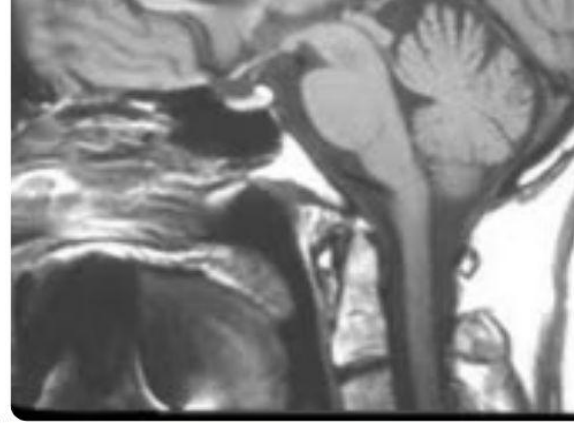




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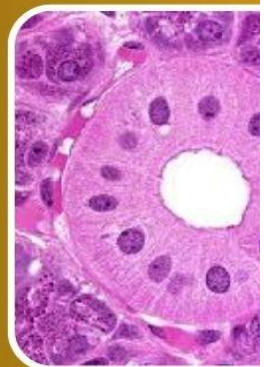
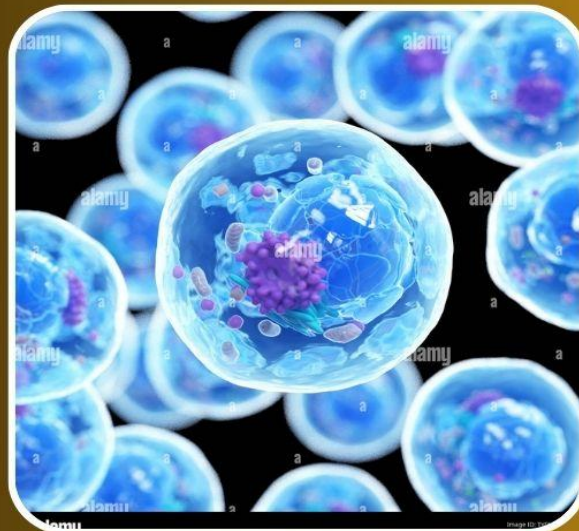
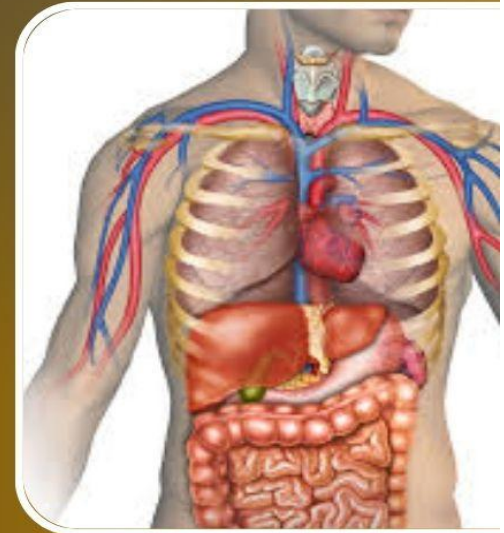
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## Editorial

# ARE RANDOMIZED CONTROLLED TRIALS AS GOLD STRANDARD FOR HIGH LEVEL EVIDENCE A PRAGMATIC APPROACH IN THE ERA OF PRECISION MEDICINE AND REAL-WORLD EVIDENCE

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## ABSTRACT:

Randomized controlled trials (RCTs) have been considered as the gold standard for evaluating medical interventions due to their robust methodology, limited introduction of bias, and strength in establishing strong evidence to show better effect of a treatment option. However, the evolving landscape of healthcare—marked by precision medicine, digital health technologies, and expanding access to real-world data—has exposed important limitations in the traditional dominance of RCTs. These include issues of generalizability, cost, ethical constraints, and limited applicability in heterogeneous patient populations, particularly in low- and middle-income countries. Concurrently, the emergence of real-world evidence, pragmatic trials, and adaptive designs has introduced complementary paradigms that challenge the exclusivity of RCTs in evidence hierarchies. This editorial provides a critical and expanded appraisal of the role of RCTs in contemporary medicine, examining their enduring strengths alongside their limitations, and highlighting the need for an integrated, context-sensitive approach to evidence generation.

**Keywords:** Phase III clinical trials, Randomized Control Trials, hierarchy of scientific evidence, clinical research  
**INTRODUCTION**

The importance of randomized controlled trials (RCTs) in clinical research is deeply embedded in the philosophy of evidence-based medicine. Since their formalization in the mid-20th century, RCTs have provided a robust methodological framework for minimizing bias through randomization, blinding, and controlled comparisons. Thus, required for approvals of regulatory authorities for use of drugs in clinical practice. This design enables researchers to isolate the effect of an intervention with a high degree of internal validity, making RCTs indispensable for regulatory decision-making and clinical guideline continue to be developed on RCT driven evidences. Major global institutions, including the World Health Organization (WHO) and the U.S. Food and Drug Administration (FDA), continue to rely on RCT-derived evidence as the cornerstone for approving therapeutics and shaping public health policies. However, the concept of RCTs as the unquestioned gold standard is increasingly being scrutinized. Modern medicine is no longer confined to controlled experimental environments; it operates within complex, dynamic health systems characterized by diverse patient populations, variable resource availability, and rapidly evolving technologies.

### *Validity-generalizability of results in strict controlled environment versus really world patients*

RCTs are optimized for internal validity, ensuring that observed outcomes can be attributed with confidence to the intervention under investigation. Yet this rigor often comes at the expense of external validity. Strict eligibility criteria frequently exclude patients with comorbidities, polypharmacy, advanced age, or atypical disease presentations. As a result, trial populations may not accurately reflect the patients encountered in routine clinical practice. This disconnect has tangible consequences. Clinicians are often required to extrapolate findings from idealized trial settings to complex real-world scenarios, where treatment responses may differ significantly. For instance, oncology trials frequently enroll younger, fitter patients, whereas real-world cancer populations include frail individuals with multiple comorbidities. The resulting evidence gap raises concerns about the applicability of RCT findings across diverse healthcare settings. Also the spectrum of side effects is much wider in real world patients as compared to the controlled carefully selected trial population. Thus generalizability of trials of needs to be interpreted carefully. However, still considering it as the highest level of evidence in the given scenario.

### *Economic and financial Constraints*

The financial burden associated with conducting RCTs is substantial. Large multicenter trials require extensive infrastructure, regulatory compliance, monitoring systems, and long follow-up periods. These requirements limit the feasibility of RCTs in resource-constrained environments, including many institutions in low- and middle-income countries. Establishment of Clinical Trial Units with approval from regulatory authorities is itself an expensive undertaking. For academic centers such as those in Pakistan, the reliance on externally funded RCTs may inadvertently skew research priorities toward globally driven agendas rather than locally relevant health challenges. Consequently, diseases with high regional burden but limited commercial interest may remain under-investigated. This imbalance underscores the need for alternative evidence generation strategies that are both cost-effective and contextually relevant.

### ***Ethical Complexities***

Ethical considerations further complicate the implementation of RCTs. The principle of clinical equipoise—genuine uncertainty regarding the comparative effectiveness of interventions—is a prerequisite for ethical randomization. However, in rapidly evolving fields such as oncology or during public health emergencies like COVID-19, maintaining equipoise can be challenging. In life-threatening conditions, withholding a potentially beneficial therapy for the sake of randomization may be ethically contentious. Similarly, patient preferences and physician judgment increasingly influence treatment decisions, potentially undermining recruitment and adherence in RCTs. These challenges necessitate more flexible and patient-centered research designs.

### ***The Rise of Real World Evidence***

The digital transformation of healthcare has facilitated the generation of vast amounts of real-world data through electronic health records, insurance databases, disease registries, and wearable technologies. Real-world evidence, derived from these sources, provides valuable insights into treatment effectiveness, safety, and long-term outcomes in routine clinical practice. Unlike RCTs, real world evidence captures the heterogeneous set of patient populations and healthcare delivery systems. It is particularly useful for post-marketing surveillance, rare adverse event detection, and evaluation of interventions in populations typically excluded from trials. Regulatory bodies including FDA, have increasingly recognized the value of real world evidence in supplementing traditional clinical trial data. However, real world evidence is not without limitations. Observational data are inherently susceptible to confounding, selection bias, and data quality issues. These issues cannot be sorted without having proper randomization and strict selection criteria.

### **Precision Medicine and the Fragmentation of Evidence**

The advent of precision medicine challenges the traditional RCT paradigm by focusing on individualized treatment strategies based on genetic, molecular, and phenotypic characteristics. In such contexts, the concept of a treatment effect becomes less meaningful without considering molecular parameters. For example, targeted therapies in oncology may be effective only in small, biomarker-defined subgroups, making large-scale randomization impractical. This necessitates alternative designs, including single-arm trials with historical controls, while these approaches offer practical solutions.

For healthcare systems in LMICs, the debate is not merely academic but deeply pragmatic. The exclusive reliance on RCTs may limit the generation of locally relevant evidence due to financial, infrastructural, and logistical constraints. Conversely, well-designed observational studies and pragmatic trials can provide actionable insights tailored to regional disease burdens and healthcare realities. By embracing methodological diversity and encouraging high-quality non-RCT research, they can facilitate evidence generation that is both scientifically robust and contextually meaningful. This includes promoting standardized reporting guidelines, fostering interdisciplinary collaboration, and prioritizing research with direct clinical and policy relevance.

### **CONCLUSION**

Randomized controlled trials remain a foundational pillar of clinical research, offering unmatched rigor in establishing high level of clinical evidence. However, their designation as the singular gold standard is increasingly incongruent with the complexities of modern medicine. The future of evidence-based practice lies in a pluralistic, integrated approach that combines the strengths of RCTs with the complementary insights of real-world evidence and innovative trial designs. This requires moving beyond rigid hierarchies toward a more nuanced, context-sensitive paradigm that prioritizes relevance, inclusivity, and methodological rigor in equal measure.

### **Conflict of Interest**

Author declare no conflict of interest.

## Original Article

# PERCEPTION AND AWARENESS OF PHYSIOTHERAPY IN MIGRAINE AND ITS ASSOCIATION WITH QUALITY OF LIFE AMONG MIGRAINE SUFFERERS

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This study was design to assess awareness and perception of physiotherapy among migraine sufferers and to examine its association with health-related quality of life among university students. This was a cross-sectional study including 132 university students aged 18–30 years with migraine, selected through convenience sampling. Migraine diagnosis was confirmed using the ICHD-3 criteria or a positive ID-Migraine screening test. Data were collected using the MINDS questionnaire, the Migraine Disability Assessment Scale (MIDAS), and the SF-36 health survey. Statistical analysis was performed using SPSS version 30, applying descriptive statistics and Pearson correlation analysis. Pearson correlation analysis showed statistically significant weak negative associations between SF-36 total scores and migraine characteristics. Quality of life was negatively correlated with the number of migraine attacks ( $r = -0.205$ ,  $p = 0.009$ ), attack intensity ( $r = -0.205$ ,  $p = 0.009$ ), medication intake ( $r = -0.185$ ,  $p = 0.017$ ), and headache-related disability ( $r = -0.155$ ,  $p = 0.038$ ). This study concludes that physiotherapy is significantly associated with improvement in migraine symptoms and overall quality of life among migraine sufferers.

**Keywords:** Awareness, Migraine, Physiotherapy, Quality of Life

## INTRODUCTION

Migraine is the second most common neurological condition in the world and causes more disability than all other neurological conditions combined, according to the Global Burden of Disease Study (1). In Iran's general population, migraine was more common in women than in men, with a prevalence of 15.1% (2). The prevalence of migraine varies by region. Some studies suggest that migraine is less common in Asian countries compared to other regions (3). The prevalence of migraine headaches was reported to be 37.2%, with females having a higher prevalence (81.1%) and students having the highest prevalence (43.3%) (4).

Migraine is a severe headache characterized by symptoms including sensitivity to light or sound, nausea, and vomiting. Migraines are typically characterized by throbbing pain on one side of the head that lasts from four to seventy-two hours. Before or during a migraine attack, some individuals experience visual disturbances (aura) such as flashing lights or zigzag lines (5). Migraine is characterized by headache attacks of specific duration accompanied by symptoms such as nausea, phonophobia, and photophobia (6). Aura is defined as brief localized neurological symptoms that often occur prior to, but sometimes during, the headache phase of a migraine attack. Chronic migraine is defined as  $\geq 15$  headache days per month for more than three months, fulfilling the ICHD-3 criteria for migraine on at least eight days per month (7). Peripheral projections of the trigeminal nerve release neurotransmitters such as pituitary adenylate cyclase-activating polypeptide (PACAP) and calcitonin gene-related peptide (CGRP), which cause vasodilation and alter nociceptive transmission upon activation (8). When these neurotransmitters are administered intravenously, migraine sufferers may experience migraine episodes, whereas healthy volunteers usually experience only mild headaches (9).

Migraine is diagnosed using the International Classification of Headache Disorders, Third Edition (ICHD-3) criteria, along with clinical symptoms, physical findings, and medical history. The aim of migraine treatment is to reduce the frequency and severity of attacks and the need for analgesics. Treatment strategies include behavioral therapy, acute symptomatic treatment, and preventive therapy. Lifestyle modification is an important component of behavioral therapy (10). Migraine is a common health problem, and its treatment remains a challenge. The role of physiotherapy in migraine management is increasingly being explored. Progressive muscle relaxation (PMR) has been shown to reduce migraine frequency. Instrument-assisted soft tissue mobilization (IASTM) therapy may decrease headache frequency, improve neck alignment, and reduce headache-related disability (11). Combining different therapeutic approaches may produce better outcomes. Manual therapy techniques used in physiotherapy

for chronic migraine have shown reduction in pain and improvement in quality of life (QOL), enabling patients to return to activities of daily living (ADLs) and social interaction (12).

The Migraine Disability Assessment Scale (MIDAS) questionnaire is commonly used to evaluate the burden of migraine. MIDAS consists of five questions that assess migraine-related disability in terms of missed work or school, reduced productivity, and limitations in social, recreational, or family activities. Awareness and perception of physiotherapy, including previous experiences with physiotherapy, can be assessed using the MINDS (Migraine and Physiotherapy) questionnaire (13).

Physiotherapy may improve the trigemino-cervical system and reduce migraine symptoms by decreasing cervical muscle tension and modulating pain through techniques such as manual therapy. Physiotherapeutic interventions may also focus on improving neck biomechanics and posture, which may contribute to persistent migraine symptoms (14).

Children and adolescents with primary headaches require a multimodal interdisciplinary treatment approach including medication, physical therapy, cognitive behavioral therapy, and lifestyle modification. Literature suggests that brisk walking for 20–30 minutes five days per week may serve as an effective aerobic exercise (15). Recent epidemiological studies indicate that migraine affects a large proportion of adults worldwide and is strongly associated with reduced health-related quality of life (16).

Enhancing awareness of the therapeutic role of physiotherapy in migraine management may improve clinical outcomes and support development of comprehensive patient-centered treatment strategies. The objective of this study was to evaluate the perception and awareness of physiotherapy in migraine management and its association with quality of life among university students.

## METHODS

This cross-sectional study was conducted over a period of four months following approval of the research synopsis. A total sample of 132 participants was calculated using Rao software, and a purposive sampling technique was employed to recruit eligible participants from Riphah International University. Students aged 18–30 years, both male and female, who were diagnosed with migraine according to the ICHD-3 criteria and screened positive on the ID-Migraine Scale ( $\geq 2$  positive responses) were included in the study (13). Individuals with other neurological disorders (such as brain tumors, trigeminal neuralgia, and temporal arteritis), cervicogenic headache, or headache secondary to hypertension were excluded (20). Data were collected after obtaining informed consent, and participants completed self-administered questionnaires, including the MINDS questionnaire to assess awareness and perception of the role of physiotherapy in migraine management, the Migraine Disability Assessment Scale (MIDAS) to evaluate migraine-related disability and its impact on daily functioning and work productivity, and the SF-36 questionnaire to assess quality of life. Confidentiality of all responses was strictly maintained.

### Statistical Analysis

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 26. Descriptive statistics were calculated to summarize demographic characteristics and study variables, including mean, standard deviation, frequencies, and percentages. Pearson correlation analysis was applied to assess the relationship between migraine characteristics (number of attacks, intensity of attacks, medication intake, and headache-related disability) and quality of life measured through SF-36 scores. A p-value of  $\leq 0.05$  was considered statistically significant. Results were presented in tables to demonstrate the association between migraine-related variables and quality of life outcomes. Appropriate inferential statistical tests were applied according to the nature of the variables to ensure validity and reliability of the findings.

## RESULTS

### Demographic Characteristics of Participants

A total of 132 students diagnosed with migraine from Riphah International University were included in the final analysis. The age of participants ranged from 18 to 30 years, with a mean age of  $22.59 \pm 2.393$  years, as presented in Table 1. The relatively narrow standard deviation indicates that most participants were within a similar age range, representing a young adult population commonly affected by migraine

**Table 1:** Descriptive statistics of age of participants

Variable	Minimum	Maximum	Mean	Std. Deviation
Age of participants	18	30	22.59	2.393

### Physiotherapy Exposure and Migraine Characteristics

Among the 132 participants, 34 were male and 98 were female. The majority of participants had not undergone physiotherapy for migraine management (104 participants; 26 males and 78 females), whereas only 28 participants (8 males and 20 females) reported receiving physiotherapy treatment. Regarding perceived effectiveness of physiotherapy, 36 participants (10 males and 26 females) reported improvement in symptoms, while 96 participants (24 males and 72 females) reported no perceived benefit.

With respect to migraine characteristics, most participants reported no increase in the number of migraine attacks (117 participants; 30 males and 87 females) and no increase in attack intensity (119 participants; 29 males and 90 females). Similarly, the majority of participants reported no regular medication intake for migraine management (114 participants; 28 males and 86 females). Only a small proportion of participants reported disability due to headache (9 participants; 2 males and 7 females). These findings indicate that although migraine was prevalent among the study population, relatively few participants had undergone physiotherapy or experienced severe disability related to migraine. Detailed descriptive statistics of participant responses according to gender are presented in Table 2.

**Table 2:** Descriptive statistics of participants according to gender

Variable	Male (n)	Female (n)
<b>Have you ever undergone physiotherapy for your headache</b>		
No	26	78
Yes	8	20
<b>Did you benefit from physiotherapy</b>		
No	24	72
Yes	10	26
<b>Number of attacks increased</b>		
No	30	87
Yes	4	11
<b>Intensity of attack increased</b>		
No	29	90
Yes	5	8
<b>Medication intake required</b>		
No	28	86
Yes	6	12
<b>Disability due to headache</b>		
No	32	91
Yes	2	7

### Association Between Migraine Characteristics and Quality of Life

Pearson correlation analysis demonstrated statistically significant weak negative associations between migraine characteristics and quality of life measured using the SF-36 total score, as shown in Table 3.

A significant weak negative correlation was observed between the number of migraine attacks and SF-36 total score ( $r = -0.205$ ,  $p = 0.009$ , one-tailed), indicating that an increase in migraine frequency was associated with a reduction in quality of life. Similarly, migraine intensity showed a statistically significant weak negative correlation with quality of life ( $r = -0.205$ ,  $p = 0.009$ , one-tailed), suggesting that higher pain intensity was associated with poorer health-related quality of life.

Medication intake also demonstrated a statistically significant weak negative association with SF-36 total score ( $r = -0.185$ ,  $p = 0.017$ , one-tailed), indicating that increased reliance on medication was associated with lower quality of life. Furthermore, headache-related disability showed a statistically significant weak negative correlation with quality of life ( $r = -0.155$ ,  $p = 0.038$ , one-tailed), suggesting that participants experiencing greater disability due to migraine had poorer quality of life outcomes.

Overall, these findings suggest that migraine-related factors, including frequency of attacks, intensity of symptoms, medication use, and headache-related disability, are significantly associated with reduced quality of life among migraine sufferers, although the strength of these correlations remains weak.

**Table 3:** Association between mean SF-36 score and migraine characteristics

Variable	Correlation	Number of attacks	Intensity of attack	Medication intake	Disability due to headache
Mean SF-36 total	Pearson Correlation	-0.205	-0.205	-0.185	-0.155
	Sig. (1-tailed)	0.009	0.009	0.017	0.038

## DISCUSSION

This study primarily examined the relationship between different characteristics of migraine and health-related quality of life (HRQOL) among university students. The SF-36 questionnaire was used to assess quality of life. Migraine burden was evaluated based on the number of attacks, intensity of attacks, medication intake, and disability due to headache.

Buse et al. demonstrated that increased headache frequency is associated with a substantial decline in physical functioning, vitality, and role participation, as measured by health-related quality of life (HRQOL) instruments such as the SF-36 (17). Similarly, Alahmadi et al. reported that patients experiencing more frequent migraine attacks had significantly lower scores on the SF-36, particularly in domains related to physical functioning and role limitation (18). The findings of the present study support this evidence and suggest that frequent migraine episodes may negatively affect academic performance, social engagement, and daily activities among university students.

In contrast to attack frequency, the association between migraine intensity and quality of life, although statistically significant in the present study, was relatively weak. This finding differs from some previous studies that reported a stronger relationship between pain severity and reduced quality of life. However, other studies are consistent with the present findings, suggesting that pain intensity alone may not fully explain the reduction in quality of life. Pociūtė and Jakavonytė-Akstinienė highlighted that although pain severity contributes to patient discomfort, functional limitations and frequency of migraine attacks are more important determinants of overall quality of life (19). Variations in findings may be attributed to individual differences in pain tolerance, coping mechanisms, and adaptation to recurrent symptoms over time, whereas frequent attacks tend to cause consistent disruption of daily functioning.

Medication intake also demonstrated a significant negative association with quality of life in the present study. Participants who reported greater use of medication had lower SF-36 scores, indicating a higher disease burden. These findings are consistent with previous evidence suggesting that frequent use of acute medication may indicate inadequate migraine control and greater functional impairment. Buse et al. reported that individuals requiring frequent medication often experience poorer quality of life and increased disability, particularly when preventive treatment strategies are insufficient (20). Although some studies suggest that appropriate preventive therapy may improve quality of life despite medication use, the findings of the present study indicate that medication alone may not significantly improve quality of life if the overall migraine burden remains high.

Headache-related disability was another factor significantly associated with reduced quality of life. Participants reporting greater disability due to migraine also demonstrated lower SF-36 scores, indicating impaired physical, emotional, and social functioning. These findings are supported by previous studies demonstrating a strong association between migraine-related disability and reduced health-related quality of life. Alahmadi et al. reported that higher disability scores were associated with poorer outcomes in both physical and emotional domains of the SF-36. Similarly, Bazargan et al. observed that migraine-related disability significantly affects both physical and psychological aspects of quality of life, highlighting the broader impact of migraine beyond pain symptoms alone (21). These findings emphasize the importance of addressing functional impairment as a critical component of migraine management.

When comparing the magnitude of associations observed in this study with those reported in previous literature, it is important to note that most correlations were statistically significant but relatively weak. Similar findings have been reported in several recent cross-sectional studies demonstrating modest associations between migraine characteristics and quality of life (18,19). In contrast, some large-scale clinical studies have reported stronger associations, which may be explained by differences in study population, migraine severity, or research design (22).

The relatively modest associations observed in the present study may be attributed to the young age of university students, who may develop adaptive coping mechanisms that allow them to maintain daily functioning despite migraine symptoms.

## **CONCLUSION**

This study concludes that physiotherapy is significantly associated with improvement in migraine symptoms and overall quality of life among migraine sufferers. Increasing awareness regarding the role of physiotherapy in migraine management may help improve patient outcomes. Educational initiatives should be developed to promote the use of physiotherapy as part of migraine treatment. Physiotherapy should be considered an important component of a multidisciplinary approach to migraine management. Future research using longitudinal or experimental study designs is recommended to establish causal relationships.

## **Conflict of Interest**

Authors declare no conflict of interest.

## **Ethical consideration**

The study was approved by local research ethics committee.

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*Original Article*

## EFFECTS OF APPLE CIDER VINEGAR ON VEGF165 AND GLUCOSE LEVEL IN DIABETIC MELLITUS TYPE-II PATIENTS

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**ABSTRACT:**

The purpose of this clinical trial was to evaluate the effect of apple cider vinegar on VEGF165 and glucose levels in type-II diabetes Mellitus (DM) patients. A randomized clinical trial using a non-probability convenience sampling technique was conducted on 110 eligible types-II diabetes Mellitus patients who failed to control their glucose levels and were scheduled for senile cataract surgery. Participants were given 15-20 ml of apple cider vinegar in 200 ml water before sleep at night for 6 months (with follow-up after each 3 months). HbA1C, Fasting Blood Sugar, and VEGF165 tests were performed Pre and Post operatively and analysed using SPSS version 21. A total 110 type-II diabetic patients with NPDR in both eyes were included. The highest proportion of patient was in the age group of 51-60 years (54.4%), females were 61.5% and majority were illiterate about (37.2%). About 58.2% patients strictly followed their medication, about 53.1% patients strictly followed their diet plan and about 48.2% patients strictly took apple cider vinegar daily. Significant mean changes were found in VEGF165 ( $p < 0.002$ ), HbA1C ( $p < 0.023$ ), and blood sugar fasting ( $p < 0.012$ ). Regular use of apple cider vinegar was effective in controlling diabetes and reducing the abnormal production of VEGF165 (retinal protein) in type-II DM patients and it helped improve ocular condition allowing ophthalmologist to perform cataract surgery more easily and remove the dense cataract.

**KEYWORDS:** Apple Cidar Vinegar, Diabetes type II, Randomized controlled trial (RCT)

### INTRODUCTION

Diabetes mellitus (DM) commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar levels over a prolonged period of time (1). Diabetes is due to either when the pancreas does not produce enough insulin, or when the cells of the body do not respond properly to the insulin produced (2).

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. The most common cause is a combination of excessive body weight and insufficient exercise (3). As of 2019, an estimated 463 million people had diabetes worldwide (8.8% of the adult population), with type 2 diabetes making up about 90% of the cases (4). Rates are similar in women and men. And trends suggest that rates will continue to rise (5).

In 2021, diabetes was the direct cause of 1.6 million deaths and 47% of all deaths due to diabetes occurred before the age of 70 years. Another 530 000 kidney disease deaths were caused by diabetes, and high blood glucose causes around 11% of cardiovascular deaths (6). The primary complications of diabetes due to damage in small blood vessels including damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina, and can result in gradual vision loss and eventual blindness(7). The platelet-derived growth factor (PDGF) family includes VEGF. VEGF-A, VEGF-B, VEGF-C, VEGF-D, and placental growth factor, which are located on chromosome 6p12, make up the VEGF gene family (8). VEGF plays a crucial role in angiogenesis by binding to its receptors, which promotes the formation of new blood vessels and the proliferation of endothelial cells. A cascade of receptor activation is necessary for the complex and well-coordinated process of new vessel formation and development. VEGF is a crucial rate-limiting step in physiological angiogenesis (9). The deletion of a single VEGF allele, which results in poor vascularization, has highlighted the crucial role that VEGF plays in angiogenesis. VEGF121, VEGF145, VEGF148, VEGF162, VEGF165, VEGF165b, VEGF183, VEGF189, and VEGF206 are the nine isoforms of VEGF-A (10). VEGF165 is the most prevalent isoform in the eye (11). Cells

in the body produce a protein called vascular endothelial growth factor (VEGF). When the body needs new blood vessels, VEGF stimulates their formation. However, cells can sometimes produce too much VEGF, which leads to abnormal blood vessels formation in the eye. These abnormal blood vessels impair vision and can damage the eye. The causes and origins of age-related eye illnesses are multifactorial and complex. Oxidative stress has been identified as a common contributing factor because the eye has high oxygen consumption, high levels of polyunsaturated fatty acids, and cumulative exposure to high-energy visible light, making it vulnerable to oxidative stress. Antioxidants may help maintain vision or even reverse visual damage, according to some theories. Therefore, the role of dietary antioxidants and the possible therapeutic benefits of antioxidant supplements as an easy and affordable method of disease prevention and control are of great research interest (12).

Apple cider vinegar is produced from apple juice, through fermentation. During fermentation, yeast convert the alcohol into acetic acid. To avoid issues such as tooth enamel erosion, 1 to 2 tablespoons (15–20 ml) should be diluted in water or tea before consumption (13).

Consuming apple vinegar may help people with diabetes and dyslipidaemia improve their glycaemic control and reduce oxidative stress, according to a 2019 clinical trial. A review of research trials conducted in 2021 also suggested that glycemic status may improve with ACV consumption. Apple cider vinegar has been investigated in recent years as a potential weight loss, heart health, and even dandruff treatment (14).

Drinking vinegar may help combat obesity, according to research from Japanese scientists. According to one tiny study, vinegar helped a group of individuals with type 2 diabetes with their insulin and blood sugar levels (15).

Consuming large amounts of apple cider vinegar can have negative effects on the stomach, throat, and teeth due to its strong acidity. Additionally, it may reduce the effectiveness of some medications, including drugs for heart disease and diabetes, as well as laxatives and diuretics (16).

## **METHODS**

The Randomized Clinical Trial (RCT) was conducted in accordance with the term of Helsinki Declaration and also was approved by the institutional Research and Ethical Committee.

A total 110 patients with Non-Proliferative Diabetic Retinopathy (NPDR) and types-II Diabetic Mellitus were included in the study. There was no gender restriction, and patients aged between 40 to 70 years were included in the study. A non-probability convenience sampling technique used. Patients were included in the study if they were diagnosed with type-II diabetes mellitus and had non-proliferative diabetic retinopathy (NPDR) in both eyes. Only patients aged between 40-70 years were eligible for inclusion. Additionally, patients with a history of diabetes mellitus were included in the study. All participants who were willing to use apple cider vinegar regularly and provided written informed consent were included in the study. Patients were excluded from the study if they were younger than 40 years or older than 70 years of age. Patients with a history of diabetes mellitus for less than five years were also excluded. Individuals with other types of diabetes mellitus such as type I diabetes or gestational diabetes, were not included in the study. Patients suffering from other systemic diseases that could affect the study outcomes were excluded. Furthermore, patients with proliferative diabetic retinopathy (PDR) in one or both eyes were excluded from the study. The study was performed according to a protocol approved by the hospital's Institutional Ethics Committee, in accordance to the ethical principles of the Helsinki Declaration and written informed consent (English and Urdu) was obtained from each patient. A preliminary screening test was done, including history of diabetes, blood sugar level, type of diabetes, Patients were educated about the about apple cider vinegar, its benefits, method of use and recommended daily quantity.

Collection of aqueous humor samples was performed in the operating theatre under sterile conditions on first visit without using apple cider vinegar and after using (3 months and 6 months). Samples (0.1 – 0.2 ml) of aqueous humor were collected in sterile tubes by way of limbal anterior chamber puncture with a 27-gauge needle of a 1-ml insulin injector. These samples were then stored frozen at  $-80^{\circ}\text{C}$  within a few minutes of collection.

The concentration of the VEGF165 isoform was measured by enzyme-linked immunosorbent assay (ELISA) with human VEGF kit (Invitrogen U.S.A.-BioSource Human VEGF Immunoassay kit Catalog # KHG0112 / KHG0111). The linear detection range of the assay was 5–1500 pg/ml.

Data were analysed using SPSS version 21. Descriptive data were presented as frequencies and percentages. One-way ANOVA was used to compare the group means. Pearson correlation analysis was used to measure the strength of the relationship between the variables. The 95% confidence intervals of the tests were determined;  $P < 0.05$  was accepted as statistically significant.

## RESULTS

Among the patients, 48.2% strictly used apple cider vinegar, 36.4% used it moderately, and 25.4% used it irregularly (Table 1). The results are summarized and analysis of the groups was done by using the ANOVA-One way test. However, VEGF165, HbA1C and Blood Sugar Fasting significantly changed after using apple cider vinegar for 3 months and 6 months.

Aqueous VEGF165 before intervention (BI) Mean  $\pm$  S.D was  $320.6 \pm 239.3$  pg/ml, after intervention (AI) Mean  $\pm$  S.D was  $242 \pm 72.5$  pg/ml on 3 months and  $133.3 \pm 58.5$  pg/ml on 6 months. (Table 2).

HbA1C before intervention (BI) Mean  $\pm$  S.D was  $9.32 \pm 1.74$ , after intervention (AI) Mean  $\pm$  S.D was  $8.65 \pm 1.81$  on 3 months and  $8.08 \pm 1.36$  SD on 6 months. (Table 3).

Blood Sugar Fasting before intervention (BI) Mean  $\pm$  S.D was  $170.14 \pm 62.42$ , after intervention (AI) Mean  $\pm$  S.D was  $157.34 \pm 58.16$  on 3 months  $133.2 \pm 58.16$  on 6months. (Table 4).

The Mean  $\pm$  S.D value of Aqueous VEGF165 (Vascular Endothelial Growth Factor) was  $242 \pm 72.5$  pg/ml, Blood Sugar Fasting was  $157.34 \pm 58.16$  and HbA1C was  $8.65 \pm 1.81$  on first follow-up (3 months) and  $133.3 \pm 58.5$  pg/ml of VEGF165, Blood Sugar Fasting was  $133.2 \pm 58.16$  and HbA1C was  $8.08 \pm 1.36$  on second follow-up (6 months).(Table 5).

**Table 1: Distribution of patients using apple cider vinegar**

	Characteristics	Percent
<b>Apple cider vinegar follow-up</b>	Strictly follow	48.2%
	Moderately follow	36.4%
	Irregular	25.4%
	<b>Total</b>	<b>110</b>

**Table 2: Effects of Apple cider vinegar on VEGF 165 at 3 months and 6 months**

Apple Cider Vinegar	Aqueous VEGF <sub>165</sub> (Mean $\pm$ S.D)	P-value
<b>Before Intervention</b>	$320.6 \pm 239.3$ pg/ml	
<b>First follow up (3-months)</b>	$242 \pm 72.5$ pg/ml	<b>0.002</b>
<b>Second follow up (6-months)</b>	$133.3 \pm 58.5$ pg/ml	

**Table 3: Effects of Apple cider vinegar on HbA1C at 3 months and 6 months**

Apple Cider Vinegar	HbA1C (Mean $\pm$ S.D)	P-value
<b>Before Intervention</b>	$9.32 \pm 1.74$	
<b>First follow up (3-months)</b>	$8.65 \pm 1.81$	<b>0.023</b>
<b>Second follow up (6-months)</b>	$8.08 \pm 1.36$	

**Table 4: Effects of Apple cider vinegar on Blood Sugar Fasting at 3 months and 6 months**

Apple Cider Vinegar	Blood Sugar Fasting (Mean ± S.D)	P-value
<b>Before Intervention</b>	170.14 ± 62.42	
<b>First follow up (3-months)</b>	157.34 ± 58.16	<b>0.012</b>
<b>Second follow up (6-months)</b>	133.2 ± 58.16	

**Table 5: Effects of Apple cider vinegar on VEGF 165, Blood Sugar Fasting & HbA1C at 3 months and 6 months**

After using apple cider vinegar		
Clinical tests	First follow-up at 3 months (Mean ± S.D)	Second follow-up at 6 months (Mean ± S.D)
<b>Aqueous VEGF<sub>165</sub></b>	242 ± 72.5 pg/ml	133.3 ± 58.5 pg/ml
<b>Blood Sugar Fasting</b>	157.34 ± 58.16	133.2 ± 58.16
<b>HbA1C</b>	8.65 ± 1.81	8.08 ± 1.36

## DISCUSSION

In current study VEGF<sub>165</sub> were significantly reduced on both follow-up periods (3 months and 6 months ( $p < 0.002$ )) in patients with diabetic retinopathy. Previous studies support the generally accepted assumption that the VEGF<sub>165</sub> level in the aqueous humor collected from the anterior chamber adequately reflects the VEGF<sub>165</sub> activity in retinal tissues, despite a lower level of VEGF<sub>165</sub> levels compared to the vitreous humor (17). Based on these clinical data, we investigated the relationship between the severity of diabetic retinopathy and VEGF<sub>165</sub> level through aqueous humor sampling.

In our study, the aqueous VEGF<sub>165</sub> levels observed in type-II diabetic patients with NPDR were consistent with results of the previous studies regarding the role of VEGF<sub>165</sub> in retinopathy (severity to generate new vessels in retina of eye). A correlation between elevated VEGF<sub>165</sub> in ocular fluids and the presence of retinopathy has been revealed by some clinical studies, suggesting that VEGF<sub>165</sub> is a mediator for hypoxic inflammation (18).

The aqueous levels of VEGF<sub>165</sub> were elevated in eyes and were also correlated with the severity of diabetic retinopathy. There was a statistically significant difference between aqueous VEGF<sub>165</sub> levels in after intervention in patients with type-II diabetes mellitus.

In the current study, HbA1C and blood sugar fasting were significantly reduced HbA1C ( $p < 0.023$ ), blood sugar fasting ( $p < 0.012$ ). Previous study results showed HbA1C ( $p = 0.002$ ) and blood sugar fasting ( $p = 0.006$ ) significantly reduced in the intervention group but not significantly changed in these parameters of the placebo group (19). Another study showed a significant reduction in fasting blood sugar ( $p = 0.05$ ), in vinegar (750 mg) ingestion group when compared with vinegar pills (40 mg acetic acid) as control group after 12 weeks trail but no significant change in Hb1C and post prandial glucose was found (20).

In the current study, diet remained the same, no significant difference was found in any dietary component before and after the intervention. Previous study human studies also reported that diet should remain the same before and after the acetic acid intervention in type-II diabetic patients to ensure comparability (21).

A study conducted on human subjects also showed physical activities and life style remained the same before and after the invention and no significant effect of these confounders was found.

Apple cider vinegar was most effective in controlling diabetes and reducing the abnormal production of VEGF<sub>165</sub> (retinal protein) in type-II diabetes mellitus patients, thereby helping to control the progression of the eye complications. Furthermore, improved ocular conditions may facilitate ophthalmologists in performing cataract surgery more easily and removing dense cataract.

## Conflict of Interest

Authors declare no conflict of interest.

## Ethical consideration

The study was approved by Institutional Research Ethics Committee.

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## Original Article

# EFFECTIVENESS OF ARM ABILITY TRAINING WITH BIOFEEDBACK TECHNIQUES TO IMPROVE NEUROPLASTICITY, DEXTERITY AND QUALITY OF LIFE AMONG SUBACUTE STROKE SURVIVORS

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### ABSTRACT:

One of the main causes of physical disability is stroke, and 80% of stroke survivors suffer upper extremity dysfunction characterized by reduced muscle strength and functional limitation in muscle control and life quality. Arm ability training with biofeedback techniques is reported to enhance the functional recovery of the upper limb by improving the dexterity of the upper limb and life quality. An experimental study to find out the effects of Arm Ability Training with Biofeedback techniques on upper limb dexterity, functional ability, and quality of life in sub-acute stroke survivors. Sixty participants were chosen and randomly allocated to two groups. Group A received Arm ability training with biofeedback techniques, and Group B received conventional therapy for 60 minutes, 5 days/week for 3-4 weeks. The outcome measures were Modified standardized nine-hole peg test (mS-NHPT), Fugl-Meyer Assessment Upper Extremity, 12-item stroke-specific quality of life scale, and Wolf Motor Function Test. The mean completion time for the m-S NHPT decreased (from 113.78 ± 3.14 to 88.36 ± 2.49), and the FMA-UL increased (from 79.08 ± 2.54 to 90.52 ± 2.92). SS-QOL-12 (19.76 ± 0.99 to 40.12 ± 1.24), WMFT (Functional Ability) (from 46.76 ± 1.47 to 56.92 ± 2.03), and the time score improved (from 478.64 ± 2.9 to 435.16 ± 2.22). The variables indicates a statistical significance ( $p < 0.05$ ). The above result statistically shows significant improvements in dexterity, functional ability, and life quality of sub-acute stroke subjects.

**KEYWORDS:** mS-NHPT, FMA-UE, SS-QOL-12, and WMFT

## INTRODUCTION

A stroke is a sudden, focal neurological impairment brought on by central nervous system vascular damage (haemorrhage or infarction). Globally, stroke ranks as the second most common cause of death and disability. Post stroke, more than two-third of the patients have impairment in the motor function of the upper limb. As a result, there is difficulty in performing activities of daily living. Eighty five percent of strokes are ischemic, mostly due to large artery cardioembolism, small vessel arteriolosclerosis, and atherothromboembolism. Fifteen percent of younger adults develop ischemic strokes due to factors, including intracerebral haemorrhage and extracranial dissection (1). According to the GBD 2019 (the Global Burden of Disease) research, the majority of deaths worldwide (18.6 million [17.1–19.7]) in both sexes were attributed to cardiovascular illnesses (CVDs). Stroke was the second most common cause of death among CVDs, accounting for 3.33 million stroke deaths in men (3.04–3.62) and 3.22 million stroke deaths in women (2.86–3.54) (2). A major cause of death and morbidity in both developed and, increasingly, low-middle-income (LMIC) nations, stroke is a serious worldwide health concern. Seventy percent of all strokes occur in Strokes LMICs, and the resulting illness burden is higher than in high-income nations. In India, stroke is now the fourth leading cause of mortality and the fifth major cause of disability due to a rise in age-related, non-communicable diseases brought on by the country's recent increase in life expectancy to over 60 years (3).

One of the main causes of physical disabilities is stroke. Up to 80% of stroke survivors experience upper extremity disability. Paresis, its most prevalent symptom, is distinguished by decreased muscle strength (due to decreased motor unit recruitment and muscle changes as atrophy), followed by loss or limitation of function in muscle control,

movement, or mobility, which can subsequently have a detrimental impact on one's ability to support oneself and one's quality of life (4).

Hemiplegia is present in over 85% of stroke survivors (Kim, 2017; Santisteban et al., 2016), and over 69% of those with hemiplegia show functional motor impairment in their upper limbs. Following a stroke, changes in muscle tone, muscular weakness, joint laxity, and reduced motor control are common signs of upper limb motor impairment. According to Hatem et al. (2016), these challenges may make it difficult to carry out daily tasks, including reaching for, picking up, grabbing, and holding onto objects. (5)

Approximately 75% of strokes are caused by damage to the middle cerebral artery, which provides a large amount of blood to the area of the brain responsible for the motor functions of the hands and upper extremities. While a slight recovery of the lower extremities allows for functional gait, recovery of the distal parts and fine motor functions (such as grasping and manipulating) is required for functional recovery of upper extremity functions (6). Over 50 percent of stroke survivors need assistance (typically mild to moderate) with dressing or bathing because of upper extremity dysfunction, and most need full assistance with certain daily living activities like cooking or cleaning. Few of them are able to resume their pre-stroke job routines and dedicate themselves to their personal, family, and leisure activities. Therefore, from the perspective of preserving functional independence, upper limb disability is an important therapeutic target. (7)

Three months after a stroke, more than half of stroke survivors still exhibit markedly delayed distal pinch grip performance, making hand motor outcome one of the clinically most important measures. In order to maximize upper limb function, current perspectives on the efficacy of rehabilitation include relearning fundamental skills related to activities of daily living (ADL) and practicing ADL intensively. Stroke patients' quality of life (QoL) is negatively impacted by upper-limb impairment. Because it affects the majority of basic ADLs (such as crawling, balancing, walking, writing, eating, washing, and manipulating items), it makes it more difficult for them to live independently.

Robotics, electromyographic biofeedback, mental practice with motor imagery, and constraint-induced movement therapy all showed improvements in arm function recovery. Repetitive task training, biofeedback, and training on a moving platform were found to improve transfer ability or balance. These results indicate that several emerging interventions, such as constraint-induced movement therapy (CIMT), non-invasive brain stimulation (NIBS), selective serotonin receptor inhibitor (SSRI) antidepressants, mirror therapy (MT), and motor imagery/mental practice, can improve motor recovery after a stroke. (9)

Arm Ability Training (AAT) is designed to assist individuals with stroke who have mild to moderate arm paresis in regaining their manual dexterity. Our "dexterity" in daily life is influenced by a variety of sensorimotor arm and hand skills, including steadiness, finger dexterity, coordinated visually guided movements, the ability to produce accurate goal-directed arm movements, and the speed of selective motions. (10)

The AAT incorporates eight distinct tasks to explicitly and repeatedly train each of these sensorimotor skills at an individual's performance limit. Variable task difficulty levels and enhanced feedback in the form of intermittent knowledge of results are also included. The AAT is clinically helpful in promoting "dexterity" recovery in stroke subjects with reduced focal disability and mild to moderate arm paresis. (11) The Arm Ability Training rehabilitation protocol markedly enhanced the function, strength, grip strength, and dexterity of the upper extremities in stroke patients (12).

By improving sensory feedback, biofeedback is a flexible method that gives people control over physiological functions. Biofeedback is frequently used in physical therapy, neuromuscular rehabilitation, and stress management to treat diseases like motor dysfunction, anxiety, incontinence, and chronic pain. The procedure starts with the measurement of a chosen physical parameter using non-invasive equipment. The result is either shown immediately or transformed into a tactile, visual, or audio feedback signal. The patient consciously modifies the physical parameter in order to practice manipulating the feedback signal. Biofeedback provides enhanced or extrinsic feedback, which supplements the body's intrinsic sensory system. (13)

Hence the study is that there are studies conducted to know the effectiveness of AAT with biofeedback techniques for upper limb rehabilitation. The need for this study is to determine how effective Arm Ability Training with biofeedback techniques is compared to conventional physiotherapy is to improve upper limb dexterity and quality of life in sub-acute stroke.

## METHODS

A single-blinded experimental study was conducted with sixty participants. Data on gender, age, stroke duration, side of involvement, Mini-Mental State Examination (MMSE), and Brunnstrom recovery stage were collected from participants aged 30 to 60 years who had been diagnosed with a stroke at the outpatient Department of Jaya College of Paramedical Sciences, College of Physiotherapy. Male and female participants with body mass index (BMIs) ranging from 24 to 29.9 who encountered both ischemic and hemorrhagic strokes during their initial episode of unilateral MCA stroke. Endocrine disorders like diabetes, hypertension, subacute stroke lasting longer than three months, upper extremity Brunnstrom scores between stages II and III (14.15), and Mini-Mental State Examination scores (MMSE)  $\geq 24$  (21 for illiterate) (16). Participants in the study must be able to sit on their own for 30 minutes. Neurological disease (Parkinson's disease, Alzheimer's disease), musculoskeletal problems (deformities, recent fracture), any systemic disease, Pain (score 1 or at least 2 joints), Patients with severe somatosensory deficit, visual or hearing impairment, or severe shoulder pain. Any comorbid condition that might impair function in the upper extremities. Patients with psychological problems are excluded from the study. The Ethical approval obtained from institution Ethical Committee (EC/JCP/ 06/ 2024), and informed consent from the participants were obtained. Participants of Group A received AAT and Group B received Conventional Exercises for 3 weeks, 5 days/week, each session 60 min/session. Measurements were taken before and after the treatment. Based on inclusion and exclusion criteria, subjects clinically diagnosed with stroke were selected. The study was approved by the Ethical Committee (EC/JCP/8/2025). Every participant gave their informed consent after being fully aware of the study's purpose. By random sampling, 50 participants who satisfied the inclusion and exclusion criteria were divided into two study groups, each consisting of 25 persons. The following outcome measures were evaluated: Modified Standardized Nine Hole Peg Test (mS-NHPT) (17, 18), Fugl-Meyer Assessment Upper Extremity (FMA-UE) (19, 20). Stroke-specific quality of life (SS-QOL) (21, 22, 23). Wolf Motor Function Test (24, 25)

### Randomization and Grouping

Fifty participants meeting inclusion and exclusion criteria were randomly assigned into two groups (n = 25 each):

- Group A: Arm Ability Training (AAT)
- Group B: Conventional Physiotherapy

Both groups underwent intervention for 3 weeks, 5 days per week, with each session lasting 60 minutes. Outcome measures were assessed before and after the intervention.

### Outcome Measures

The following assessments were conducted:

- Modified Standardized Nine Hole Peg Test (mS-NHPT) (17, 18)
- Fugl-Meyer Assessment for Upper Extremity (FMA-UE) (19, 20)
- Stroke-Specific Quality of Life (SS-QOL) (21–23)
- Wolf Motor Function Test (WMFT) (24, 25)

### Intervention Protocols

#### Group A: Arm Ability Training (AAT)

Participants in Group A performed structured AAT exercises targeting upper limb dexterity:

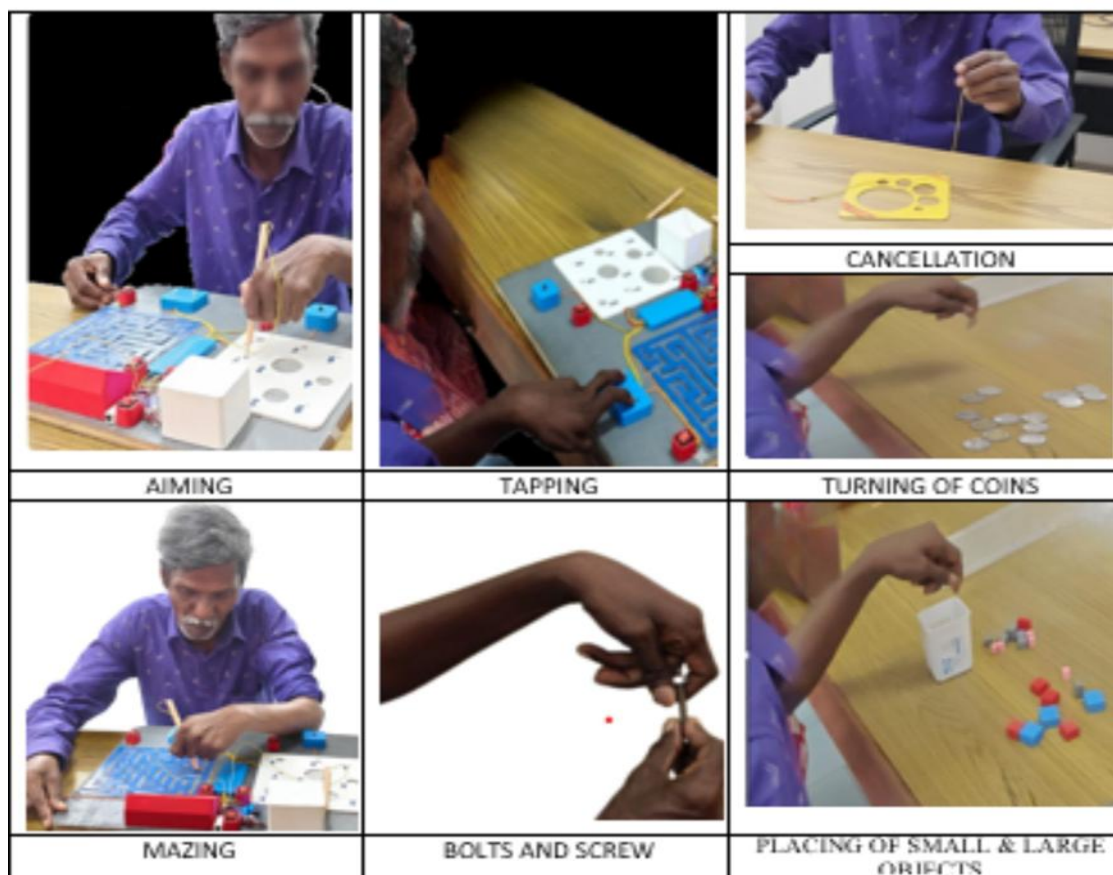
1. Aiming: Using a stylus, hit targets 18–23 cm away, 3–50 mm wide, and 30 cm above the table surface. Aim at specific targets displayed on a screen.
2. Tapping: Quick, repetitive, alternating movements of the thumb, index, and middle fingers on a sensor.
3. Cancellation: Mark circles of various sizes with a pen.
4. Turning Coins: Manipulate coins of 18 and 23 mm diameter.
5. Maze Tracking: Follow specified tracks along with music without losing contact on the track.
6. Bolts and Nuts: Pick up bolts of 3, 5, and 12 mm.
7. Placing Smaller Objects: Precision placement of small items.
8. Placing Larger Objects: Placement of larger objects to enhance motor control.

#### Group B: Conventional Physiotherapy (26)

Participants in Group B performed conventional upper extremity exercises to improve functional mobility:

- Functional tasks such as folding towels, twisting bottle lids, flipping cards, turning keys, drawing lines with a pencil, and placing coins in a piggy bank.
- Slow, continuous stretching and strengthening exercises for the paretic upper extremities.

SPSS 23.0 is used for statistical analysis. A paired-sample t-test is used to compare within the groups. A p-value < 0.05 was considered statistically significant.



**Figure 1: Arm Ability Training**

## RESULTS

The average age of participants in Group A was  $44.00 \pm 9.61$  years, while in Group B it was  $46.92 \pm 9.86$  years. The mean difference in age between the two groups was 2.92 years.

**Table 1: Age of participants in Group A and Group B**

		Mean ( $\mu$ )	S.D.	MD	"t" value	"p" value
Age	Group – A	44.000	9.605	2.92	1.073	0.294
	Group – B	46.920	9.857			

S.D.: Standard Deviation MD: Mean Difference

In Group A, the mean completion time for the m-S NHPT decreased from  $113.78 \pm 3.14$  at pre-intervention to  $88.36 \pm 2.49$  post-intervention, showing a mean improvement of 125.42 ( $t = -42.368$ ,  $p < 0.05$ ).

The mean FMA-UL score increased from  $79.08 \pm 2.54$  at pre-intervention to  $90.52 \pm 2.92$  post-intervention, with a mean difference of 11.44 ( $t = 11.73$ ,  $p < 0.05$ ).

The mean SS-QOL-12 score improved from  $19.76 \pm 0.99$  at pre-intervention to  $40.12 \pm 1.24$  post-intervention, with a mean difference of 20.36 ( $t = 57.29$ ,  $p < 0.05$ ).

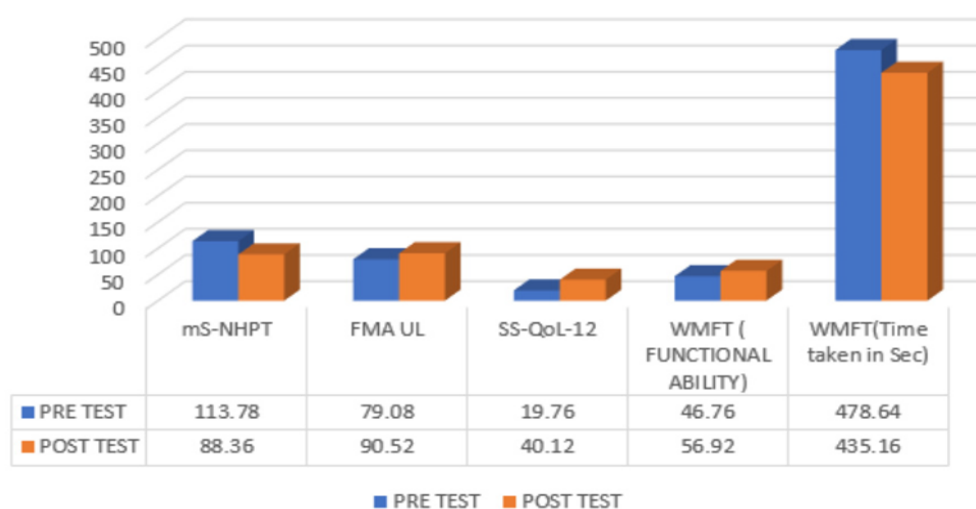
The mean WMFT (Functional Ability) score improved from  $46.76 \pm 1.47$  at pre-intervention to  $56.92 \pm 2.03$  post-intervention, with a mean difference of 10.16 ( $t = 20.93$ ,  $p < 0.05$ ). The mean WMFT (time in seconds) score improved from  $478.64 \pm 2.9$  at pre-intervention to  $435.16 \pm 2.22$  post-intervention, with a mean difference of 43.64 ( $t = -62.15$ ,  $p < 0.05$ ).

The above result statistically shows significant improvements in terms of mS-NHPT, FMA-UL, SS-QoL-12, and WMFT (functional ability and time taken in seconds) for sub-acute stroke subjects AAT with biofeedback techniques.

**Table 2: Pre- and Post-scores of Arm Ability Training with Biofeedback Techniques**

		Mean ( $\mu$ )	S.D.	MD	"t" value	"p" value
<b>mS-NHPT</b>	<b>Pre-test</b>	113.78	3.14	25.42	-42.368	0.3746
	<b>Post-test</b>	88.36	2.49			
<b>FMA-UL</b>	<b>Pre-test</b>	79.08	2.54	11.44	11.7355	0.01906
	<b>Post-test</b>	90.52	2.913			
<b>SS-QoL- 12</b>	<b>Pre-test</b>	19.76	0.99	20.36	57.2972	0.03538
	<b>Post-test</b>	40.12	1.24			
<b>Functional Ability WMFT</b>	<b>Pre-test</b>	46.76	1.477	10.16	20.9318	0.1816
	<b>Post-test</b>	56.92	2.038			
<b>WMFT (Time seconds)</b>	<b>Pre-test</b>	478.64	2.924	43.64	-62.1571	0.0174
	<b>Post-test</b>	435.16	2.221			

**Effects of AAT with Biofeedback techniques**



**Figure 2: Pre- and Post-scores of Arm Ability Training with Biofeedback Techniques**

**DISCUSSION**

The study objective was to find the effects of arm ability training with biofeedback techniques on improving the dexterity, functional ability of the upper limb, and quality of life in subacute stroke subjects. The outcome measures used were mS-NHPT, FMA-UL, SS-QOL-12, and WMFT. These outcomes were measured before the treatment and after the treatment in each group.

Strokes impair the brain's structural and functional integrity. The brain's intrinsic capacity to reorganize its structure and function in response to injuries and stimuli is known as plasticity. The process of plasticity begins after a stroke. Changes in neural activity and connection in terms of function and structure have been observed in the contralateral hemisphere's peri-lesional and distant areas. A number of interventions have been developed to improve the recovery of post-stroke subjects, some of which actively encourage the remaining neural circuits to promote plasticity (27).

Sensory inputs interact with the motor system as feedback for successful motor behaviours; they enable us to interact with the environment. The feedback for the somesthetic system originates from proprioceptive and cutaneous receptors and reaches to the parietal cortex. Cutaneous inputs are crucial for honing dexterous motions and enable people to do manual tasks in daily life, such as holding things or playing musical instruments. For upper extremity motor planning and adaptation, proprioceptive inputs are required (28).

The AAT with BF focuses on improving brain remodeling and restoration. The primary objective of Arm Ability Training (AAT) is to train the unique rehabilitation needs of stroke subjects by enhancing sensorimotor capabilities. AAT is a sophisticated motor training program designed specifically for survivors of stroke who have mild to moderate arm paresis. "High density" elements relevant to attaining significant recovery induced from training focusing on impairment are purposefully included in the design of AAT. Its design promotes intrinsic motivation, emphasizes motor learning, and has long-term advantages and effectively enhances a variety of sensorimotor hand and arm skills for stroke subjects.

#### CONCLUSIONS:

Based on the results, AAT led to statistically significant improvements in dexterity (mS-Nine Hole Peg Test), upper limb motor function (FMA-UL), WMFT, and life quality (SS-QOL) within the groups. Arm Ability Training with BF demonstrated significantly greater improvements in FMA-UL, WMFT, and SS-QOL scores, indicating a more pronounced effect on upper limb dexterity and perceived life quality. Arm Ability Training with BF may offer more focused gains in structured motor control and perceived life quality. Thus, incorporating arm ability training along with biofeedback techniques may enhance the recovery process in a sub-acute stroke rehabilitation program.

#### Conflict of Interest

Authors declare no conflict of interest.

#### Ethical consideration

The study was approved by institution Ethical Committee (EC/JCP/ 06/ 2024).

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*Original Article*

## BRIDGING HEALTHCARE AND COMMUNITY BY EXPANDING THE SCOPE OF MEDICAL SOCIAL WORK IN PUBLIC HEALTH CARE IN SINDH, PAKISTAN: CHALLENGES AND SOLUTIONS

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**ABSTRACT:**

This research study aimed to bridge healthcare and community and to expand the scope of medical social work in public health care, specifically in Sindh, Pakistan, by identifying challenges and proposing solutions within this context. Using qualitative semi-structured interviews with a sample of 18 participants (or respondents), our study explored the opinions of psychiatric social workers who provide professional help to patients with psycho issues through their service delivery in mental care hospitals, clinics, and community centers. However, our research findings explored many challenges, as expressed by participants during qualitative interviews, including the role ambiguity of health social workers among communities, resource scarcity, community-public power imbalances, the shortage of physical infrastructure, prevalent diseases, cultural barriers to treatment, people with disabilities, the impact of public organizational culture on their service delivery, and patients' education and poverty. Our research suggests that health policymakers in Sindh address those challenges as solutions, thereby effectively enhancing the role and responsibilities of social workers in public health care at the provincial level.

**KEYWORDS:** Challenges, Communities, Public Health Care, Medical Social Work, Solutions

### INTRODUCTION

Medical social work and services, a profession dedicated to enhancing the well-being of individuals and communities, have historically played a crucial role in the intersection of healthcare and societal welfare (1). Originating from late 19th-century efforts to address the social determinants of health, its evolution reflects a bidirectional influence between medicine and social work, profoundly shaping public health practices (2). This interdisciplinary approach recognizes that health outcomes are not solely determined by biological factors, such as child and maternal health, but are also significantly influenced by socioeconomic conditions, cultural contexts, and systemic inequalities (3). Hence, community health services are implicitly interconnected with public health care services in the current century.

In Sindh, Pakistan, this integrated approach is particularly pertinent, as the region grapples with significant disparities in healthcare access and pervasive socioeconomic challenges, especially in rural areas (4). In this context, this paper will explore the expanding scope of medical social work within Sindh province's public health care setting and thoroughly investigate the potential to bridge policy gaps between healthcare institutions and underserved poor communities, thereby fostering more equitable health outcomes.

A previously conducted study (1) concluded that the effectiveness of social work interventions, specifically in less developed regions such as Sindh province in Pakistan, significantly impacts public health policies and challenges the involvement of social workers in health care. Their findings will examine the specific challenges and opportunities for medical social workers in Sindh, advocating for their integral role in multidisciplinary healthcare teams and for the development of robust community-based health initiatives (5). The growing recognition of social workers' contributions in multidisciplinary teams within hospital settings further underscores their capacity to enhance holistic patient care and facilitate inter-professional collaboration, which is often lacking in many developing nations, like Mozambique, Tanzania, Malawi, Zambia, Zimbabwe, South Africa, and the Philippines (6,5,7). Furthermore, the implementation of medical social work in provincial hospitals in countries like Vietnam highlights its potential to significantly improve the quality and efficiency of healthcare services, especially when tailored to specific client needs (8). This becomes particularly vital in regions where social determinants of health, such as poverty, illiteracy, and low social capital, profoundly affect health outcomes and access to care (3). Hence,

the implementation of the Sustainable Development Goals (SDGs) is vital for bridging healthcare and communities as a solution, through efficiency in health services, improvement in health results, and advancement in community resilience, as the independent nature of SDGs only highlights the importance of integration of health care and communities within public health care (9). Hence, there is significant potential to integrate community health care services with public health care services.

### Background of Medical Social Work

The historical trajectory of medical social work demonstrates a continuous adaptation to evolving healthcare paradigms, moving from initial efforts focused on individual patient advocacy to a broader public health orientation that addresses systemic inequities and promotes community well-being (10). This evolution has been critical in solidifying the profession's role in addressing the complex interplay between social determinants of health care, particularly evident during global health crises such as the COVID-19 pandemic-related health challenges, where social workers provided crucial interventions, support, and advocacy for vulnerable populations (1). The expansion of medical social work into public health care services in low-income countries like Mozambique further underscores its critical role in promoting health equity and addressing multifaceted challenges through collaboration with public health professionals, thereby advancing the Sustainable Development Goals (SDGs) as elaborated by (6). Thus, the increasing complexity of patient needs and the growing recognition of integrated care necessitate the continued involvement and expansion of medical social work within diverse healthcare systems in Mozambique (11). This integration is essential because medical social workers provide individualised, client-centred support that addresses patients' psychosocial needs, complementing the routine clinical care provided by nurses and physicians and ultimately enhancing treatment adherence and patient satisfaction (12). Various recent studies, amongst others, highlight that the integration of social work in Karachi's public hospitals serves as a vital strategy for patient welfare, yet the efficacy of these services is often undermined by the "stigmatized labour" and high stress levels experienced by frontline workers (1, 13). Furthermore, (13) previously noted that the prevailing perception of these professionals as mere "charity distributors" rather than skilled clinical practitioners limits their role to financial gatekeeping, thereby preventing the provision of standard professional services required to address the complex psychosocial needs of vulnerable populations. This narrow mandate is particularly problematic in Karachi's major facilities like Jinnah Hospital, where the daily influx of 2,500 to 3,000 patients creates an acute demand for counselling and guidance that existing officers, crippled by financial constraints and a lack of local knowledge components in their training, are unable to meet (14). This resulted in a critical disconnect, with non-social work graduates frequently appointed to these roles, further diluting the professional standards necessary for effective interprofessional collaboration within the healthcare system (6). The systemic dysfunction is compounded by a lack of clear career progression beyond the director level and a deficiency in clinical supervision, both of which demotivate practitioners and hinder the proper application of direct practice methods. In addition to these structural deficits, (13) also report that the lack of private counselling rooms in public hospitals compromises patient confidentiality, while the absence of official transport prevents social workers from conducting essential field visits for follow-up care. The authors explain that the professional environment is further constrained by an entrenched hierarchical structure that prioritizes the medical model, positioning physicians as the primary authority figures while often disregarding the specialized competencies of social case workers in patient recovery. Beyond these internal hierarchies, practitioners are increasingly subjected to external interference from political and religious factions when managing sensitive cases like domestic violence or sexual assault, which often compromises their ability to provide impartial advocacy for vulnerable patients (13). This environment is further complicated by the fact that many Social Welfare Officers hold degrees in sociology rather than specialized social work, leading to a profound lack of familiarity with assessment methodologies necessary for clinical case management (13). This study was a qualitative study designed to explore challenges in medical social work in a limited resource region of Sindh, Pakistan.

## METHODS

### *Study Design, Methods and Sampling*

This research utilizes a qualitative descriptive approach, conducted during March to May 2025, employing semi-structured face-to-face interviews to capture respondents' perceptions, opinions, and socio-economic descriptive data (15) related to the effective involvement of social workers in bridging psychiatric health care for communities with their enhanced role in public medical care across Sindh,

Pakistan. Using purposive sampling, a qualitative questionnaire was administered to interview 18 psychiatric social workers, working in different types of community health centers, and non-governmental organizations (NGOs), like social service agencies, in collaboration with diverse public or private health institutions, such as psychiatric hospitals and mental health clinics, to evaluate their professional satisfaction and the specific barriers they face with implications of theoretical frameworks in clinical settings to ensure holistic care for patients (16). Following a previous study (6), during the final survey, the semi-structured questionnaire was tested with four respondents to ensure the validity of questions related to the aim of this study and to make minor modifications immediately.

### *Data Collection and Analysis*

Using semi-structured interviews mirroring the aim of the study was to collect qualitative data on a comprehensive range of topics from respondents (or psychiatric social workers) on the role ambiguity of health social workers among communities, resource scarcity, community-public power imbalances, the shortage of physical infrastructure, prevalent diseases, cultural barriers to treatment, people with disabilities, the impact of public organizational culture on their service delivery, and patients' education and poverty. Our qualitative survey results indicate that there were 11 male and 7 female participants, as the number of female social workers is usually lower than that of male social workers due to socio-cultural constraints on women across Pakistan. Furthermore, the results show that the average age of respondents was 35 years, with most holding certificates in university and social work training. On average, psychiatric social workers had 5 years of experience in the field.

## **RESULTS**

A total of 18 participants were included in this study including 11 males and 7 females, aged between 20 to 60 years. A summary of the demographic characteristics is given in Table 1.

**Table 1: Socio-economic characteristics of participants (social workers)**

<b>Characteristics (Variables)</b>	<b>Statistics/ Number</b>	<b>Average</b>
<b>Age (years)</b>		
20 – 30	4	35
31 – 40	11	
> 40	3	
<b>Education / Training</b>		
Primary education	1	-----
Secondary education	3	
University education	6	
Social training or a degree certificate	5	
Psychology training or a degree certificate	3	
<b>Years of Social work experience (years)</b>	-----	5 years
<b>Total Sample (n) = No. of respondents</b>	<b>18</b>	-----

Most the participants had university level education (n=6) or a social training (n=5), only a small number had early education (Table 1). The findings of the study indicate that medical social work in Sindh is severely compromised by a lack of specialized supervisory personnel, as many hospital placements are currently managed by non-professional staff who lack the necessary social work educational background to provide clinical oversight.

Various social workers' opinions are explained as follows;

*Oh ... many community members don't even know the social worker's status. They perceive social workers as nice human beings who help patients, even without proper education and training. Sometimes, they give some money to social workers as a gift (Respondent 9).*

Another respondent was interviewed and explained.

*Communities and NGOs have inadequate resources. They rely heavily on donations or charity coming from middle-class and/or poor people. As a result, it affects our health delivery services (Respondent 4).*

Many participants expressed that the public organizational health care culture, cultural barriers, patients' education and poverty mainly affect psychiatric social workers' performance. This research, therefore, also explored these issues to bridge the gap between communities and health care with an effective involvement of public health care in Sindh province of Pakistan.

Regarding the above issue, a few participants expressed.

*... We don't see appropriate or supportive consideration from health professionals in the public health sector when performing this social work, on the one hand, especially in marginalized areas. On the other hand, communities have cultural barriers, a lack of education, and poverty, which affect our role and responsibilities (Respondents 2, 6 and 13).*

Regarding a question raised about the professional silos and unequal power dynamics that often relegate social workers to secondary status within multidisciplinary teams, various interviewees expressed.

*Umm .... We social workers have often found that there is a power inequality, specifically when we perform in multidisciplinary teams. We also found inadequate physical infrastructure and insufficient counselling space for dedicated staff and patients in most hospitals in Sindh province. As a result, these issues stop us from performing private counselling sessions effectively (Respondents 10, 17, 18).*

The two interviewees revealed.

*Oh . . . shortages of finances are a big challenge in conducting this social work. Low salaries and a shortage of service delivery inputs and infrastructure adversely affect our social work performance (Respondents 1 and 14).*

## DISCUSSION

Our research findings from Sindh province of Pakistan mirror organizational challenges observed in Saudi Arabia and Iran, where medical social workers are increasingly recognized as vital human resources for national health strategies yet remain constrained by a semi-professional status that triggers high levels of work-related stress and exhaustion (18,19). Driven primarily by the fact that many practitioners are forced to perform non-specialized tasks, such as medicinal procurement and price auditing, for which they have no formal pharmacological training (18). This displacement from clinical practice to clerical oversight is symptomatic of a top-down bureaucratic structure (or power imbalance) where practitioners often follow orders rather than exercising professional discretion, a reality reflected in reports that a significant portion of their daily labor is dictated by administrative mandates rather than patient-centered psychosocial needs (19). This erosion of professional autonomy is further compounded by the communities or public's limited understanding of social casework's specialized reputation in developing countries, like in Sindh, Pakistan, where extreme poverty and inadequate healthcare financial resources currently representing only 2.8% of Pakistan's GDP often reduce the perceived role of the psychiatric social worker to a mere facilitator of financial aid rather than a trained clinician capable of managing complex psychological and economic anxieties (13). This professional distress is further intensified in the Sindh context as practitioners must navigate a "hybrid" role, where they are pressured to adapt to externally dictated organizational policies that favor administrative efficiency over the core clinical values of social inclusivity and patient advocacy (13). In contrast to the private sector, where specialized welfare services for non-affording patients are virtually non-existent, the authors further elaborate that social workers in Sindh's public hospitals must single-handedly manage the "Parchi fee" (or money gift) system and navigate a landscape devoid of any formal government monitoring mechanism to audit service quality or clinical standards. Also, a shortage of infrastructure and space in medical centers poses a big obstacle for social workers when they do psychiatric counselling. Due to a lack of education and specialized training of social workers, in addition to patients' cultural barriers, illiteracy and poverty are other equivalent issues to be addressed if public health policy makers in Pakistan make a health policy in the future, aiming at bridging healthcare and community and expanding the scope of medical social work in public health, specifically in Sindh, Pakistan. Following previously reported studies (6) and (19), that specifically addressed the professional silos and unequal power dynamics that often relegate social workers to secondary status within multidisciplinary teams, our study also explores that this power imbalance is further intensified by a critical shortage of physical infrastructure, as the lack of dedicated office space in many Sindh province's hospitals prevents social workers from conducting

private counseling sessions, thereby compromising the dignity and confidentiality of patients during sensitive psychosocial assessments.

Moreover, the lack of professional field supervisors in many Sindh hospitals forces students and practitioners to navigate complex psychosocial cases without adequate clinical mentorship, a situation exacerbated by gendered perceptions that frame social work as a welfare-oriented female profession rather than a technical healthcare discipline (20). This perception is deeply rooted in a national cultural ethos that continues to view social work as a voluntary, unpaid activity of a "selfless sort" rather than a paid professional practice, leading to a systemic abhorrence toward the idea of professional social workers receiving wages for what the public considers inherently noble service (14). Consequently, this cultural preference for unpaid sacrifice undermines the development of professional social work education in Pakistan, which struggles to establish a distinct indigenous identity while relying heavily on American philosophical frameworks and techniques that may not fully align with the local socioeconomic reality (21). This theoretical disconnect is further exacerbated by the absence of a "National Council for Social Work Education and Training," leaving the province without standardized licensing or a governing body to distinguish qualified professionals from non-specialized humanitarian actors (14). The above statements align with previous literature, such as studies reported previously (6) and (19), which specifically address professional silos and unequal power dynamics that often relegate social workers to secondary status within multidisciplinary teams. Thus, our study also explored that this power imbalance is further intensified by a critical shortage of physical infrastructure, as the lack of dedicated office space in many hospitals in Sindh province prevents social workers from conducting private counselling sessions, thereby compromising the dignity and confidentiality of patients during sensitive psychosocial assessments. Consequently, the lack of professional authority and institutional autonomy within the broader healthcare hierarchy prevents these workers from executing complex tasks, as their contributions are frequently overshadowed by administrative constraints and the dominance of medical practitioners (19). This systemic marginalisation is further evidenced by data showing that nearly two-thirds of social workers feel they lack the same level of professional authorisation as their medical colleagues, a disparity that actively discourages them from introducing innovative psychosocial interventions or grief counselling techniques (19), (22). The authors further explain that this absence of mentorship is linked to a rigid centralization of authority and outmoded hospital hierarchies that prevent practitioners from participating in key organizational decisions or establishing formal linkages with another medical unit.

The statements of respondent 10, 17 and 18 were aligned with previous literature, such as studies by (6) and (19), which specifically address professional silos and unequal power dynamics that often relegate social workers to secondary status within multidisciplinary teams. Thus, our study also explored that this power imbalance is further intensified by a critical shortage of physical infrastructure, as the lack of dedicated office space in many hospitals in Sindh province prevents social workers from conducting private counselling sessions, thereby compromising the dignity and confidentiality of patients during sensitive psychosocial assessments. Consequently, the lack of professional authority and institutional autonomy within the broader healthcare hierarchy prevents these workers from executing complex tasks, as their contributions are frequently overshadowed by administrative constraints and the dominance of medical practitioners (19). This systemic marginalization is further evidenced by data showing that nearly two-thirds of social workers feel they lack the same level of professional authorization as their medical colleagues, a disparity that actively discourages them from introducing innovative psychosocial interventions or grief counseling techniques (19), (22). The authors further explain that this absence of mentorship is linked to a rigid centralization of authority and outmoded hospital hierarchies that prevent practitioners from participating in key organizational decisions or establishing formal linkages with another medical unit. The research results reveal that the challenges as mentioned above are exacerbated by a significant budgetary shortfall (or shortage of financial resources), with current funding allocations for professional development often amounting to less than 200 dollars per worker, rendering specialized training in advanced psychosocial interventions (17). In addition to these financial constraints, the professional growth of social case work in Sindh has been significantly stunted by a fifteen-year government ban on new appointments that lasted until 2016, a policy gap that forced existing staff to manage Patient Welfare Association funds from sources like Zakat and Bait-ul-Maal without sufficient manpower (13). This personnel deficit is compounded by rigid bureaucratic protocols, as more than half of the surveyed practitioners expressed that inflexible hospital policies and the requirement to refer all minor procedural matters to higher-level administrators severely restrict their ability to respond effectively to immediate social issues (19). The research results reveal that the challenges as mentioned above are exacerbated by a significant

budgetary shortfall (or shortage of financial resources), with current funding allocations for professional development often amounting to less than 200 dollars per worker, rendering specialized training in advanced psychosocial interventions (17). In addition to these financial constraints, the professional growth of social case work in Sindh has been significantly stunted by a fifteen-year government ban on new appointments that lasted until 2016, a policy gap that forced existing staff to manage Patient Welfare Association funds from sources like Zakat and Bait-ul-Maal without sufficient manpower (13). This personnel deficit is compounded by rigid bureaucratic protocols, as more than half of the surveyed practitioners expressed that inflexible hospital policies and the requirement to refer all minor procedural matters to higher-level administrators severely restrict their ability to respond effectively to immediate social issues (19). In detail, the systemic lack of professionalization, coupled with inadequate infrastructure and pervasive resource scarcity, contributes significantly to psychological distress and burnout among healthcare workers, particularly female professionals, in Sindh. This phenomenon is particularly pronounced among women doctors who face significant work-life conflicts, gender discrimination, and an unsafe work environment, leading to high attrition rates within the Pakistani healthcare system (26). Furthermore, medical students themselves frequently report elevated levels of anxiety, depression, and a diminished sense of accomplishment, underscoring a broader systemic issue of mental health challenges within the medical education and practice pipeline (27). These pervasive stressors, compounded by hierarchical institutional structures that limit voice and autonomy, create a challenging environment for fostering a robust professional identity and patient advocacy (28).

The consistent exposure to these demanding conditions, including long working hours and emotional labor, significantly contributes to the elevated burnout rates and mental health issues observed among medical professionals, particularly women in gynecology and emergency departments, across Pakistan (29). This professional burnout is further exacerbated by systemic issues such as poor healthcare infrastructure, high patient loads, and limited career progression opportunities, which are prevalent in many low- and middle-income countries (30). The absence of adequate mental health facilities and the pervasive stigma surrounding mental illnesses exacerbate these issues, with mental health conditions often attributed to supernatural causes (31). These factors collectively contribute to a higher susceptibility to stress, anxiety, and depression among medical students and practicing professionals, hindering the effective provision of patient care and often leading to devastating outcomes such as physician suicide (32,33). Therefore, addressing the root causes of burnout and psychological distress among healthcare workers, especially women, through comprehensive support systems and improved working conditions is crucial for maintaining the well-being of the healthcare workforce and enhancing the resilience of the healthcare system in Sindh. The challenges faced by female healthcare professionals, including medical students, are particularly acute, with studies indicating higher rates of depressive symptoms among them, suggesting a need for gender-specific interventions to mitigate disparities and address the unique stressors they face (35,36).

Our research overall suggests that the combination of social work in Karachi's public hospitals serves as a vital strategy for patient welfare, yet the efficacy of these services is often undermined by the "stigmatised labour" and high stress levels experienced by frontline workers. Keeping in view the above challenges faced by social workers in their roles and responsibilities, while working in parallel with the affected communities, and the challenges they confront, besides their appropriate recognition, the provincial health department, the government of Sindh, Pakistan, must address these challenges appropriately, which already offer solutions, in their health policy in the near future.

#### CONCLUSIONS:

Our study aimed to bridge healthcare and community and expand the scope of medical social work in the public health sector, specifically in Sindh, Pakistan. Using qualitative semi-structured interviews, with a sample of 18 respondents, our study explored the opinions of psychiatric social workers, working to professionally help psycho patients using their service deliveries, like transportation, patients' admission at public and private hospitals and clinics, psycho social counselling. However, many challenges, as expressed by participants during qualitative interviews, were recognized, including the role ambiguity of health social workers among communities, resource scarcity, community-public power imbalances, the shortage of physical infrastructure, prevalent diseases, cultural barriers to treatment, people with disabilities, and impact of public organizational culture on their service delivery, and patients' education and poverty.

## Conflict of Interest

Authors declare no conflict of interest.

## Ethical consideration

The study was approved by local Research Ethic Committee.

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### Case Report

## ANTERIOR MEDIASTINAL MASS CAUSING SUPERIOR VENA CAVA OBSTRUCTION: A CASE REPORT

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#### ABSTRACT

Anterior mediastinal masses are uncommon but potentially life-threatening, particularly when they cause vascular compromise such as superior vena cava (SVC) obstruction. Thymoma is the most frequently encountered anterior mediastinal tumour in adults and may produce critical complications including complete SVC occlusion, haematological toxicity, and post-treatment pulmonary sequelae.

**CASE PRESENTATION:** A 53-year-old woman from Gilgit Baltistan presented with a 20-day history of fever and cough. Contrast-enhanced computed tomography of the chest revealed a large infiltrative anterior mediastinal mass encasing the great vessels and causing complete SVC obstruction with significant collateral venous formation. She was treated with concurrent chemoradiotherapy (CCRT), with serial imaging demonstrating partial tumour regression. However, persistent SVC obstruction, post-radiation pulmonary fibrosis, and progressive haematological toxicity — including dimorphic anaemia, leucopenia, and thrombocytopenia — developed as sequelae of treatment. This case highlights the importance of early imaging evaluation, a multidisciplinary treatment approach, and diligent haematological surveillance in patients with anterior mediastinal masses complicated by SVC obstruction. Holistic nursing care addressing both the physical and psychosocial burden of long-term malignancy is equally essential to optimise patient outcomes.

**KEYWORDS:** superior vena cava obstruction; anterior mediastinal mass; thymoma; concurrent chemoradiotherapy; haematological toxicity

### INTRODUCTION

The mediastinum is the central compartment of the thoracic cavity, situated between the lungs and extending from the sternum anteriorly to the vertebral column posteriorly. It is anatomically divided into the superior, anterior, middle, and posterior regions, each housing vital structures including the heart, trachea, oesophagus, thymus, major blood vessels, and lymph nodes. The mediastinum plays a crucial role in supporting cardiopulmonary function and protecting these essential organs, and its central location renders it a common site for various pathological conditions, including tumours (1).

In this case, the diagnosis is thymoma, a tumour arising from thymic epithelial cells and most commonly located in the anterior mediastinum. Thymic epithelial tumours are rare, with an estimated annual incidence of 1–5 per million population globally (2). In Asian countries, and particularly in China, anterior mediastinal masses are reportedly more prevalent, with thymomas accounting for 30.6% to 30.7% of all mediastinal neoplasms, surpassing benign mediastinal cysts and neurogenic tumours (3). Thymoma arises from thymic epithelial cells and is most commonly found in the anterior mediastinum (4). In 2015, the World Health Organization classified tumours of the thymus into three main categories: thymomas, thymic carcinomas, and thymic neuroendocrine tumours (5).

### CASE PRESENTATION

A 53-year-old woman from Gilgit Baltistan presented to the Emergency Department of a private tertiary care hospital in Karachi, Pakistan, on 19 December 2022, with a 20-day history of fever and cough. A chest computed tomography (CT) scan had been performed at a district hospital in Gilgit Baltistan, following which she was referred to the cardiothoracic service in Karachi for further evaluation.

On admission, the patient was alert, afebrile, and mildly tachypnoeic and hypertensive. Respiratory examination revealed bilateral crepitations and diminished air entry. Chest radiography demonstrated bilateral pleural effusions. Neck veins were distended; no lymphadenopathy or peripheral oedema was observed.

### Imaging Findings

Serial contrast-enhanced CT scans of the chest demonstrated progressive reduction in the size of the anterior mediastinal mass, consistent with the therapeutic effect of concurrent chemoradiotherapy (CCRT) (Table I). Despite partial tumour regression, the residual mass continued to cause complete obstruction of the superior vena cava (SVC) and non-visualisation of both brachiocephalic veins, resulting in significant collateral venous circulation through the anterior and posterior chest wall soft tissues. Dilated azygos and hemiazygos veins were noted, with a small filling defect in the azygos vein at the T8–T10 level.

Post-radiation fibrosis and traction bronchiectasis were identified in the anterior segment of the right upper lobe, the medial right middle lobe, and the posterior right lower lobe, with minimal ground-glass opacities and fibrotic changes in both lungs. No pleural effusion, pulmonary nodules, or distant metastases were identified, findings consistent with local disease control and treatment-related pulmonary sequelae.

Date of CT Scan	Mass Dimensions (AP × T × CC, mm)	Key Findings
29 March 2023	52 × 44 × 115	Baseline; complete SVC obstruction; collateral venous circulation
12 March 2024	48 × 17 × 76	Partial regression post-CCRT; persistent SVC occlusion; post-radiation fibrosis
8 April 2025	43 × 16 (two dimensions)	Further size reduction; infiltrative mass; traction bronchiectasis; no metastases

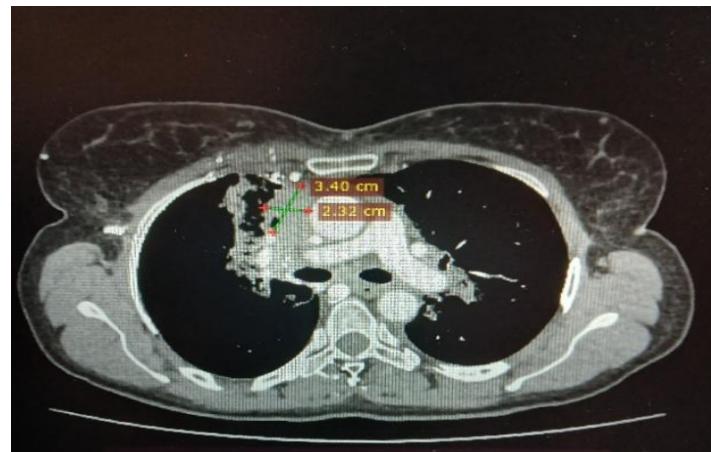
**Table I:** Serial CT chest findings demonstrating tumour response to CCRT and persistent SVC obstruction. AP = anteroposterior; T = transverse; CC = craniocaudal; CCRT = concurrent chemoradiotherapy; SVC = superior vena cava.

#### Before Chemo radiotherapy

#### After Chemo radiotherapy



29<sup>th</sup> March 2023 (52x44x115mm)



12<sup>th</sup> March 2024(48x17x76mm)

## DISCUSSION

Anterior mediastinal masses encompass a range of pathologies, including thymomas, lymphomas, germ cell tumours, and thyroid conditions. In adults, thymic neoplasms and lymphomas are the most frequent causes. Given the confined space of the mediastinum, these tumours can exert significant pressure on surrounding structures, resulting in catastrophic complications such as SVC obstruction. [6] We report a case of an infiltrating anterior mediastinal tumour in a 53-year-old woman who initially presented with systemic symptoms and subsequently developed complete SVC obstruction.

The initial symptoms of fever and cough were non-specific, which may have contributed to diagnostic delay. Subsequent imaging, however, demonstrated a marked anterior mediastinal mass. This case illustrates the pivotal role of contrast-enhanced CT in evaluating tumour size, extent of infiltration, and vascular encasement. The CT findings demonstrated not only tumour invasion but also collateral venous formation and haemodynamic changes consistent with SVC obstruction, necessitating urgent oncological attention.

The haematological complications in this case followed a progressive course, beginning with iron deficiency anaemia (7), evolving to dimorphic anaemia, and ultimately culminating in pancytopenia comprising leucopenia and thrombocytopenia. This progression is attributable to the combined effects of chronic disease and CCRT (8). Dimorphic anaemia arises from concurrent nutritional deficiencies and may coexist with anaemia of chronic disease or megaloblastic processes. The development of neutropenia and thrombocytopenia following CCRT is consistent with bone marrow suppression, a well-recognised adverse effect of combined modality therapy (9). These findings underscore the importance of close haematological monitoring in patients receiving intensive oncological treatment.

Although partial tumour regression was achieved, the patient continued to experience complications from residual tumour burden, as well as treatment-associated pulmonary fibrosis and bronchiectasis. These post-radiation changes may necessitate long-term respiratory support and surveillance. Furthermore, the persistence of SVC obstruction despite tumour response suggests irreversible structural damage or fibrotic occlusion of the vessel, and endovascular or surgical intervention should be considered based on clinical presentation.

Several important clinical lessons emerge from this case. First, early detection and characterisation of mediastinal pathology are paramount, as delayed treatment can result in compression of critical structures within the mediastinum. Second, the management of such tumours necessitates a multidisciplinary approach incorporating oncological intervention, supportive care, radiological surveillance, and, where appropriate, surgical consultation. Third, this case emphasises the integral role of holistic nursing care, encompassing monitoring for treatment side effects, promoting respiratory function, and addressing the psychosocial burden of chronic malignancy.

Concurrent chemoradiotherapy can achieve tumour reduction and disease control in anterior mediastinal masses with vascular involvement (10). However, residual complications such as SVC syndrome and haematological toxicity require close ongoing monitoring. This case reinforces the value of both advanced diagnostic assessment and comprehensive nursing care in achieving optimal patient outcomes.

### ***Clinical Recommendations***

Based on the findings of this case, the following clinical recommendations are proposed:

- Prompt imaging with contrast-enhanced CT should be performed in patients with unexplained respiratory symptoms and systemic signs, particularly prolonged fever, when mediastinal pathology is suspected. Early diagnosis may prevent the development of SVC obstruction.
- Regular full blood count monitoring is essential in patients receiving CCRT, as early detection of anaemia, leucopenia, or thrombocytopenia enables proactive management, including transfusions, haematopoietic growth factors, or dose adjustments, thereby preventing serious clinical sequelae.
- Nurses play a pivotal role in recognising signs of SVC syndrome, monitoring respiratory status, managing treatment side effects, and providing emotional and psychosocial support. Patient education regarding symptom reporting and medication adherence is critical.
- Long-term follow-up with serial imaging and pulmonary function testing is recommended given the risk of post-treatment complications including pulmonary fibrosis, bronchiectasis, and vascular compromise. Interventional radiology or surgical approaches may be indicated for persistent SVC syndrome.

### **CONCLUSION**

This case illustrates the importance of clinical expertise and a multidisciplinary approach in managing anterior mediastinal masses complicated by SVC obstruction. The clinical course — characterised by initially non-specific respiratory symptoms followed by progressive haematological toxicity — underscores the need for early imaging evaluation, collaborative oncological management, and diligent supportive care. Although the vascular response to CCRT was only partial, long-term follow-up of the vascular architecture and haematological profile reflects the chronic nature of these malignancies and their treatment effects. For nursing professionals, this case reaffirms the importance of holistic, patient-centred care addressing both the physical and psychosocial dimensions of living with chronic malignancy. Early recognition, interdisciplinary collaboration, and compassionate patient support represent the cornerstones of achieving the best possible outcomes in patients with these challenging thoracic pathologies.

### **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

### **PATIENT'S CONSENT**

Written informed consent was obtained from the patient for publication of this case report and accompanying clinical data.

### **ETHICAL CONSIDERATION**

This case report was conducted in accordance with the principles of the Declaration of Helsinki. Patient confidentiality was strictly maintained throughout.

### **Authors' Contribution**

RS and AM contributed to the study conception, clinical data acquisition, and manuscript drafting. GA contributed to clinical management and critical revision. HA contributed to data collection and manuscript review. All authors approved the final version for publication.

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