with 3 mL Normal Saline and showed average blood loss of 39.44 ± 2.62 mL and 86.9 ± 9.28 mL respectively.⁶ These studies compared the effect of adrenaline and normal saline on different individuals but the amount of blood lost during tonsillectomy varies with an individual's age, gender, weight, hemoglobin level, coagulation profile, and pre-operative use of antibiotics. Given the magnitude of morbidity associated with hemorrhage during tonsillectomy, I have designed a study to compare pre-incisional peritonsillar infiltration of Adrenaline and Normal Saline (placebo) in terms of mean operative blood loss during tonsillectomy in the same patient. Since age, gender, weight, tonsillar size, and character will be the same in each patient, the effect of both drugs will be evaluated more accurately. Moreover, $2\mu\text{g/kg}$ of patient's body weight low dose Adrenaline 1;200,000 will be used instead of a fixed amount of 1;100,000 Adrenaline used in the above-mentioned studies as it has been reported to have equal Vasoconstrictive efficacy and lower adverse effects on heart rate, and Mean Arterial Pressure.⁷ By decreasing per-operative blood loss during tonsillectomy using this technique, life-threatening complications like cerebral hypoxia, aspiration, hypotensive shock and asphyxia will be avoided.

Objective of the study is to compare pre-incisional peritonsillar infiltration of Adrenaline and Normal Saline in terms of mean per-operative blood loss during tonsillectomy.

METHODS

The study conducted was double-blinded randomized clinical trial conducted in the department of otorhinolaryngology and head and neck surgery of Benazir Bhutto Hospital, Rawalpindi. The Study was done over a period of six months from 22-08- 2022 to 22-07-2023. Patients were chosen through convenience, non-probability sampling technique. Total sample size was 60 which was determined through the open EPI calculator at level of significance 5% and the power of test $(1-\beta)$ 95%. Population mean blood loss in Adrenaline group \pm S.D = $39.44 \pm 2.62.6$ Population means blood loss in Normal Saline group \pm S.D.= 86.9 ± 9.28 .⁶ Patient of age of 6-18 years from both genders which were diagnosed case of recurrent tonsillitis admitted for bilateral elective tonsillectomy under general anesthesia or patients with ASA grade I-II¹⁰ were included in this study. The potential patients that can be subjected to this study having co- morbidities (cardiovascular, hematological, pulmonary, hepatic or, renal disorders) or having the history of heparin, warfarin or, any-other anticoagulant use were excluded. Also patients having gross asymmetry in the size of both tonsils, history of unilateral

peritonsillar abscess or patients undergoing adenoidectomy with tonsillectomy were excluded. All data were entered in SPSS version 23 for Windows. Descriptive statistics were used to analyze qualitative and quantitative variables. Qualitative variables including gender, ASA grade, and tonsil grade were represented by frequency and percentage. For quantitative variables including age, weight, and amount of blood loss Mean

\pm Standard Deviation was calculated. To compare the amount of blood loss between the adrenaline-injected side and the Normal Saline-injected side, the independent sample's t-test was applied at 5% level of significance. Hence, age, gender, weight, and tonsillar size were same in each patient. Effect modifiers like age, gender, and weight were controlled by stratification. A post-stratification student t-test was applied. P-value ≤ 0.05 was taken as significant.

RESULTS

A total of 60 cases were enrolled in this study. Adrenaline was injected to the right side if the last digit of the number was even and vice versa.

Age range of the patients was 6-18 years. Mean age of the patients was 11.7 ± 3.4 years. There were 35 males (58.3%) while 25 females (41.7%). Mean weight of the patients was 35.5 ± 7.6 kg. According to Brodsky grading scale for tonsil size, 33 patients (55%) were having tonsil size 1 -2 while 27 patients (45%) were having tonsil size 3 -4 (**Table-1**). Out of 60 patients, 24 belonged to ASA grade-I and 36 patients belonged to ASA grade-II (**Table-2**). Mean per-operative blood loss was found to be 41.0 ± 10.4 mL and 86.4 ± 11.3 mL in adrenaline and normal saline, respectively. The difference between two groups was statistically significant ($p < 0.001$) (**Table-3**). Stratification for age, gender and weight was also carried out (**Tables-4**).

Table 1: Distribution of patients by tonsil size according to the Brodsky grading scale

Tonsil size	Number	Percentage
1-2	33	55.0
3-4	27	45.0
Total	60	100.0

Table-2: Demographic Distribution of Patients.

Age (Year)	Number	Percentage
6-10	26	43.3
11-18	34	56.7
Total	60	100.0
Gender	Number	Percentage
Male	35	58.3
Female	25	41.7
Total	60	100.0
Weight	Number	Percentage
≤ 30	18	30.0
> 30	42	70.0
Total	60	100.0
ASA grade	Number	Percentage
Grade I	24	58.3
Grade II	36	41.7
Total	60	100.0

Table 3: Comparison of Per-operative blood loss (mL)

Group	Blood Loss		P value
	Mean	S.D	
Adrenaline	41.0	10.4	P<0.001
Normal saline	86.4	11.3	

Table 4: Stratification of age, gender, weight with regard to per-operative blood loss (mL)

Age (Year)	Group	Blood Loss (mL)		P-value
		Mean	S.D	
6-10	Adrenaline	43.3	11.8	P<0.001
	Normal saline	84.7	9.5	
11-18	Adrenaline	39.3	8.8	P<0.001
	Normal saline	87.7	12.5	

Weight (Kg)	Group	Blood Loss (mL)		P value
		Mean	S.D	
≤ 30	Adrenaline	41.6	11.8	P<0.001
	Normal saline	84.0	10.3	
> 30	Adrenaline	40.8	9.8	P<0.001
	Normal saline	87.4	11.7	

Gender	Group	Blood Loss (mL)		P-value
		Mean	S.D	
Male	Adrenaline	44.1	8.6	P<0.001
	Normal saline	86.1	11.6	
Female	Adrenaline	36.8	11.2	P<0.001
	Normal saline	86.8	11.2	

DISCUSSION

Although tonsillectomy is one of the most commonly performed surgeries, a review of the literature reveals only a few articles dealing with the study of intraoperative blood loss in tonsillectomy and adenotonsillectomy, and the factors influencing it. Estimation of blood loss during tonsillectomy is difficult but important especially in patients who cannot tolerate blood loss, e.g., children, patients with anemia or factor VIII deficiency, and patients receiving anticoagulant therapy. Also, in children the normal physiological mechanisms are less adaptable to a rapid blood loss, and breakdown of these compensatory mechanisms may be initiated by a smaller loss than in adults.⁸

There are many proven methods of tonsillectomy that include cold-knife dissection, LASER, guillotine, snare with suture, suction cautery, hot-knife dissection, microdissection, bipolar and unipolar Electrocautery, and most recently described bipolar electrosurgical scissors.⁹ Though surgeons are trying newer and more effective methods, the cold knife technique has remained the standard procedure for many years. To measure operative blood loss accurately and continuously is difficult especially in adenotonsillectomy. Several methods of estimation such as the calorimetric method of estimation (swab weighing technique), repeated volume determination, weighing the patient etc, are based on different principles.⁸ In current study amount of blood loss was calculated using the Gravimetric method.¹⁰

In the present study, a total of 60 patients were included. The mean age of these patients was 11.7 ± 3.4 years with an age range from 6 to 18 years. The peak incidence was observed in the age group 11 to 18 years. A study by Moonka regarding tonsillectomy described the most common incidence of tonsillectomies in the age group 11 to 20 years.¹¹ The sample size of Moonka study was large ($n=376$) as compared to our study patients where 60 patients were included. Another study carried out by Adel and Ahmed in Iraq also reported the

occurrence of tonsillectomies in the age group 15 to 20 years ($n=250$).¹² In the present study, males were the predominant gender. A study done by Beigh et al in Iran also reported the domination of males.¹³ Adoga and Okeke in their study demonstrated male predominance.¹⁴

In our study, mean peroperative blood loss was found to be 41.0 ± 10.4 and 86.4 ± 11.3 in adrenaline and normal saline, respectively. The difference between two groups was statistically significant ($p < 0.001$). Our findings are consistent with a study conducted by Junaid et al.⁶ Prasad et al, pretreated patients, undergoing tonsillectomy, with antibiotics and reported that the average blood loss in 46 patients who received antibiotics was 80.75 ml whereas in the other group of 54 patients who had not received the antibiotics the average blood loss was 97.06 ml.⁸ In the current study, the mean per-operative blood loss in males of the Adrenaline group was 44.1 ± 8.6 ml and in females, it was 36.8 ± 11.2 ml while in normal saline group the blood loss was found to be 86.1 ± 11.6 ml in males and 86.8 ± 11.2 ml in females. The blood loss in males and females of both groups was statistically significant ($p < 0.001$). Similar to our results, Broadman et al have demonstrated the benefits of using peritonsillar infiltration with adrenaline and concluded that infiltrations should be performed with either normal saline containing or plain Adrenaline.¹⁵

CONCLUSION

In conclusion, peritonsillar infiltration of adrenaline had a significant reduction in per-operative blood loss when compared to normal saline group ($p < 0.001$). Furthermore, the per-operative blood loss in both age groups 6 to 10 and 11-18 years was statistically significant ($p < 0.001$). Considering the life-threatening potential of intraoperative blood loss, it is recommended that patients, undergoing tonsillectomy should be injected with adrenaline, immediately before surgery, to minimize the rate of intraoperative blood loss.

Conflict of interest:

All authors have declared that they have no conflict of interest to disclose.

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Contribution:

Conceptualization: Z.S, A.H.A

Data curation: M.A, A.A.J

Formal analysis: N.R, Z.S

Writing and editing: A.H.A, N.R, Z.S

Project administration: Z.S

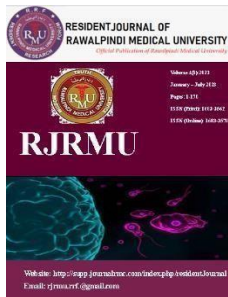
Review and approval: M.A, A.H.A

Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Case Report: Unilateral Perisylvian Polymicrogyria Syndrome

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ABSTRACT

Perisylvian polymicrogyria syndrome is a rare congenital neurological condition due to defective cortical development. It is one of the syndromes associated with polymicrogyria and may be bilateral or unilateral (the latter being rarer than the former with only a handful of cases reported to date). We report a case of a 16 years old male from Pakistan who presented with recent episodic loss of consciousness, with a background history of long-standing seizures, developmental delay, and body weakness. MR brain of the patient depicted a right-sided widened Sylvian fissure, perisylvian cortical thickening, and polymicrogyria. The findings were consistent with the diagnosis of unilateral perisylvian polymicrogyria syndrome.

INTRODUCTION

Polymicrogyria syndromes are a well- established cause of medically refractory seizures. Depending on the site of cortical involvement, these syndromes present with a spectrum of associated neurological disorders; including (but not limited to) oromotor paralysis and cognitive impairment. Two forms of the perisylvian polymicrogyria syndrome have been described, based on whether one or both of the perisylvian regions are affected. Bilateral abnormalities are more common than their unilateral counterpart. Bilateral cases present with pseudobulbar palsy while unilateral cases present with contralateral hemiparesis.¹ Although there have been various articles published on the bilateral form of the disease, only a handful of cases of unilateral disease have been reported worldwide. No such case has previously been documented from Pakistan. We present a rare case of unilateral polymicrogyria syndrome of a young boy who presented with epilepsy, hemiplegia, and a recent episode of short- interval loss of consciousness.

CASE REPORT

A 16-year-old boy from Skardu presented to OPD with two episodes of loss of consciousness and a seven-year history of refractory generalized tonic-clonic seizures and left-sided body weakness.

On physical examination, his left plantar was upgoing indicating a positive Babinski sign. The power in both the left upper and left lower limbs was 3/5 (reduced), while on the right-side power was 5/5. Apart from mildly elevated serum alkaline phosphatase levels (162 U/L), all lab investigations at the time of presentation were unremarkable. Past medical history revealed that he was on tablet Tegral 200mg TDS. The provided birth history did not suggest any perinatal complications, overt hypoxic-ischemic insult, or hospital admission. Developmentally, the child had delayed milestones and impaired speech.

His MRI brain (epilepsy protocol) showed a widening of the right-sided perisylvian fissure, along with cortical thickening and an increased number of gyri in the right perisylvian area consistent with polymicrogyria. The left perisylvian fissure and adjacent cerebral cortex were unremarkable. The imaging findings, in the context of the given clinical history, were in favor of the diagnosis of Perisylvian Polymicrogyria Syndrome.

DISCUSSION

Polymicrogyria (PMG) is a formational abnormality of the cerebral cortex after defective neuronal migration and development. It results in an increased number and decreased size of gyri separated by shallow sulci, resulting in a characteristic appearance at the cortex and grey-white matter junction.² Cortical malformation defects may be caused by interruption of the normal developmental stages due to the absence of normal gene expression, the creation of an abnormal gene, or the malfunction of a gene due to external factors such as infection or ischemia.³ In the past, the diagnosis of polymicrogyria was often missed due to imaging limitations and it was often confounded

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with pachygyria and schizencephalic clefts. However recent radiological advances have aided the diagnosis and classification of this relatively common abnormality.⁴ Thin section MR imaging is a reliable tool for diagnosis, with the best determination on sagittal images in comparison with axial images, where different angulations may result in erroneous reporting.⁵ Polymicrogyria has various patterns including focal, multifocal, or diffuse, and it may be unilateral or bilateral. Although the exact incidence of PMG is unknown, it is one of the most common congenital cortical defects and an established cause of medically refractory

epilepsy. The commonest cerebral locations are the insula and the perisylvian cortex.⁶ Both the unilateral and bilateral perisylvian form of the disease have similar radiological features with differences confined to laterality. However clinically, the presentation of bilateral type is dominated by suprabulbar signs and more severe mental retardation and epilepsy.⁷ The involvement of bilateral hemispheres or more than half of a single hemisphere indicates poor prognosis and severe motor and developmental impairment.⁸ Congenital unilateral perisylvian polymicrogyria (CUPP) presents with hemiplegia and pyramidal tract dysfunction contralateral to the side of the cortical malformation. Delayed cognitive development and seizures may commonly be associated.⁹

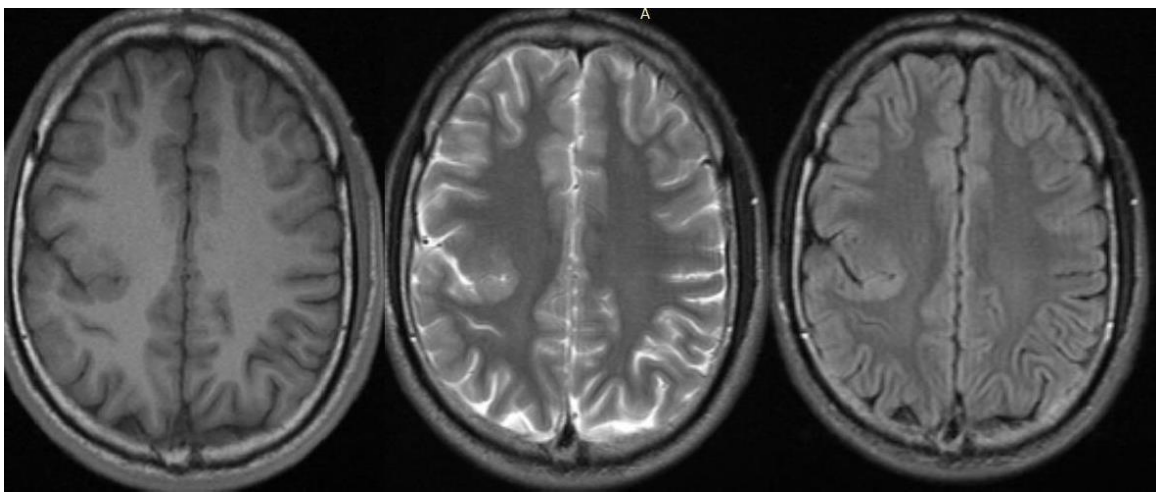


Figure 1: MRI brain axial T1WI (a), T2WI (b) and FLAIR (c) sequences showing irregular and uneven polymicrogyria along the right sylvian fissure.

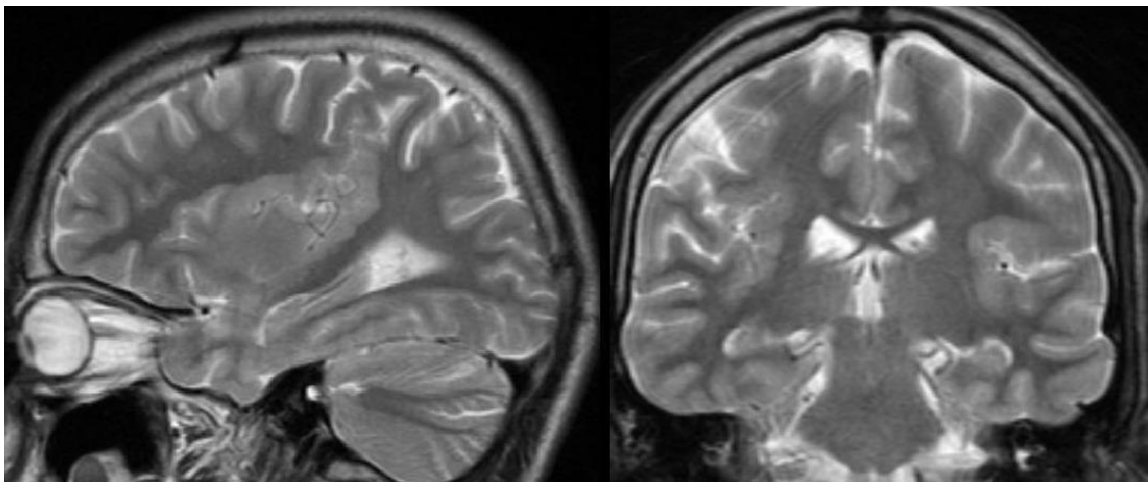


Figure 2: MRI brain T2WI Sagittal (a) and T2WI Coronal (b) images showing the presence of irregular lumpy polymicrogyria along the right perisylvian region.

CONCLUSION

We reported the case of an adolescent male who presented with established epilepsy, hemiplegia, and two recent episodes of loss of consciousness. Although cerebral polymicrogyria is commonly associated with seizures and the perisylvian region is the most common site of this structural defect, the unilateral form is extremely rare. Early and prompt diagnosis can save the patient from a myriad of unnecessary diagnostic tests and hospital visits, where the cause of epilepsy has not been established.

Conflict of interest:

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Contribution:

Conceptualization: S.S, A.I.S

Data curation: A.I.S

Formal analysis: S.S

Writing and editing: S.S, A.I.S

Project administration: S.S

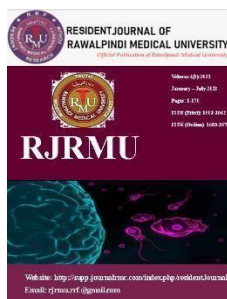
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Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Intra Ventricular Aspergilloma Presenting with Hydrocephalus in Immunocompetent Patient: A Case Report

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ABSTRACT

Introduction CNS Fungal infections are opportunistic Infections that may be mistaken for another differential diagnosis in immunocompetent patients. Most are diagnosed on biopsy of mass lesions and culture of CSF/excised tissue. Antifungal medications such as amphotericin B and voriconazole show promising results in management.

Case Report A young male presented with a history of frontoparietal headache, fever, and projectile vomiting. He had B/L papilledema. MRI showed non communicating hydrocephalus, supra sellar lesion and a hypo- intense lesion in the third ventricle. An endoscopic biopsy of the lesion was done. Histopathology showed aspergillus species. The patient was treated with voriconazole. On a 4-month follow-up, the patient is stable and symptom-free.

Conclusion CNS aspergillosis is rare and may present with a variety of symptoms mimicking cerebral tumors, meningitis, or abscess. A high index of suspicion and timely biopsy/culture is required for optimal management.

INTRODUCTION

Fungal infections usually present as opportunistic infections in immunocompromised patients, however, they can rarely present in immunocompetent patients. Therefore in the CNS, they are usually mistaken for other differentials such as tumors, tuberculous meningitis, and brain abscess. One of the rare causes of CNS fungal infections is Aspergillosis caused by Aspergillus species (most commonly by Aspergillus fumigatus).¹ Aspergillus spores are inhaled by the host and are spread to the CNS either by paranasal sinus or direct hematogenous spread.² These spores germinate hyphae at body temperature in

immunocompromised patients. In immunocompetent patients, the hyphae are killed by the activation of neutrophils.³ CNS fungal infections usually present with meningitis, abscess or granuloma, vascular invasion with thrombosis, infarction and hemorrhage, and aneurysm formation. Most cases are managed with antifungal medication such as Amphotericin B, voriconazole, itraconazole, and flucytosine.⁴

We present a rare case of a young immunocompetent male presenting with communicating hydrocephalus secondary to aspergillosis.

CASE REPORT

A 25-year-old male, an automobile mechanic by profession, presented in the emergency of DHQ Hospital Rawalpindi with complaints of on-and-off headaches for the past 2 months. Fever and vomiting for the last 15 days. Headache was sudden in onset, increases during exertion, with the frequency of 2 to 3 times per week, lasting for one to two hours, severe in intensity, mostly in the frontoparietal region, non-radiating relieved by over-the-counter analgesics, associated with vomiting for last 15 days.

Vomiting was projectile in nature, mostly containing food particles, with two to three episodes per day. The patient also complained of fever for the last 15 days which was undocumented with no diurnal variation. There was no history of diabetes mellitus, steroid intake, or any other immunocompromised state. On examination, the patient had GCS 14/15, pupils B/L reactive, visual field normal in both eyes, all cranial nerves intact, moving all limbs. Systemic examination was unremarkable. Fundoscopy showed grade 3 papilla edema. His CT scan showed communicating Hydrocephalus. MRI showed communicating Hydrocephalus, and mild frontal sinusitis along with suspicion of a hyperintense lesion within the suprasellar region extending into the floor of the

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third ventricle on T1WI and mixed intensity lesion in the suprasellar region with hypointense lesion within the third ventricle on T2WI (**Figure 1,2**). The patient was admitted to the neurosurgery department, DHQ, and an endoscopic third ventriculostomy along with a biopsy of the third ventricle mass was performed. Biopsy report showed fungal hyphae consistent with aspergillus species. Patient remained well post operatively and started oral voriconazole after consultation from infectious department of Holy Family Hospital and discharged at 5th post operative day on oral voriconazole. Patient remained well on 2 weeks OPD follow up but again presented after 3 weeks with meningitis. LP was performed and CSF R/E and C/S done which were consistent with fungal meningitis. Patient then managed on IV amphotericin B for 1 week along with oral voriconazole and ventriculoperitoneal shunting was done, after CSF was clear of fungal meningitis. Post shunting scan was done which showed normal sized ventricles (**Figure 3**)

Patient was again discharged on oral voriconazole and remained on regular OPD follow ups for 4 months which showed no further deterioration in patient. On each follow up patient was examined for complications of CNS aspergillosis such as brain abscess, meningitis, sinus thrombosis etc.

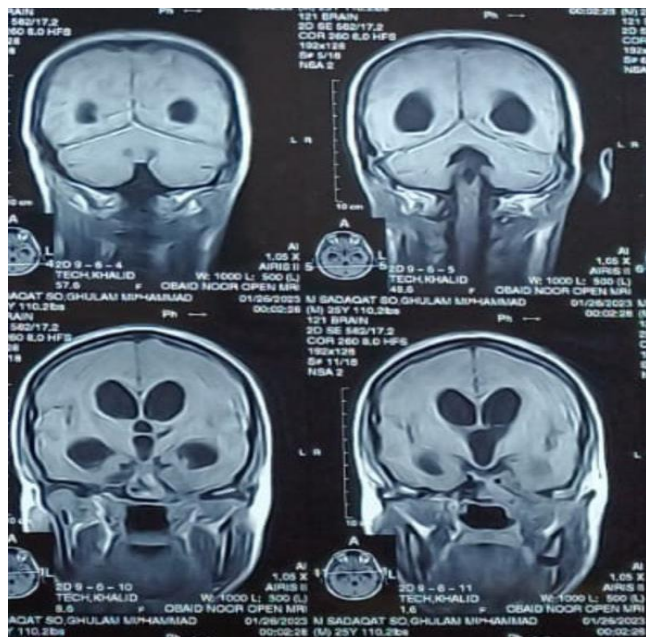


Figure 1. T1 diffusion-weighted MRI showing hypo to hyper intense supra sellar lesion.

DISCUSSION

Cerebral aspergillosis is rare in immunocompetent patients. However, when it does occur, it is usually due to infection spread from tissues adjacent to the brain such as prolonged sinusitis, as was the case in our patient. It can also occur after cerebral or cardiac surgery or lumbar puncture. It is more common in patients with diabetes mellitus.⁵⁻⁸ Aspergilloma commonly occurs in frontal region followed by para-sellar region. In immunocompetent patients, CNS aspergillosis forms granulomas due to immune response.⁹ Amphotericin B and voriconazole are commonly used in the treatment of aspergillosis but voriconazole has superiority over amphotericin B as it shows better penetration in CSF.¹⁰ A similar case of a young male with right frontal aspergilloma was reported in Iran, that presented with lower limb weakness. It was successfully managed with craniotomy and complete excision of the mass, followed by voriconazole treatment for 3 months.⁹ Our case is a very rare presentation of aspergillosis as patient had communicating hydrocephalus and intra ventricular aspergilloma. Very few such cases have been reported in the literature.

CONCLUSION

CNS aspergillosis is a rare and may present with a variety of symptoms mimicking cerebral tumors, meningitis or abscess. A high index of suspicion and timely biopsy/culture is required for optimal management.

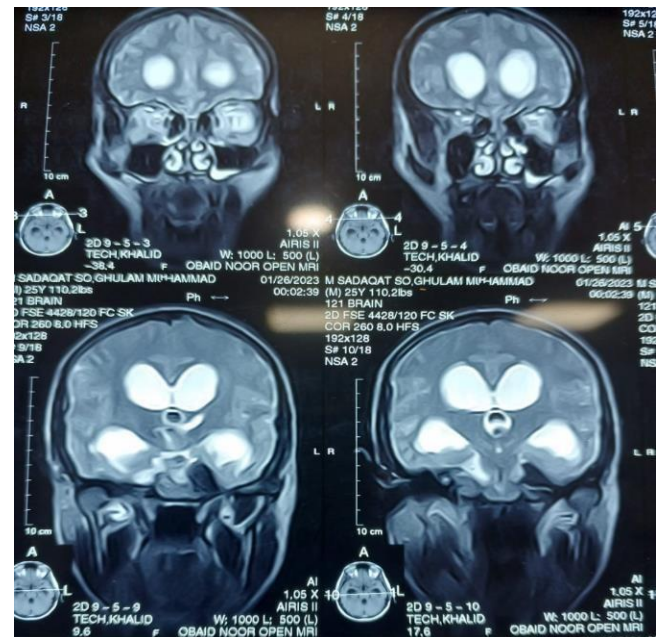


Figure 2. T2 diffusion weighted MRI showing hypo intense lesion in 3rd ventricle.

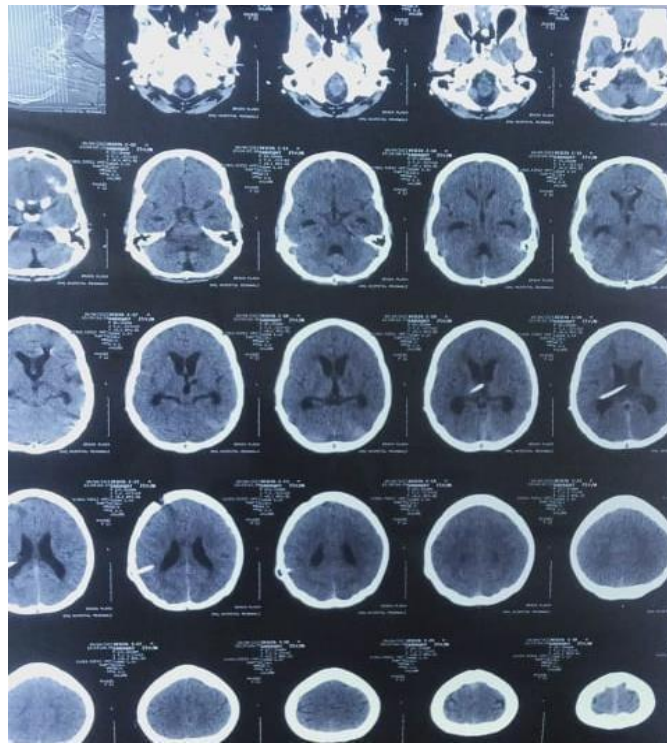


Figure 3: Post op CT scan showing normal size ventricles.

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Contribution:

Conceptualization: H.A.F, Q.A.Y

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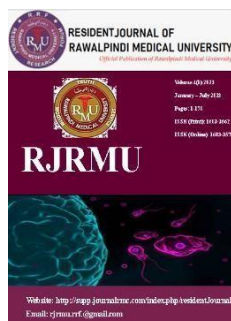
Review and approval: H.A.F, N.A

Availability of data and materials:

All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Role of Inferior Vena Cava Diameter (IVCd) and Inferior Vena Cava Collapsibility Index (IVCc) in Determining Adequacy of Fluid Resuscitation in Dengue Patients: One Step Forward Towards Dengue Management

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INTRODUCTION

Dengue is defined as an acute febrile disease caused by the bite of mosquito named *Aedes aegypti* which acts as a vector in transmission of Dengue viruses (DENVs), consisting of four serotypes (DENV 1-4) and belonging to family *flaviviridae* and genus *flavivirus*.¹ All four DENV serotypes have emerged from sylvatic strains in the forests of South-East Asia. DENV is the most common cause of arboviral disease throughout the globe, affecting through all its four strains (DENV 1-4). According to world health organisation (WHO), the number of cases of dengue is on the rise from last two decades, as 505,430 cases in 2000, to over 2.4 million in 2010, and 5.2 million in 2019 with more prevalence in young population.² DENV covers a spectrum of diseases, ranging from simple dengue fever to haemorrhage and shock with incubation period of 4-10 days.

The laboratory evaluation represents the presence of thrombocytopenia, lymphopenia, raised haematocrit, and elevated aspartate aminotransferase levels.³ The signs and symptoms of DENV vary between fever, nausea, vomiting, arthralgia, myalgias, abdominal ascites, pleural effusion, rising haematocrit, and narrow or absent pulse pressure, depending upon the type of dengue: dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS).⁴ Two pathological mechanisms associated with severe form of dengue are plasma leakage and haemorrhage leading to hypovolemia shock and death if not treated with aggressive approach. The fluid management is of paramount importance in acute management of DSS that have greater impact on future outcomes and overall survival (OS) of the patients having DSS.⁵

The choice of fluid regimens is of greater importance in treatment of DSS. Several randomised controlled trials have been conducted to determine the choice of fluid in DSS, however; the crystalloids solutions such as 0.9% saline and ringer lactate are most commonly administered fluids being studied in management of dengue. The role of colloids can be evaluated in severe cases of DSS due to greater osmotic effects, but they are also associated with significant adverse events limiting their utilization in management of dengue.⁶ The assessment adequacy of fluid resuscitation become more valuable in order to avoid fluid overload and related complications. The serial measurements of haematocrit reflect the balance between fluid therapy adequacy and ongoing plasma leakage.

Central Venous Assessment (CVA) through 2D ultrasonography using inferior vena cava (IVC) parameters like inferior vena cava diameter (IVCd) and inferior vena cava collapsibility index (IVCc) can be used as valuable adjunct to serial haematocrit measurements in assessment of fluid resuscitation adequacy in patients with DSS.⁷ The IVCd is measured for 20 seconds of spontaneous breathing at 2-3 cm from junction of IVC and right atrium. The maximum IVCd (IVCdmax) is measured at end expiratory phase and in the same vein, the minimum IVCd (IVCdmin) is measured at end-inspiratory phase. The IVCc index is measure of difference between IVCd max and IVCd min divided by IVCd min, $[IVCdmax - IVCdmin] / IVCdmax \times 100$ and expressed as percentage.⁸ A normal IVCd is measured as less than 1.7cm and normal IVCc is valued as 30% in normal healthy individuals.

According to inferior vena cava parameters

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(IVCd, IVCc), hypovolemic shock is defined as IVCd of less than 1.5cm and IVCc of greater than 50%.⁹ According to a study by Thanachartwet et al. the IVCd become less than 1.5cm and IVCc index increased above 50% in patients with DSS, when measured at day 4 and 5 validating the state of hypovolemia in DSS.¹⁰

RECOMMENDATIONS

In the highlight of literature, the utilization of IVCd and IVCc should be now implemented in valued guidelines for fluid resuscitation and management in patients with DSS. Its should be the standard practice now to evaluate the inferior vena cava parameters along with serial measurements of haematocrit to determine the fluid resuscitation adequacy. Measuring inferior vena cava parameters is a non-invasive technique that can be achieved easily through 2D USG and at very cost-effective way.

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Conceptualization: A.J

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Writing and editing: A.R, A.J

Project administration: S.M, M.S.A

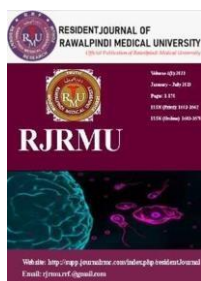
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Role of Artificial Intelligence In Advancement of Medicine

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INTRODUCTION

In recent era, Artificial Intelligence has made a remarkable progress in analysing the Sensory Data that allowed the machine in interpreting the complex data more efficiently ¹. Artificial intelligence as a machine learning tool is now being used in analysing medical data and creating a new gateway to help and improve healthcare services. Besides this, Machine learning algorithms and other AI powered software are now used in helping the professionals in hospital and community-based research.

As of now, Machine Learning is helping in making clinical decisions, and with that medical imaging is an important role where AI has been given some important role, as being used in analysing different diagnostic and radiological scans like CT, MRI, and X-Rays ². Some of the decision-making tools are helping professionals in making treatment and medication decisions that are increasing the efficiency of the healthcare system and improving little error- making possibilities. While Covid-19 as a pandemic has been a major disruption globally, especially in introducing new means of technology to help the overall economic system, it has also led the healthcare system to introduce new means of monitoring patient care by introducing AI-related tools that are efficiently monitoring the patients. As in Diagnostic Radiology, AI has been a major disruptor where different oncological issues are being identified using AI-based tools to detect the disease earlier ². For instance, Lung Cancer is one of the deadly tumors, and using AI-based screening tools is now a way to detect any lung-based nodule that can be potentially cancerous and automatically identify them as benign or malignant ³. Another example is colonic polyps which are usually undiagnosed or misdiagnosed and are a potential cause of Colorectal Carcinoma. Using the AI-based

screening tool is crucial in detecting the issue and being treated. And this AI-based screening technology can be used in identifying any other carcinoma from Breast to Brain Tumors as well ⁴.

In other diagnostic subjects, for instance in Histopathology where the traditional approach to detecting any biopsy sample and accurately diagnosing the problem has required certain knowledge at the morphological, cellular, and genetical level and this whole data has been well read by the AI to diagnose any tumor more accurately than a human being ⁵. With that modern approach is being made using the AI tool to accurately take a biopsy sample, and create a slide with certain stain required to detect the issue in a more accurate way with little error ⁶.

With the arrival of Deep machine learning, it has become easier to identify any gene sequence for a certain variant of the disease ⁷. An example of Clinical medicine, where AI is being used in an efficient way is Dermatology. Certain skin-related issues including skin cancer are carrying certain physical aspects like depth, color, width, and texture, and all these features being used more accurately by the Machine Learning tool are increasing the efficiency to detect any skin-related issue ⁸.

Creating a drug is a costly and time-consuming process. With the advent of Quantum Computing with AI, it has been easier to test any molecular structure of a drug quicker than ever. With that, a better molecular design of a drug using AI has made it easier today to bring a better drug. This new revolution is what mankind witnessed during the Covid-19 pandemic when the need for a Covid-19 vaccine led the drug manufacturing industry to use this AI-based tool and create a vaccine more quickly ⁹. The way things are moving forward there is little to no doubt that AI will eventually shape and carry many of the

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Healthcare tasks and increase the overall efficiency of the healthcare system. Where most of the equipment's in patient care are being used to monitor a patient such a data is being used to by the Artificial Intelligence to early detect the reasonof any harmful event, like sepsis or any cardiovascular events.¹⁰

RECOMMENDATIONS

Artificial Intelligence is progressing in a way where it is moving the humanity to the next era of Industrial Revolution and the need of human based approach in the profession is decreasing. We need to equip the profession with this new knowledge and create the awareness that can be helpful to the profession and also in the progression of the healthcare.

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Conceptualization: S.M.S

Data curation: S.M.S, T.F

Formal analysis: M.S.A, S.M.S

Writing and editing: S.M.S, T.F

Project administration: S.M.S, M.S.A

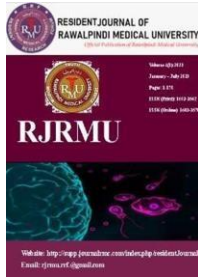
Review and approval: S.M, T.F

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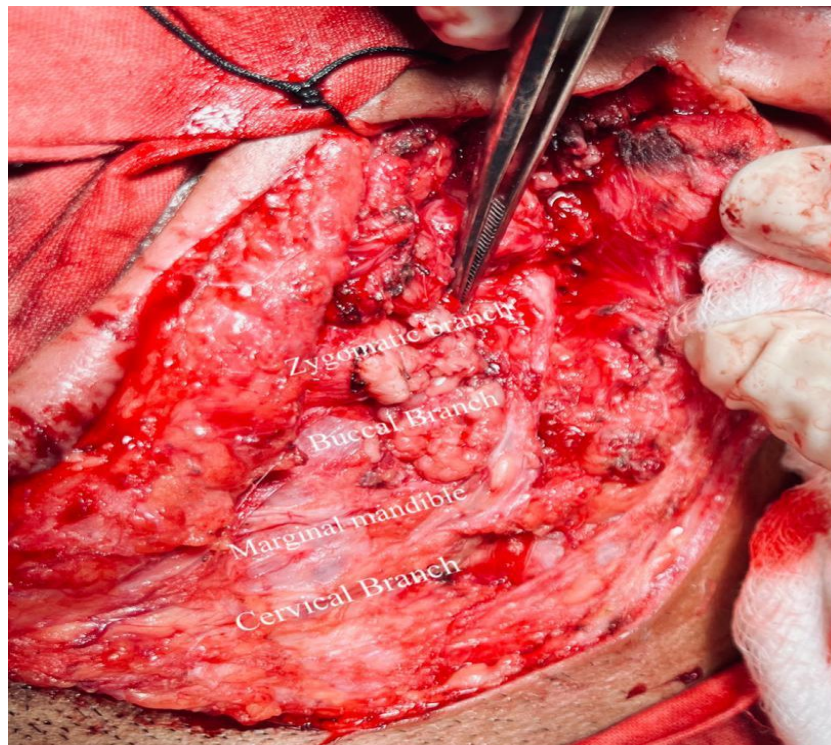
All the data generated or analyzed during this study are included in this manuscript, and can be made available on suitable request.

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Parotid Gland with Fascial Nerve Branches



A case of superficial Parotidectomy performed at Department of Otolaryngology and head and neck surgery, Benazir Bhutto Hospital Rawalpindi. In this picture, all branches of facial nerve passing through parotid gland are wonderfully delineated and highlighted.