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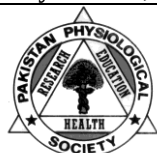
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EDITORIAL

ARTIFICIAL NEURAL NETWORKS IN PHYSIOLOGY:
EMERGING ROLES IN EDUCATION AND RESEARCH

Ahmed Badar

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Artificial neural networks (ANNs) have become central to biomedical science, offering new ways to understand complex physiological systems, enhance teaching, and accelerate research. Their capacity to model nonlinear biological processes makes them valuable tools for physiology education, where they support interactive simulations, adaptive learning, and computational training for undergraduate and graduate students. In research, ANNs enable the analysis of large datasets, prediction of physiological responses, and integration of experimental as well as computational approaches. Beyond these domains, ANNs support personalized medicine, real-time physiological monitoring, drug development and pharmaceutical manufacturing. As these technologies continue to evolve, their influence on physiology is expected to deepen, offering new opportunities for discovery and innovation.

Keywords: Artificial Neural Networks, Computational models, Physiological systemsPak J Physiol 2026;22(2):69–70, DOI: <https://doi.org/10.69656/pjp.v22i2.1958>

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Artificial neural networks (ANNs) are computational systems inspired by the structure and function of biological neural networks. They consist of interconnected nodes ('neurons and nuclei') that process information through weighted connections, allowing them to learn patterns from data and perform tasks such as classification, prediction, and pattern recognition. Their ability to model nonlinear and multidimensional relationships makes them particularly suited to physiological systems, which often involve complex interactions that cannot be captured by simple linear models. As physiology increasingly intersects with computational science, ANNs have emerged as essential tools for understanding biological complexity.¹

Physiology is inherently complex, requiring students to understand dynamic processes such as membrane potentials, cardiovascular regulation, and endocrine feedback loops. In physiology education, ANNs are reshaping how students engage with difficult concepts. ANNs enable the creation of interactive simulations that allow learners to manipulate variables and observe dynamic physiological responses, improving comprehension of processes such as membrane potentials, cardiovascular regulation, and endocrine feedback loops. These tools help bridge the gap between theoretical knowledge and system-level understanding, which is often challenging for students encountering physiology for the first time.²

ANNs also support personalized learning through adaptive educational platforms. ANN-driven systems can identify knowledge gaps by analyzing student performance data and adjust content difficulty accordingly. This approach aligns well with competency-based medical and health sciences education, where individualized progression is increasingly emphasized. Although these technologies are not exclusive to physiology, their integration into

biomedical curricula is growing, offering students a more tailored and effective learning experience.²

At the post-graduate level, training in computational physiology is becoming more prominent, and ANNs play a central role in this shift. Students are increasingly exposed to ANN-based modelling in areas such as electrophysiology, pharmacokinetics, and systems biology. This training prepares future physiologists and biomedical scientists to work in interdisciplinary environments where computational and experimental approaches are deeply intertwined. As data-driven research becomes the norm, familiarity with ANN methodologies is no longer optional but essential.

In physiological research, ANNs have become powerful tools for modelling complex biological systems. Their capacity to capture nonlinear dynamics allows researchers to simulate neuronal firing patterns, cardiac electrophysiology, metabolic regulation, and other processes that are difficult to represent using traditional mathematical models. By integrating principles from computer science, nonlinear dynamics, and chaos theory, ANNs enable the study of emergent behaviours that arise from interactions among multiple physiological variables.

ANNs also facilitate data-driven discovery in physiology. Modern research generates vast datasets from genomics, proteomics, imaging, and wearable biosensors.³ ANNs can identify patterns within these datasets, revealing relationships that may not be apparent through conventional statistical methods. For example, ANNs have been used to predict drug-target interactions, analyze chemogenomic space, and explore toxicity profiles, demonstrating their utility in bridging molecular data with physiological outcomes.⁴

Another important contribution of ANNs to physiology research is their ability to support hypothesis generation. By predicting the outcomes of physiological

experiments, ANN models can guide researchers toward the most promising experimental directions. This predictive capability accelerates research cycles and reduces the need for extensive trial-and-error experimentation, particularly in fields such as electrophysiology, where experimental procedures can be technically demanding and time-consuming.^{2,3}

Beyond drug development, ANNs are contributing to personalized and precision medicine by analyzing patient-specific data to predict therapeutic responses.³ This is particularly relevant in physiology-based specialties such as cardiology, endocrinology, and neurology, where individualized treatment strategies can significantly improve outcomes.³ ANNs also support real-time physiological monitoring through integration with wearable biosensors, enabling continuous assessment of parameters such as heart rate variability, glucose levels, and respiratory patterns.³

The integration of ANNs with emerging technologies such as digital twins, high-throughput screening platforms, and advanced biosensors further expands their potential impact on physiology. Digital twins, that are virtual models of individual patients, use ANN-based simulations to predict physiological responses and guide personalized treatment strategies. High-throughput screening platforms incorporate ANN-driven predictions to prioritize experimental testing, improving efficiency and reducing costs.¹

Artificial neural networks are thus reshaping physiology education, research, and drug development in profound ways. Their ability to model complexity, analyze large datasets, and generate predictive insights positions them as essential tools for the next generation of physiologists and biomedical scientists.⁵ As ANN technologies continue to evolve, their integration into physiology will deepen, offering unprecedented opportunities for discovery, innovation, and personalized healthcare. At the same time, responsible implementation will require attention to issues of interpretability, bias, and ethical use, ensuring that these powerful tools contribute positively to biomedical science.

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EDITORIAL

PREPARE FOR ANOTHER HOTTER SUMMER THAT MAY IMPACT
YOUR HEALTH

Tehseen Iqbal

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Globally next few years will be hotter than before. Heat wave is expected in Pakistan also. Heat stress is the leading cause of weather-related deaths and can exacerbate underlying illnesses including cardiovascular disease, diabetes, mental health, asthma. Heat stroke is a medical emergency with a high-case fatality rate. Infants and elderly persons are more prone to temperature changes. Above environmental temperature around 33–35 °C heat stress begins. When the body experiences heat stress and body temperature rises beyond normal, cells release heat shock proteins (HSP) that can trigger inflammatory responses mediated by cytokines. This process contributes to endothelial damage, vasodilation, and widespread cell death, resulting in potential organ damage. When an unacclimatized person is exposed to extreme heat for prolonged time, the person may suffer heat exhaustion or heat stroke. Heat exhaustion is a heat-related illness caused by excessive sweating, which leads to loss of water and electrolytes and a decreased blood volume. Without replacement of water and electrolytes, this will lead to decreased arterial pressure and feelings of dizziness, muscle cramps, and fainting. Heat exhaustion, if untreated, can lead to heat stroke. World Health Organization (WHO) and National Disaster Management Authority (NDMA) advised that people should drink water frequently, especially when going outside; avoid heat exposure by limiting outdoor activities between 10 AM to 4 PM; use light coloured and loose-fitting clothes; never leave children in parked vehicles.

Keywords: Heat shock proteins, Heat stress, Heat stroke, Heat wave

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Global warming damages the environment and threatens the life on earth. Globally this is expected that 2026 will be the fourth successive year in which temperature will have reached at least 1.4 °C above pre-industrial levels (1850-1900).¹ Summer 2026-2027 in Pakistan is expected to be intensely hot and the Pakistan Meteorological Department (PMD) has warned of severe heat waves across the country, creating significant health risks²

A heatwave is a period where local excess heat accumulates over a sequence of unusually hot days and nights. Heatwaves and prolonged excess heat conditions are increasing in frequency, duration, intensity and magnitude due to climate change. Even low and moderate intensity heat waves can impact the health and well-being of vulnerable populations. It is difficult to complete work or learning in very hot weather and heatwaves may lead schools and other institutions to close. Heatwaves can also be associated with hazardous air pollution events. Heat stress is the leading cause of weather-related deaths and can exacerbate underlying illnesses including cardiovascular disease, diabetes, mental health, asthma, and can increase the risk of accidents and transmission of some infectious diseases. Heat stroke is a medical emergency with a high-case fatality rate.³

Environmental temperature has greater impact on those who engage in physical work in the outdoors, such as labourers, farmers, military personnel, and fire-fighters. Infants and elderly persons are more prone to

temperature changes. Although heat production and heat loss mechanisms are functional in neonates and children, these are easily exhaustible, leading to the development of hypothermia or hyperthermia. Elderly show decreased thermos-sensitivity, causing delayed or insufficient responses to thermal changes leading them to be more susceptible to hypothermia or hyperthermia.

Essentially all the energy spent by the body is eventually converted into heat. As long as skin temperature is greater than the temperature of the surroundings, heat can be lost by radiation, conduction and convection. At very high ambient temperatures, the only means by which the body can rid itself of heat is by evaporation.⁴ The temperature range needed for the body's metabolic processes to function correctly is between 37±0.5 °C (98.6±0.9 °F). The ability to regulate body temperature within a physiological range remains a key requirement for survival and daily functions.

Temperature comfort zone for human body is between 20–25 °C; body feels warm at 25–30 °C, body feels hot above 30 °C, body's heat loss mechanisms start becoming ineffective around 33–35 °C. Above this range, heat stress begins.⁵ The human body employs several physiological mechanisms to prevent heat exhaustion when exposed to high temperatures. Sweating and evaporative cooling, cutaneous vasodilation and heat acclimatization are developed to tolerate heat. During acclimatization body starts earlier and increased sweating but the sweat contains less

amount of salts. The human body typically requires 7 to 14 days of consistent daily exposure of 60 to 90 minutes to heat to achieve full acclimatization. Physical activity in the heat accelerates the process compared to sitting still. Acclimatization is temporary and benefits begin to fade within a week and are largely lost after 2 to 3 weeks.⁶

When the body experiences heat stress and temperatures rise beyond normal, cells release heat shock proteins (HSP) that can trigger inflammatory responses mediated by cytokines. This process contributes to endothelial damage, vasodilation, and widespread cell death, resulting in potential organ damage. Untreated, patients may become comatose and hypotensive, and may experience shock, cardiac collapse and death.

Studies between year 2000 and 2019 show approximately 489,000 heat-related deaths each year, with 45% of these in Asia and 36% in Europe.⁷ When an unacclimatized person is exposed to extreme heat for prolonged time, the person may suffer heat exhaustion or heat stroke. Heat Exhaustion is a heat-related illness caused by excessive sweating, which leads to loss of water and electrolytes and a decreased blood volume. Without replacement of water and electrolytes, this will lead to decreased arterial pressure and feelings of dizziness, muscle cramps, and fainting. Heat exhaustion, if untreated, can lead to heat stroke. Heat Stroke is a body temperature more than 40 °C (104 °F) accompanied by dry, hot skin and central nervous system abnormalities such as convulsions, delirium, and/or coma. An alternative definition is that heatstroke is a form of hyperthermia associated with a systemic inflammatory response that leads to multiorgan dysfunction, especially encephalopathy.⁸

The negative health impacts of heat are predictable and largely preventable with specific public health and multi-sectoral policies and interventions. WHO has issued guidance for public health institutions to identify and manage extreme heat risks. Action on climate change combined with comprehensive preparedness and risk management can save lives now and in the future.³ WHO and NDMA advised that people should drink water frequently, especially when going outside; avoid heat exposure by limiting outdoor

activities between 10 am to 4 pm; use light coloured and loose-fitting clothes; never leave children in parked vehicles.

WHO's "Beat the Heat" initiative, running from January 2025 to June 2026, aims to protect workers, attendees, and local communities from extreme heat and other environmental hazards and to provide adequate drinking water and sanitation. Extreme heat is now recognized as a critical public health issue. The initiative will mobilize global support with a focus on developing action plans to ensure that workplaces and public spaces are equipped with heat response strategies.⁹

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ORIGINAL ARTICLE

AGE RELATED CHANGES IN ULNAR AND MEDIAN NERVE CONDUCTION PARAMETERS: A CROSS SECTIONAL STUDY

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Background: Nerve conduction study (NCS) is an important method to assess integrity of peripheral nervous system. It helps in diagnosis, treatment and prognosis of diseases of peripheral nerves. Nerve conduction study parameters, like conduction velocity (NCV), latency and amplitude are affected by several different physical factors like temperature, demography, and ethnicity. It can also be affected by age, gender, height, weight, and BMI. This study was conducted to find out the age-related changes in median and ulnar nerve conduction parameters.

Methods: This was a cross-sectional study with a total of 75 participants 40–70 years of age, conducted at Khyber Medical University, Peshawar, from July 2021 to July 2022. Participants were divided into three groups: 40–50 years, 51–60 years, and 61–70 years. The inclusion criteria were normal neurological examination, normal blood sugar, urea, creatinine, LFTs and ESR. Pregnant women and patients with bleeding disorders were excluded from study. NCS was recorded on Nihon Kohden Neuropack. Data was analysed using SPSS-22. One-way ANOVA with Tukey Post Hoc analysis for multiple group comparisons was done between groups. **Results:** There was a decline in nerve conduction study parameters associated with advancing age ($p < 0.05$). The amplitude of both nerve impulses decreased while latency increased with advancing age. There was decline in motor and sensory NCV with advancing age. **Conclusion:** The nerve functioning decreased with advancing age. This decline was more marked in motor conduction compared to sensory conduction.

Keywords: Median nerve, Nerve conduction, Nerve conduction velocity, Ulnar nerve

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INTRODUCTION

Electrodiagnostic (EDX) studies are an important tool for diagnosis and evaluation of neuromuscular disorders.¹ These studies include nerve conduction studies (NCS) and needle electromyography (EMG). The basic principle of nerve conduction study is to apply an external electrical pulse that produces a propagated nerve action potential (NAP) which can be recorded at a distal point in the same nerve. The NAP produces a compound muscle action potential (CMAP) which arises from activation of muscle fibres of a specific muscle. Sensory action potential is recorded in the form of Sensory Nerve Action Potential (SNAP). These potentials can be recorded with the help of a needle or surface electrodes.²

Neurological disorders are most common in old age which are responsible for about 50% debility after 65 years of age. There is a profound effect of aging on peripheral nerve structure and function. Central Nervous System being protected by blood brain barrier is less vulnerable to environmental insults than Peripheral Nervous System which is more likely to be affected by trauma, injury and infections.³

The nerve fibres are basically composed of axons and myelin sheath, therefore, the decline in nerve function is also attributed mainly to these two factors although there may be other contributing factors present as well like non-neural cells and nutritional factors like vitamin B₁₂ deficiency and vitamin E deficiency.⁴ Alterations in myelin sheath can cause decline in nerve conduction velocity. With advancing age, there may be decreased number of functional axons which leads to decline in amplitude of CMAP or SNAP.⁵

The proportion of elderly population over 50 years is rising especially in developed countries due to improvement in life expectancy, it is therefore important to identify the disease early and screen for curable causes.⁶ Polyneuropathy affects about 7% of elderly population and NCS is the most important tool to diagnose polyneuropathy.⁷

We don't know how much decline occurs in NCS parameters with advancing age in our population. We are still applying values of US, Europe and Canada on our population. This study will help to assess the NCS values and age related changes in ulnar and median nerve conduction parameters in our population.

METHODOLOGY

It was a cross-sectional study with a sample size of 75 who were selected through consecutive sampling. The sample size was calculated through STAT UBA (Used Better than Aged) by keeping the power of 0.80 and α value of 0.05.⁸ The study was approved from ASRB and KMU Ethical Board (Reference No. DIR/KMU-EB/AR/000532) and was carried out at Institute of Basic Medical Sciences, KMU Peshawar from July 2021 to July 2022.

The participants were divided into 3 groups of 25 each based on age. Group I were aged 40–50 years, Group II were 51–60 years, while Group III were 61–70 years old. Those people were included in the study who had no confounding medical or surgical illness like diabetes or hypertension, no history of previous upper limb injury/myopathy/neuropathy. Pregnant women, people aged >70 or <40 years, those with bleeding disorders or on anticoagulant therapy and patients with compression symptoms of median or ulnar nerve were excluded from the study.

The nerve conduction studies were performed on Nihon Kohden Neuropack M1 EP/EMG measuring system MEB-9200/MEB-9300. Temperature was set at 25 °C (room temperature). The sensory and motor nerve conduction studies were recorded for both median and ulnar nerves both proximally (elbow) and distally (wrist) in the forearm at standard sites as specified by American Association of Neurological and Electrodiagnostic Medicine (AANEM). Specific software compatible with the NC electrodes was used for recording nerve conduction parameters.⁹

Demographic parameters, blood parameters (CBC, Fasting blood sugar, LFTs, RFTs, ESR) and NCS parameters were entered and analysed using SPSS-22. The nominal variables were looked for frequencies and percentages while numerical variables were analysed for Mean $\pm$ SD. The data were normally distributed as checked by Shapiro Wilk test. The different groups were compared with each other using One-way ANOVA followed by Tukey Post Hoc analysis for multiple group comparisons.

RESULTS

The mean age of the study participants was 53.83 $\pm$ 8.33 years including 32 women and 43 men being 42.66% and 57.33% respectively. Mean height, weight and BMI and their comparative studies of different groups have been described in Table-1.

Table-2 shows comparison of median motor nerve conduction parameters. There is a significant difference between group I and III and group II and III.

Table-3 shows comparison of three groups for ulnar motor nerve conduction parameters. There was no significant difference in right ulnar motor nerve conduction parameters. The only significant difference was between group II and III in amplitude at elbow ($p=0.032$). Other results were insignificant.

Table-4 shows comparison of study groups for median sensory nerve conduction parameters. There were significant differences between group I and group III.

Table-5 shows comparison of study groups for ulnar sensory NCS parameters. Here a few significant differences were seen between group I and group III.

Table-1: Comparative studies of demographic parameters

	Mean $\pm$ SD			<i>p</i>		
	Group I	Group II	Group III	Group I vs II	Group I vs III	Group II vs III
Height (Cm)	162.22 $\pm$ 9.36	163.0 $\pm$ 7.43	162.76 $\pm$ 7.04	0.930	0.96	0.99
Weight (Kg)	73.74 $\pm$ 13.55	71.37 $\pm$ 10.05	72.64 $\pm$ 10.55	0.747	0.93	0.91
BMI (Kg/m ²)	27.74 $\pm$ 3.9	26.82 $\pm$ 4.0	27.38 $\pm$ 3.1	0.659	0.93	0.85

Table-2: Comparison of Group I, II and III for Median Motor Nerve conduction parameters

	Mean $\pm$ SD			<i>p</i>		
	Group I	Group II	Group III	Group I vs II	Group I vs III	Group II vs III
Right median motor nerve conduction parameters (wrist)						
Latency (ms)	3.29 $\pm$ 0.35	3.44 $\pm$ 0.36	3.77 $\pm$ 0.51	0.38	0.000*	0.021*
Amplitude (mV)	10.12 $\pm$ 2.4	9.76 $\pm$ 2.4	8.07 $\pm$ 2.09	0.83	0.007*	0.031*
Right median motor nerve conduction parameters (Elbow)						
Latency (ms)	7.45 $\pm$ 0.6	7.75 $\pm$ 0.52	8.06 $\pm$ 0.745	0.20	0.003*	0.20
Amplitude (mV)	9.58 $\pm$ 2.6	9.17 $\pm$ 2.19	7.52 $\pm$ 2.41	0.81	0.10	0.05
NCV (m/s)	56.08 $\pm$ 3.9	54.68 $\pm$ 3.55	54.64 $\pm$ 4.13	0.41	0.39	1.00
Left median motor nerve conduction parameters (Wrist)						
Latency (ms)	3.16 $\pm$ 0.32	3.34 $\pm$ 0.32	3.5 $\pm$ 0.52	0.25	0.009*	0.32
Amplitude (mV)	10.38 $\pm$ 2.54	9.98 $\pm$ 2.43	7.66 $\pm$ 1.98	0.82	0.000*	0.002*
Left median motor nerve conduction parameters (Elbow)						
Latency (ms)	7.21 $\pm$ 0.61	7.55 $\pm$ 0.49	7.71 $\pm$ 0.85	0.18	0.027*	0.67
Amplitude (mV)	9.9 $\pm$ 2.42	9.52 $\pm$ 2.49	7.28 $\pm$ 2.56	0.84	0.001*	0.006*
NCV (m/s)	57.38 $\pm$ 4.19	56.1 $\pm$ 3.75	55.95 $\pm$ 5.49	0.58	0.51	0.99

Table-3: Comparison of Group I, II and III for ulnar motor nerve conduction parameters

	Mean±SD			p		
	Group I	Group II	Group III	Group I vs II	Group I vs III	Group II vs III
Right ulnar motor nerve conduction parameters (Wrist)						
Latency (ms)	2.38±0.25	2.46±0.33	2.47±0.37	0.60	0.57	0.99
Amplitude (mV)	9.22±1.4	9.7±2.35	8.76±1.58	0.61	0.65	0.17
Right ulnar motor nerve conduction parameters (Elbow)						
Latency (ms)	6.42±0.58	6.6±0.49	6.64±0.72	0.57	0.43	0.97
Amplitude (mV)	8.72±1.62	9.02±2.45	8±1.68	0.85	0.39	0.16
NCV (m/s)	56.52±5.16	55.88±4.68	56.04±5.94	0.90	0.94	0.99
Left ulnar motor nerve conduction parameters (Wrist)						
Latency (ms)	2.42±0.34	2.5±0.26	2.46±0.38	0.67	0.93	0.87
Amplitude (mV)	8.98±1.5	9.32±2.12	8.37±1.55	0.76	0.43	0.13
Left ulnar motor nerve conduction parameters (Elbow)						
Latency (ms)	6.28±0.75	6.46±0.5	6.55±0.82	0.65	0.38	0.89
Amplitude (mV)	8.11±1.64	8.85±2.03	7.57±1.57	0.30	0.52	0.032*
NCV (m/s)	59.43±6.21	58.71±3.97	57.13±5.9	0.88	0.30	0.56

Table-4: Comparison of Group I, II and III for right median sensory nerve conduction parameters

	Mean±SD			p		
	Group I	Group II	Group III	Group I vs II	Group I vs III	Group II vs III
Right median sensory nerve conduction parameters						
Latency (ms)	2.38±0.27	2.58±0.38	2.89±0.49	0.17	0.000*	0.01*
Amplitude (µV)	34.55±14.2	30.46±11.2	22.65±9.57	0.44	0.002*	0.05
NCV (m/s)	58.99±6.6	55.35±8.2	49.87±8.14	0.22	0.000*	0.03*
Left median sensory nerve conduction parameters						
Latency (ms)	2.29±0.25	2.51±0.34	2.64±0.38	0.05	0.001*	0.33
Amplitude (µV)	40.7±15.85	34.31±12.04	26.81±9.09	0.18	0.001*	0.09
NCV (m/s)	61.24±6.39	56.82±7.83	54.65±7.92	0.09	0.007*	0.55

Table-5: Comparison of Group I, II and III for ulnar sensory nerve conduction parameters

	Mean±SD			p		
	Group I	Group II	Group III	Group I vs II	Group I vs III	Group II vs III
Right ulnar sensory nerve conduction parameters						
Latency (ms)	1.97±0.32	2.08±0.4	2.12±0.28	0.60	0.40	0.94
Amplitude (µV)	38.95±17.98	33.12±11.36	28.5±14.8	0.35	0.04*	0.52
NCV (m/s)	60.56±7.83	57.45±8.4	59.59±12.7	0.50	0.93	0.72
Left ulnar sensory nerve conduction parameters						
Latency (ms)	1.96±0.23	2.04±0.23	2.23±0.43	0.67	0.01*	0.08
Amplitude (µV)	39.8±20.1	37.24±16	29.84±14.3	0.85	0.10	0.28
NCV (m/s)	60.35±5.93	57.06±5.51	56.88±9.77	0.25	0.22	0.99

DISCUSSION

The nerve conduction parameters decline with advancing age which was significant in all the groups but mostly seen between group I and III (40–50 years vs 61–70 years). It was found that amplitude of CMAP and SNAP declined with advancing age. Similar findings were observed by Loewenbrück KF *et al*, who found out that there was a decline in median and ulnar peak sensory amplitudes during four years follow-up study.¹⁰ As amplitude is representative of total number of functioning axons in a nerve fibre, the decrease in amplitude may be attributed to decline in number or function of nerve axons with advancing age.¹¹ Increasing age is also associated with peripheral oedema and increase in skin resistance which might be the reason behind low amplitudes with advancing age.¹² There was also an increase in sensory and motor latency of both the median and ulnar nerve with advancing age which means there is more delay in transmission of nervous signals to the nerve fibre with advancing age. This is in accordance with a study

conducted by Singh R *et al* who showed similar results.⁸ This may be due to many factors like alterations in myelin sheath (myelin figures/myelin balloons), loss of nerve fibres, decreased neurotransmitters.¹³

In the present study, the median and ulnar nerve conduction velocities also showed decline with advancing age. This finding is similar to a follow-up study in which it was found out that ulnar sensory NCV declined at a rate of 0.14 m/s per year while median sensory NCV declined at a rate of 0.21 m/s per year.¹⁴ Falco *et al*¹⁵ reported a 10% decline in NCV over 60 years of age. In another longitudinal study on median and ulnar sensory nerves Suthar HR *et al*¹⁶ demonstrated that median sensory NCV declined at a rate of 0.29 m/s while ulnar sensory NCV declined at a rate of 0.42 m/s per year. They also reported a decline in both sensory and motor NCV of median and ulnar nerves in aging study groups.¹⁶

Fong *et al*¹⁷ did NCS on different ethnicities for effect of demographic and physical factors on NCS

parameters, it was seen that advancing age was associated with reduced motor as well as sensory nerve conduction velocities.¹⁷ As NCV is the measure of degree of myelination of peripheral nerve fibres, the decline in NCV with advancing age may be due to loss of myelinated nerve fibres.¹⁸

CONCLUSION AND RECOMMENDATIONS

The age-related changes are more marked in median nerve than ulnar nerve. More accurate results could have been obtained by following the same study population and having a large sample size. Further longitudinal studies are needed to determine the rate at which NCS parameters decline with advancing age.

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SF: Proof reading

MK: Data analysis

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ORIGINAL ARTICLE

IMPACT OF PROPYLTHIOURACIL-INDUCED HYPOTHYROIDISM DURING PREGNANCY ON POST-NATAL LOCOMOTOR DEVELOPMENT IN RAT PUPS

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Background: The foetus depends on maternal thyroid hormones for neurogenesis during early days of pregnancy. The objective of this study was to determine the impact of maternal hypothyroidism on cortical lamination, resulting in impaired locomotion in rat pups. **Methods:** This study was conducted in the Anatomy Department of Islamic International Medical College over 9 weeks. Twenty-four female and 12 male Sprague-Dawley rats were divided into two equal groups. Control group received a standard diet and drinking water, while the hypothyroid group was given 4.5 mg propylthiouracil/rat/day via drinking water. Treatment began one week before mating and continued for three weeks after delivery. Pups were born after three weeks and nursed freely for 21 days. On day 22, locomotor testing was performed before dissection. Brains were extracted, and motor cortex was examined. Data from inclined plane test and microglial counts were analysed with *t*-test, while Chi-square test was applied for forelimb placing and cortical lamination assessment. **Results:** The control group exhibited typical locomotion, as evidenced by their performance in locomotor tests, which reflected a healthy pattern of neurogenesis. In contrast, the hypothyroid groups demonstrated a significant decline in their ability to stay on an inclined plane and a delayed response in forelimb placement, indicating atypical neurogenesis evidenced by an elevated number of microglia and disrupted cortical lamination. **Conclusion:** Experimentally induced maternal hypothyroidism in Sprague Dawley rats had a detrimental impact on the locomotion of pups associated with abnormal neurogenesis.

Keywords: Antenatal care, Impaired locomotion, Maternal hypothyroidism, Motor cortex, Neurogenesis

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INTRODUCTION

Maternal hypothyroidism is characterized by elevated levels of Thyroid Stimulating Hormone (TSH) in the bloodstream during pregnancy, affecting the development of the foetus.¹ During human development, the activation of foetal thyroid hormones typically takes place between the 10th and 16th week of gestation, which closely coincides with the second trimester of pregnancy. However, it is vital to recognize that the primary phase of neurogenesis occurs predominantly in the first trimester. Similarly, in rats, the activation of thyroid hormone typically begins after the 18th day of embryonic development, aligning with the critical period for normal brain development, which spans from the 12th to 18th embryonic days. Consequently, during this early developmental period, the foetus depends on maternal thyroid hormones for neurogenesis. Their impact extends beyond influencing neurons' proliferation, migration, and differentiation, along with myelination and is of vital importance.^{2,3}

The neocortex, a prominent cortical region, orchestrates the planning, initiation, and execution of voluntary movements in rodents. It also serves as the hub for receiving input from diverse brain regions and seamlessly integrating sensory data with motor

directives. Rats can acquire and enhance motor skills through repetitive training, with the neocortex assuming a pivotal role in storing and adjusting motor representations.⁴

Propylthiouracil (PTU) is classified as an anti-thyroid agent, hindering the transformation of inactive thyroid hormones into their active forms, thereby influencing the retention of thyroid hormones in the thyroid gland.⁵ It is used for the induction of maternal hypothyroidism in animal models, including rats.⁶

Maternal thyroid hormone deficiency affects the expression of approximately 500–1000 genes directly or indirectly and impairs the antioxidant defence system.^{7–9} This leads to oxidative stress and potential gene mutations, which significantly disrupt the laminar architecture of the cerebral cortex and cerebellum, ultimately provoking a microglial response.¹⁰ Additionally, thyroid hormone deficiency alters neuronal progenitor cell division dynamics, causing delayed symmetrical divisions and a reduced progenitor pool, factors that may contribute to behavioural deficits in the offspring.²

Numerous rat studies have demonstrated the impact of maternal hypothyroidism on cognitive functions and coordinated motor skills. However, most

of these studies have primarily focused on biochemical parameters and gene expressions, with limited research on histological parameters.^{3,11}

This study aims to evaluate how maternal hypothyroidism impacts the locomotor activity associated with abnormal neurodevelopment within the motor cortex of rat pups. This research proposes the implementation of thorough and structured screening initiatives aimed at ensuring optimal foetal brain development. Furthermore, it underscores the significance of incorporating serum TSH biochemical testing as a valuable indicator for detecting maternal hypothyroidism during prenatal checkups.

METHODOLOGY

This controlled interventional study, conducted in collaboration with the National Institute of Health and the Anatomy Department of the Islamic International Medical College, was executed for 9 weeks after obtaining approval for the study synopsis from the Ethics Review Committee, Reference No. Riphah/IRC/22/2087. A total of twenty-four female and twelve male Sprague Dawley rats were included in the study, with an age range of 12 to 16 weeks and weighing between 250 to 300 grams, selected by simple convenience sampling. The sample size was adequate according to the Resource Equation Method.¹² Animals were housed under carefully regulated environmental conditions. These conditions included maintaining a constant temperature of 22 ± 0.5 °C, a 12-hour light and dark cycle, and a humidity level of 50%.¹³

Twenty-four female and twelve male Sprague Dawley rats, aged 12 to 16 weeks and weighing between 250 and 300 grams, along with 12 of their offspring who were full-term rat pups (3 weeks) of both sexes without congenital abnormalities, were included in this study. Rats less than 12 weeks of age, >250 grams or <300 grams, along with pups born prematurely and pups born with visible congenital defects, were excluded.

The rats were divided into two distinct groups, with their dietary and water regimens beginning one week before mating and continuing consistently throughout gestation, weaning, and up to the 22nd day postpartum.¹⁴

Control group rats were provided with a standard chow diet and given plain drinking water through the oral route, and Experimental group rats were subjected to a daily oral administration of 4.5 mg of propylthiouracil/rat¹³, administered through drinking water. This treatment protocol began one week before mating and was maintained throughout gestation and the weaning period, continuing until the 22nd day postpartum.¹⁴

The study involved assessing the serum TSH levels in female rats before mating to ensure they didn't have natural hypothyroidism. Mating was conducted in

12 cages, with 3 cages serving as controls and 9 as experimental. Each cage contained 2 females and 1 male rat, and pregnancy was confirmed on the first day of gestation by observing a vaginal plug.¹⁴ On the 10th day of gestation, maternal serum TSH levels were reassessed to evaluate thyroid function, with values ranging from 25 ng/mL to 41 ng/mL confirming a sustained hypothyroid state (Table-1).

The pups were born at the end of pregnancy, and they were left with their mothers in the same cages to have unrestricted access to mother's milk for the next three weeks.¹⁵ At the end of three weeks after birth, the locomotor activity of 12 pups from each group was assessed.

Table-1: Serum TSH levels in the females of the hypothyroid group at the 10th day of gestation

Rat #	Serum TSH ng/ml	Rat #	Serum TSH ng/ml
1	25	7	32
2	35	8	51
3	36	9	38
4	65	10	39
5	45	11	56
6	35	12	41

Each pup's movement was assessed individually by placing it on an inclined plane. A unique inclined plane model was designed for this purpose, and the angle of descent of each rat pup was measured (Figure-1A). Between each measurement session, there was a one-hour gap. To ensure accuracy, the average of two readings were computed for each rat, providing a representative measure of their locomotion.¹⁶

The primary goal of the forelimb placing reaction test is to assess the motor function of the animal, particularly its ability to respond to sensory stimuli by accurately placing its forelimbs on a flat surface. Each pup's forelimb placing response was observed and evaluated for one minute¹⁷ (Figure-1B).

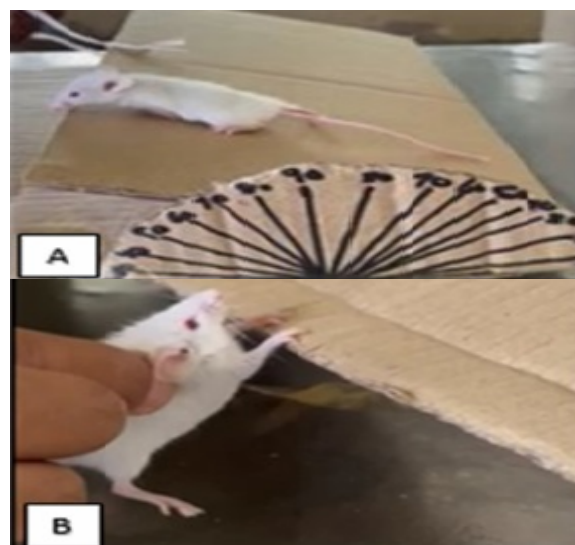


Figure-1: (A) The inclined plane test, (B) The forelimb placing reaction

This assessment employed a four-point scoring system as: 0= No observable reaction, 1= Weak and uncoordinated lifting of limbs without contacting the horizontal surface, 2= Delayed placement of the forelimb on the horizontal surface, and 3= Fast and accurate placement of both forelimbs on the horizontal surface.¹⁷

On the 22nd postpartum day, the same pups from each group were anesthetized and sacrificed. Subsequently, the skulls of each animal were split open, allowing access to the cerebrum, which was then carefully dissected. A portion of the specimens was preserved in neutral buffered formalin (10%) for 24 hours, followed by a process of dehydration using increasing concentrations of alcohol (50%, 70%, 80%, 90%, and 100%). These specimens were then subjected to clearing and embedding in paraffin wax. Afterward, 5-micron-thick tissue sections were obtained, and these sections were stained with H&E.¹⁸

High-resolution images of the slides were obtained using an Olympus BX53 microscope at magnifications of 4×, 10×, and 40×. Images captured were then transferred to a laptop for further analysis, utilizing Image J software. Parameters (Microglial count and differentiation of cortical layers) at the microscopic level were methodically evaluated in sections derived from both cerebral hemispheres. This assessment covered four distinct regions in each hemisphere, beginning at the midline and extending towards the right and left sides.

Microglial count was performed at 40× magnification to evaluate the cortical inflammatory response, which is associated with disrupted neurogenesis, impaired myelination, and altered locomotor activity. Neuronal migration is essential for forming the layered structure of the cerebral cortex during normal brain development. However, some neurons may fail to migrate correctly, forming ectopic clusters within the cortex.¹⁹ Arrangement of cortical neurons was observed at 10× magnification and graded using the following scale.²⁰

Grade 0, No Differentiation: None of the six cortical layers are preserved in any of the 4 HPF (high-power fields) per rat.

Grade 1, Minimal Differentiation: All six layers are preserved in 1 out of 4 HPF/rat.

Grade 2, Mild Differentiation: All six layers are preserved in 2 out of 4 HPF/rat.

Grade 3, Moderate Differentiation: All six layers are preserved in 3 out of 4 HPF/rat.

Grade 4, Well Differentiated: All six cortical layers are preserved in all 4 HPF/rat.

The data obtained from the calibrated images were recorded and analysed using SPSS-26. The Kolmogorov-Smirnov test was applied to assess the normality of the data. A significant p-value showed

normal distribution of data. Independent samples *t*-test was applied to assess potential differences in means for inclined plane test and microglial count (quantitative variables), with the results expressed as Mean±SD. For comparing group differences in forelimb placing reaction and lamination of cortical layers (qualitative variable), the Chi-square test was used. A significance level of $p<0.05$ was set by standard statistical practice.

RESULTS

The locomotive capabilities of the rat pups were evaluated based on their tendency to fall from an inclined plane. The outcomes demonstrated a notably strong statistical significance, ($p<0.001$). (Table-2).

In the forelimb placement reaction, the control group exhibited a quicker response than the hypothyroid group. In the control group, 83.3% of the rats showed a prompt forelimb placing reaction, while 16.7% exhibited a delayed response. In contrast, among the hypothyroid group, 66.7% showed no response, 25% displayed a weak reaction, and 8.3% had a delayed response. The Chi-square analysis revealed a significant disparity between the two groups (Table-3).

The hypothyroid group displayed microglial cells with oval-shaped nuclei (Black arrows in Figure-2), indicative of an inflammatory response, whereas the control group showed no microglial cells. There was a high statistical significance ($p<0.001$), indicating a substantial differences between the two groups (Table-4).

Table-2: Mean degree of fall, *t*-test of pups by inclined plane test

Groups	Mean Degree of Fall±SD
Control	41.66±6.06*
Hypothyroid	31.66±3.58*

* $p<0.001$

Table-3: Chi-square analysis of pups in forelimb placing reaction [n (%)]

Forelimb Placing Reaction	Control	Hypothyroid
Prompt Response	10 (83.3)	0 (0.0)
Delayed Response	2 (16.7)	1 (8.3)
Weak Response	0 (0.0)	3 (25.0)
No Response	0 (0.0)	8 (66.7)

Table-4: Mean microglial count in both groups *t*-test

Groups	Mean Microglial Count (cells/hpf)±SD
Control	0±0.0
Hypothyroid	6.63±0.52

* $p<0.001$

In the control group, 100% of the rats demonstrated good differentiation across all 6 cortical layers, with no observed clusters of ectopic cells (Black circles in Figure 2). In contrast, within the hypothyroid group, 8.3% of the rats exhibited minimal differentiation (Grade 1) across all six cortical layers, 50% showed mild differentiation (Grade 2), and 41.7% demonstrated

moderate differentiation (Grade 3). The statistical analysis, conducted using the chi-square test, highlighted an extremely significant difference ($p < 0.001$) between the two groups concerning the severity of differentiation. (Table 5).

Table-5: Percentage of rats with different grades of differentiation of cortical layers [n (%)]

Severity of Cortical Layer Differentiation	Control	Hypothyroid
Grade 1 (Minimal Differentiation)	0 (0.0)	1 (8.3)
Grade 2 (Mild Differentiation)	0 (0.0)	6 (50.0)
Grade 3 (Moderate Differentiation)	0 (0.0)	5 (41.7)
Good Differentiation (All 6 Cortical Layers)	12 (100)	0 (0.0)

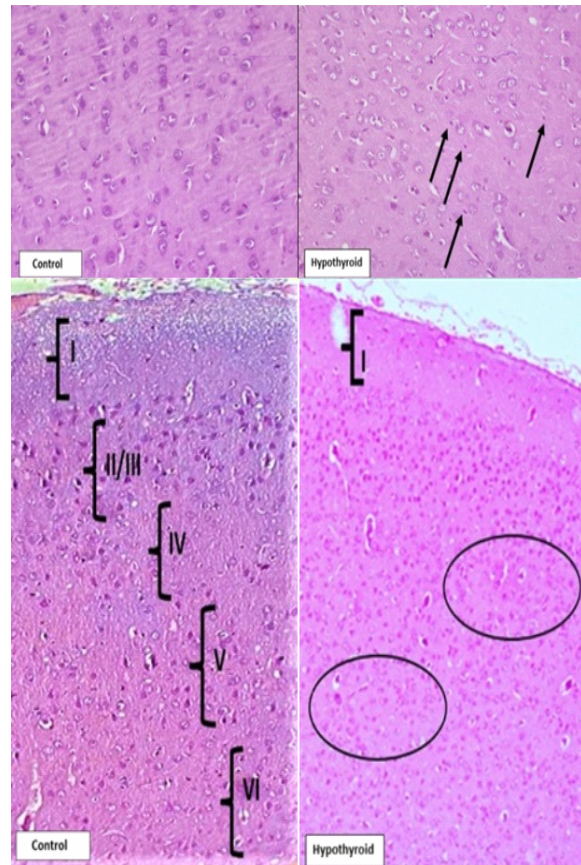


Figure-2: Microglia, represented by black arrows at 400× and ectopic cell clusters, represented by black circles at 400× in hypothyroid groups while Control groups showed no microglia with normal cortical lamination (I–VI)

DISCUSSION

Maternal thyroid hormones play a crucial role in foetal neurogenesis, and their significance is particularly pronounced during pregnancy. This heightened importance arises from the increased demands placed on the maternal thyroid gland due to physiological changes in the mother's body. Of particular note is the fact that, up to the 12th week of gestation, the foetus relies entirely on the maternal provision of thyroid hormones²¹. The

findings of this study align with those reported in previous research.

In this study, the offspring of hypothyroid rat mothers showed impaired motor coordination and balance, struggling to maintain posture and adjust body position on an inclined plane. Their task performance lacked the precision and stability observed in pups. These motor deficits are likely linked to reduced expression of key proteins involved in neuronal maintenance, migration, and plasticity. Similar alterations in motor skills were reported by Barez-Lopez S *et al*²² and Khairinisa MA *et al*²³.

Forelimb placing reactions were assessed using a four-point scoring system to evaluate motor activity in rats. The control group showed quick and strong responses, whereas the hypothyroid group exhibited delayed and weakened reactions. These differences are likely due to maternal hypothyroidism and disrupted cortical lamination, potentially driven by oxidative stress and down regulation of key genes related to motor function. Similar motor deficits were reported by Manoj P. Dandekar, supporting the findings of this study.²⁴

Microglia serve as a supportive element in neuronal survival and engage in phagocytic activities²⁵, primarily in inflammatory response to the demise of neuronal precursors and the surplus of neurons during perinatal development. When faced with stressful conditions, there is an observable rise in microglia²⁶. Recent research has furnished substantiating evidence of this phenomenon, with the hypothyroid group exhibiting a more pronounced prevalence of microglial cells when contrasted with the control group. In 2022, Chamas L conducted research indicating that hypothyroidism, specifically within the hippocampus of mice leads to the activation of glial cells.²⁷ This finding was further supported by Yizhen Wang *et al*, who also found a connection between hippocampal hypothyroidism in rats and an uptick in inflammatory immune responses.²⁸

In this study, a significant disruption in the organization of cortical layers within the hypothyroid group was observed. This irregularity was characterized by blurred boundaries between layers II, III, and IV, primarily resulting from the infiltration of layer III pyramidal cells into layer IV, as well as the migration of large pyramidal cells from layer V into layer IV. The root cause of these irregularities in cortical layer differentiation associated with hypothyroidism has been associated to reduced expression of the reelin gene. In 2020, O'Shaughnessy KL's research demonstrated that chemicals disrupting thyroid function during developmental neurotoxicity could lead to abnormalities in cortical lamination.²⁹ Furthermore, in 2021, Montero *et al*, indicated that rats experiencing dysfunction in thyroid hormones exhibited downregulated genes and delayed neuronal radial migration.³⁰

Although the study gave invaluable insight into the histological parameters of the developing motor cortex. The current research did not provide insights into ultrastructural alterations, molecular mechanisms, or the dynamics of gene expression due to limited resources.

Future studies should incorporate molecular and gene expression analyses to further elucidate the mechanisms underlying the observed effects. Given the critical role of thyroid hormones in neural development, effective prenatal monitoring and timely management of maternal thyroid function are essential to prevent neurodevelopmental deficits and promote healthy brain development in offspring.

CONCLUSION

This study highlights the detrimental effects of maternal hypothyroidism on locomotor activity. The observed disruptions in neuronal layer organization underscore a critical connection between maternal thyroid dysfunction, especially under stress, as evidenced by increased microglial cell counts, and altered motor cortex development.

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ORIGINAL ARTICLE

ROLE OF β -2 GLYCOPROTEIN 1, ANTI-CARDIOLIPIN AND LUPUS ANTICOAGULANT ANTIBODIES IN DIAGNOSIS OF ANTI-PHOSPHOLIPID SYNDROME

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Background: Anti-Phospholipid Syndrome (APS) is an autoimmune disease in which the patient is in a hypercoagulable state leading to vascular thrombosis and obstetric morbidity and mortality. The aim of my study is to see the presence of Anti- β 2 Glycoprotein 1 (Anti- β 2GP1), Anti-cardiolipin (aCL) and lupus anticoagulant antibodies (LA) in patients suspected of APS. **Methods:** This cross-sectional study was performed in the Department of Chemical Pathology, Liaquat National Hospital and Medical College, Karachi. A total of 115 patients from Rheumatology and Gynaecology Departments having thrombotic episodes were tested for the presence of one or more of the antibodies namely, Anti- β 2GP1, Anti-Cardiolipin and Lupus Anticoagulant Antibodies in their sera. Data was analysed using SPSS-27. **Results:** Among 115 patients, 53.9% had no antibody positive and were considered to be disease free. Positivity with LA was seen in 23.5% of the population while 15.7% were positive with aCL IgM and 13% positive with aCL IgG. As regards Anti- β 2GP1 IgM 8.7% and IgG 15.7% were positive in each assay. All parameters had low sensitivity but high specificity and negative predictive value. The diagnostic accuracy of aCL IgG and IgM was 77.3% and 74.7% respectively. **Conclusion:** Anti- β 2GP1, aCL, and LA are valuable markers for the diagnosis of APS. They are better markers having a high specificity and negative predictive value.

Keywords: Anti-cardiolipin, Anti-phospholipid syndrome, Lupus anticoagulant antibodies, β 2 glycoprotein 1

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INTRODUCTION

Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by a hypercoagulable state presenting with venous or arterial thrombosis and/or obstetrical complications.^{1,2} These patients have circulating anti-phospholipid antibodies which cause thrombosis in arterial, venous, and even microvascular beds.^{3,4} The deep veins of the legs and cerebral arteries are the two most common sites of thrombosis.³ There are two types of APS: Type-I is primary APS which is half of the cases, and Type-II is secondary APS in which the patient has other systemic autoimmune diseases.⁵ Type-II APS can be seen in patients having Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Systemic Sclerosis, Sjögren's syndrome etc.^{5,6} In 1999, international experts developed the Sapporo criteria for the diagnosis of APS which was later updated in 2006 in Sydney, Australia and was named the modified Sapporo or Sydney criteria.^{7,8} In 2023 the ACR/EULAR APS classification criteria was developed which showed that at least one Anti-phospholipid antibody should be present in a patient with one APS clinical criterion and then added laboratory and clinical criteria were used to give weightage.⁹ The clinical criteria include arterial, venous or small vessel thrombosis, or pregnancy complications

which could be attributed to placental insufficiency.⁷ The laboratory criteria involve the presence of at least one positive marker of APS at least 12 weeks apart, which include, positive Lupus anticoagulant (LA), Anti-Cardiolipin Antibody (aCL) IgG or IgM, or Anti- β 2 Glycoprotein antibody (Anti- β 2GP1) IgG or IgM.⁷ If all three laboratory criteria are present with high titres of antibodies in a patient, that patient will have the maximal risk of developing APS.¹⁰ Intermittent positivity of LA or low titres of the aCL and Anti- β 2GP1 pose a low risk of development of the disease.¹⁰ Our study aimed to see the role of different antibodies in diagnosis of APS and correlation of the antibodies.

MATERIAL AND METHODS

This analytical cross-sectional study was carried out in the Department of Chemical Pathology, Liaquat National Hospital and Medical College, Karachi from 2 Mar to 13 Sep 2024 after approval of Ethical Review Committee with Ref. No. RC-LNH-Pathology-01/2025/05. A total of 115 patients suspected of suffering from APS with either thrombosis or miscarriages were recruited in the study. The age, gender and other data was collected. Five mL blood was collected in gel top tube for Anti- β 2GP1 and aCL antibodies. For LA, 3 mL blood was collected in blue

top tube containing sodium citrate as anticoagulant. Anti- β 2GP1 was analyzed semi quantitatively by Quanta Lite ELISA from INOVA diagnostics, aCL was measured by EIA/ELISA method on ETI-MAX 3000 (EVOLIS) and LA was measured by automated coagulation analyzer Sysmex CS-2500. For Anti- β 2GP1 IgG and IgM, <15 U/mL was taken as negative, 15.0–39.9 U/mL as weakly positive, 40.0–79.9 U/mL as positive and $\geq$ 80 U/mL as strongly positive. For aCL IgM, <5.0 MPL-U/mL was taken as negative, 5.0–7.2 MPL-U/mL as equivocal, and >7.2 MPL-U/mL as positive. In case of aCL IgG, <10.0 GPL-U/mL was considered negative, 10.0–14.4 GPL-U/mL as equivocal, and >14.4 GPL-U/mL as positive. For LA, LA1 screening test, 31–44 seconds was taken normal, for LA2 confirmatory test, reference interval was 30–38 seconds. LA ratio $\leq$ 1.2 was taken as normal, 1.3–1.5 as weakly positive, 1.6–2.0 as moderately positive, and >2.0 was taken as strongly positive. Data analysis was done on IBM SPSS-27. Chi-square/Fisher exact test was applied, and $p \leq 0.05$ was considered significant.

RESULTS

Out of a total of 115 patients 79.1% were females 20.9% were males; 47% were aged $\leq$ 35 years, 30.4% were between 36 and 50 years, and 22.6% were >50 years old. Sixty-two (53.9%) patients had no antibody positive and were considered free of disease or had no risk of thrombosis; 31 (27%) had only one antibody positive, and 19 (16.5%) had two positive antibodies.

Table-3: Diagnostic accuracy of Anti- β 2 Glycoprotein (IgG, IgM) and Anti-Cardiolipin ((IgG, IgM)

	Lupus Anticoagulant		<i>p</i>	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
	Positive	Negative						
β2Glycoprotein IgG								
Positive	4	14	1.000	14.8%	84.1%	22.2%	76.3%	67.82%
Negative	23	74						
β2Glycoprotein IgM								
Positive	4	6	0.241	14.8%	93.2%	40%	78.1%	74.78%
Negative	23	82						
Anti Cardiolipin IgG								
Positive	8	7	0.007*	29.6%	92%	53.3%	81%	77.39%
Negative	19	81						
Anti Cardiolipin IgM								
Positive	8	10	0.033*	29.6%	88.6%	44.4%	80.4%	74.78%
Negative	19	78						

Chi-square/Fisher exact test was applied, *Significant

DISCUSSION

The main antigen which is targeted by the antibodies in APS is β 2GP1. This antigen is responsible for complement activation and homeostasis. If antibodies are formed against β 2GP1, this can prevent homeostasis and complement activation and cause the thrombotic and obstetrical complications of APS.¹¹ Primary APS is characterized by the presence of thrombotic events or obstetrical complications and the presence of the antibodies to phospholipids.¹² Catastrophic APS has also been reported which showed the presence of the Anti-Phospholipid antibodies.¹³ One South Asian study

There were just 3 (2.6%) cases having all three tests positive. Positivity with LA was seen in 23.5% of cases while 15.7% were positive with aCL IgM, and 13% positive with aCL IgG. Regarding Anti- β 2GP1, IgM was positive in 8.7% and IgG in 15.7% (Table-1).

When LA positive and negative groups were compared, there were no significant differences in age, anti- β 2GP1 IgG and IgM, aCL IgM levels, but significant differences were found in aCL isotype IgG titres ($p=0.05$) (Table-2). The sensitivity and specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA) are tabulates as Table-3. All of these antibodies have a low sensitivity but high specificity and high NPV showing that they are better markers to rule out the disease than to diagnose the disease.

Table-1: Prevalence of different antibodies with isotypes

Antibodies Positive	IgG	IgM
Anti- β 2GP1	18 (15.7%)	10 (8.7%)
aCL	15 (13.0%)	18 (15.7%)

Table-2: Comparison of lupus anticoagulant with age and bio-chemical markers (Mean $\pm$ SD)

Parameters	Lupus Anticoagulant		<i>p</i>
	Positive	Negative	
Age (Years)	39.85 $\pm$ 15.29	39.43 $\pm$ 14.64	0.898
Anti- β 2GP1 IgG (U/mL)	10.08 $\pm$ 1.66	10.74 $\pm$ 4.29	0.435
Anti- β 2GP1 IgM (U/mL)	10.08 $\pm$ 1.66	9.71 $\pm$ 1.16	0.200
aCL IgM (MPL-U/mL)	9.86 $\pm$ 13.32	4.75 $\pm$ 5.74	0.063
aCL IgG (GPL-U/mL)	10.75 $\pm$ 11.05	6.23 $\pm$ 5.74	0.050*

*Significant

states that Catastrophic APS is more likely to occur in patients with triple antibody positivity.¹⁴ This has also been validated by another study in which they say that the presence of all three antibodies, especially high titers of aCL and β 2GP1 IgG are seen in Catastrophic APS.¹⁵ According to Keeling *et al*, the most predictive test for thrombosis is LA, and if IgG β 2GP1 or IgG aCL antibodies are also present in the patient, it will increase the specificity of the tests, and there is no role of IgM testing.¹⁶ We found no significant differences between β 2GP1 IgG or IgM in both LA groups. The presence of LA is the single most powerful predictor of thrombotic

risk and obstetric complications.¹⁷ In our study 23.50% cases showed LA positive. If LA, β 2GP1, and aCL are present in a patient, they are at highest risk of developing complications of pregnancy or thrombosis.¹⁷ We found three cases in which all three antibodies were present, so these patients are at highest risk of developing these complications and/or Catastrophic APS. Díaz-Coronado *et al*¹⁸ compared the thrombotic events and obstetrical complications between primary APS and secondary APS and found that thrombotic events were more common in the primary APS group. As regards obstetrical events like miscarriages, there were no significant differences between the two groups. Women with positive β 2GP1 IgM were at three times increased risk of developing obstetrical complications like miscarriages. This is in contrast to the study by Keeling *et al*¹⁶ who observed no role of IgM testing in APS. Mushtaq *et al*¹⁴ found the IgM aCL to be the most common antibody found in the South Asian region, followed by IgG aCL and LA. We found LA to be the most common positive antibody, followed by aCL IgM and β 2GP1 IgG respectively.

There were certain limitations to our study. These antibodies were not retested after 12 weeks as is the recommendation. This is probably due to the high financial burden in a low income country such as ours. The laboratory methods of measurement of these different antibodies were studied, and it was found that all the methods have their pitfalls.¹⁹ LA is prone to interference by many substances, aCL and β 2GP1 can be measured by a variety of methods, so causing a large variation of results.¹⁹ This may also be true in our study.

CONCLUSION

Anti- β 2GP1, Anti-cardiolipin and Lupus anticoagulant antibodies are valuable markers for the diagnosis of Anti-phospholipid syndrome. They are better markers to rule out the disease as they have a high specificity and negative predictive value.

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TP: Concept and final approval

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ORIGINAL ARTICLE

CLINICAL AND ANATOMICAL CORRELATES OF NASAL SYMPTOMS FOLLOWING INTRANASAL BECLOMETHASONE DIPROPIONATE IN ALLERGIC RHINITIS

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Background: Allergic rhinitis is a common inflammatory nasal mucosal disorder. Inferior turbinate hypertrophy may influence symptom severity and response to intranasal corticosteroid therapy. Objective was to evaluate clinical and anatomical correlates of nasal symptoms and assess changes following intranasal beclomethasone dipropionate in allergic rhinitis patients. **Methods:** This quasi-experimental pre-post study was conducted at the Department of ENT, KRL Hospital, Islamabad (Oct 2024–Jun 2025). A total of 960 consecutive patients with allergic rhinitis were enrolled. Sneezing, rhinorrhoea, nasal obstruction, and post-nasal drip were assessed in relation to inferior turbinate hypertrophy. Patients received one-week intranasal beclomethasone dipropionate. Symptom severity was evaluated using a modified Total Nasal Symptom Score and data was analyzed on SPSS-24. **Results:** Runny nose (94.8%) and sneezing (88.5%) were most prevalent, followed by nasal obstruction (82.3%). Moderate disease was observed in 43.8% of patients. Inferior turbinate hypertrophy was significantly associated with nasal obstruction. Post-treatment symptom severity declined, with greater improvement in rhinorrhoea and sneezing than nasal obstruction. **Conclusion:** Inferior turbinate hypertrophy was associated with greater symptom severity. Intranasal beclomethasone dipropionate significantly improved symptoms, and the modified Total Nasal Symptom Score effectively assessed treatment response.

Keywords: Allergic rhinitis, Beclomethasone dipropionate, Inferior turbinate hypertrophy, Nasal obstruction, Total nasal symptom score

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INTRODUCTION

Allergic rhinitis is a very common clinical chronic inflammatory immune-mediated condition in which nasal mucosa is involved. It is caused by release of immunoglobulin E (IgE) in response to environmental allergens. Other factors contributing in its aetiology are recurrent respiratory tract infections, tonsillar and adenoidal hypertrophy, rhinosinusitis, otitis media and interna.^{1,2} The common sign and symptoms of allergic rhinitis are running nose and eyes, blockage of nose and nasal sinuses, sneezing, post nasal drip and itching. All these conditions affect the life of an individual, daily activities and sleep both in personal and public places.³ Since past few decades throughout the globe, the allergic disorders including allergic rhinitis are increasing day by day with a ratio of 10–30% of the population.⁴ The World Health Organization (WHO), has introduced a program named with Allergic Rhinitis and its Impact on Asthma (ARIA). The importance of this program is to give community based awareness about the early recognition and management of allergic rhinitis as it is strongly linked asthma and other respiratory diseases.⁵ In pathophysiology of allergic rhinitis nasal cavity plays an important role. The epithelium of nasal mucosa is ciliated with rich vascular

supply. This is highly responsive to allergens. Immediately after exposure to allergens histamine is released, causing vasodilation, increases vascular permeability and ultimately leads to oedema of mucosa. All causes nasal congestion and rhinorrhoea.⁶ In nasal cavity the inferior turbinate plays a key role to humidify the inspired air and regulate the air flow by filtering the foreign particles. In allergic rhinitis, the inferior turbinate mostly undergoes hypertrophy due to continuous inflammation. Side by side the mucosal oedema also leads to narrowing of air ways and further impairing the airflow.⁷ Osteomeatal complex is another anatomical region that is located in middle meatus, that serves to drain the frontal, maxillary and anterior ethmoidal sinuses. Inflammatory swelling of the nasal mucosa can also obstruct this region, resulting in impaired drainage of sinuses and symptoms like facial pressure and post-nasal drip. This highlights the close functional relationship between the nasal cavity and paranasal sinuses in allergic conditions.⁸

The most effective treatment for allergic rhinitis is intranasal corticosteroids due to their strong anti-inflammatory action. Among these, beclomethasone dipropionate is widely used and has been shown to reduce nasal inflammation, reducing the

swelling of turbinates and improving nasal airflow. It acts locally on the nasal mucosa, leading to relief of symptoms such as rhinorrhoea, sneezing and nasal obstruction. Because of its effectiveness and safety profile, beclomethasone is commonly used as a first-line therapy in the management of allergic rhinitis.⁹ To assess the severity of symptoms in allergic rhinitis, standardized scoring systems are commonly used. One of the most widely used tools is the Total Nasal Symptom Score (TNSS), which evaluates key symptoms such as sneezing, rhinorrhoea and nasal obstruction each graded from 0–3 (no symptoms mild, moderate and severe symptoms respectively). This scoring system provides a reliable method to measure symptom severity and monitor response to treatment and is frequently used in clinical studies of allergic rhinitis.¹⁰

In Pakistan the most common allergic disorder is allergic rhinitis affecting almost 24.62% of general population and the etiological factors behind this are pollens, dust and pollution especially in urban areas.¹¹ The available literature on allergic rhinitis mainly focuses on pharmacological management, with less emphasis on the relationship between clinical symptoms and underlying nasal anatomy. Although the association between inferior turbinate hypertrophy, nasal obstruction and the effectiveness of intranasal corticosteroids is well established but there is limited local data from our population. Environmental factors such as pollen exposure in Islamabad may influence disease presentation and treatment response. Therefore, this study was conducted to evaluate allergic rhinitis in relation to nasal anatomy, particularly the inferior turbinates, using a standardized symptoms based scoring system (modified TNSS). This provides an objective assessment of symptom severity and contributes local evidence to support better patient management.

METHODOLOGY

The quasi-experimental pre-post study was conducted department of ENT KRL hospital Islamabad over a period of 09 months from October 2024 to June 2025 after obtaining ethical approval from CPSP with letter number CPSP/REU/ENT-2021-045-999. A total of 960 patients were included in the study. A formal sample size calculation was not performed. All eligible patients presenting during the study period with clinically diagnosed cases of allergic rhinitis were included by using non-probability consecutive sampling to maximize sample size and to improve the precision of estimates. Patients aged 20–60 years of either gender were included. Patients with a history of asthma, smoking, deviated nasal septum, inferior turbinate hypertrophy due to structural causes, acute upper respiratory tract infections, those already on prolonged treatment and pregnant females were excluded from the

study. After obtaining informed consent, detailed history and clinical examinations of all patients were done. Symptoms including sneezing, rhinorrhoea, nasal obstruction and post-nasal drip were recorded. This study was conducted without a control group, as all patients received intranasal corticosteroid therapy as part of routine clinical management. Patients were treated with intranasal corticosteroid beclomethasone dipropionate at a dose of 0.1 mg daily (50 µg per spray), administered as one spray in each nostril twice daily. Treatment was continued for a period of one week (the treatment duration of one week was selected to assess early clinical response to intranasal corticosteroid therapy). Symptom severity was recorded before and after treatment using a standardized scoring system, and improvement was defined as a reduction of $\geq 50\%$ in the total symptom score. Nasal examination was carried out using a nasal speculum and headlight to assess anatomical findings. This anatomical assessment is used as a part of routine evaluation. Although nasal endoscopy and imaging are available, they were not included in the study protocol to maintain uniform assessment across all patients. Clinical findings were interpreted in relation to nasal anatomy but special focus was on important anatomical areas such as the inferior turbinates due to their role in airflow regulation and nasal obstruction. A standardized symptom based scoring system adapted from Total Nasal Symptom Score (TNSS) which includes sneezing, rhinorrhoea and nasal obstruction used to assess the severity of symptoms each graded from 0 to 3 and the total score ranges from 0–9 in the modified version. A reduction of $\geq 50\%$ in score was considered significant improvement.¹⁰

Data were analysed using SPSS-24. Categorical variables were presented as frequencies and percentages. Normality of the data was assessed before applying parametric tests. Pre- and post-treatment TNSS scores were compared using paired *t*-test, while associations between variables were assessed using chi-square test, and $p \leq 0.05$ was considered significant. No formal adjustment for potential confounding variables was performed, and multivariate analysis was not conducted as the primary objective of the study was exploratory in nature.

RESULTS

A total of 960 patients with allergic rhinitis were included in the study. The most common clinical findings were rhinorrhoea, sneezing and nasal obstruction. These symptoms were interpreted in relation to underlying nasal anatomy, particularly involving the inferior turbinates. A significant association was observed between inferior turbinate hypertrophy and nasal obstruction. Assessment of treatment response following intranasal corticosteroid

therapy, specifically beclomethasone dipropionate, showed improvement in the majority of patients based on the standardized symptom score. Detailed anatomical correlations and treatment outcomes are presented in the following tables.

Table-1: Anatomical clinical findings (n=960)

Clinical Findings	Anatomical Interpretation	n	%
Nasal obstruction	Inferior turbinate hypertrophy/airway narrowing	790	82.3
Rhinorrhoea	Nasal mucosal gland hyperactivity	910	94.8
Sneezing	Nasal mucosal irritation	850	88.5
Post-nasal drip	Nasopharyngeal/sinus involvement	640	66.7

Table-2: Association of inferior turbinate hypertrophy with nasal obstruction

Inferior Turbinate Status	Obstruction		Total	p
	Present	Absent		
Hypertrophy				
Present	650	70	720	0.001
Absent	140	100	240	

Table-3: Comparison of TNSS scores before and after treatment with intranasal beclomethasone dipropionate (Mean±SD)

Symptom	Pre-treatment	Post-treatment	p
Sneezing	2.4±0.6	0.9±0.5	<0.001
Rhinorrhoea	2.5±0.5	0.8±0.4	<0.001
Nasal obstruction	2.3±0.7	1.0±0.6	<0.001

Table-4: Severity of symptoms based on modified TNSS (n=960)

Severity	Frequency	Percentage (%)
Mild	290	30.2%
Moderate	420	43.8%
Severe	250	26.0%
Total	960	100%

DISCUSSION

Allergic rhinitis is a common inflammatory disease of the upper respiratory pathway associated with symptoms like nasal obstruction, sneezing and rhinorrhoea.¹ In this study, we focused on understanding of these symptoms in relation to nasal anatomy, especially the role of the inferior turbinates.

In our study, the most common symptom (Table-1) was rhinorrhoea (94.8%), with sneezing (88.5%) and nasal obstruction (82.3%). These findings are similar to previous studies done by Siddiqui *et al* and Bernstein *et al*. They report rhinorrhoea and sneezing as the most frequent symptoms of allergic rhinitis. These are caused by inflammation of the nasal lining and release of chemical mediators such as histamine, which increases glandular activity and irritate sensory nerves.^{12,13} Our results showed that nasal obstruction in a large number of patients (82.3%). This symptom is strongly related to anatomical changes in the nose, especially involving the inferior turbinates that help to regulate the airflow and make the air breathable. When these structures become enlarged due to inflammation, they can narrow the nasal airway,

increases the resistance to airflow and cause obstruction.^{14,15} In our study, a significant association was found between inferior turbinate hypertrophy and nasal obstruction ($p=0.001$) (Table-2). This supports the idea of nasal blockage caused by enlargement of turbinates.¹⁶ The inferior turbinate has a rich blood supply. In case of allergic rhinitis this vascular tissue becomes swollen, which explains why patients experience persistent nasal blockage.¹⁷ Post-nasal drip was also present in many patients (66.7%). This symptom indicates involvement of the back of the nasal cavity and upper airway. Although in our research sinuses were not studied but the literature suggests that inflammation can affect the entire nasal passage and lead to mucus accumulation. Joo *et al* explained that excessive mucus production and reduced clearance can result in post-nasal drip, especially in allergic conditions.¹⁸

The use of a standardized scoring system to assess the severity of symptoms and treatment response was another important aspect of our study. We used a modified Total Nasal Symptom Score (TNSS) which included sneezing, rhinorrhoea and nasal obstruction. Each symptom was graded from 0–3 and the total score is 0–9, to measure the overall severity of the disease. This scoring system allowed us to objectively compare symptoms before and after treatment intranasal corticosteroids, beclomethasone dipropionate. A reduction of 50% or more in the total score was considered significant. This approach provides a reliable method to assess treatment effectiveness.¹⁰ In our study, most patients had moderate severity (43.8%), 30.2% with mild and 26% with severe disease. A significant reduction in TNSS scores was observed after treatment with intranasal beclomethasone dipropionate, as shown in Table-4. Mean scores for sneezing (pre- treatment 2.4±0.6 and post treatment 0.9±0.5), rhinorrhoea (pre-treatment 2.5±0.5 and post treatment 0.8±0.4) and nasal obstruction (pre-treatment 2.3±0.7 and post treatment 1.0±0.6) decreased markedly after treatment ($p<0.001$), indicating marked symptom improvement following treatment (Table-3). These findings are consistent with previous studies that have demonstrated the effectiveness of intranasal corticosteroids in reducing symptom severity in allergic rhinitis.⁹ The improvement was more in rhinorrhoea and sneezing as compared to nasal obstruction. This can be explained by the fact that nasal obstruction is partly due to structural changes such as turbinate hypertrophy, which may take longer to resolve even after inflammation is reduced.¹⁹ These findings are comparable to other studies where intranasal corticosteroids have been shown to significantly reduce symptom scores, particularly for rhinorrhoea and sneezing. This scoring system has been used in previous studies of allergic rhinitis done by Ripp *et al* and Restimulia *et al*, where they considered TNSS

a standard tool to evaluate the burden of symptoms and response to therapy.^{20,21} As the study did not include a comparator group, the observed improvement should be interpreted as an association following treatment rather than definitive evidence of treatment effectiveness.

LIMITATIONS

This study was conducted at a single centre and anatomical assessment was based on clinical examination without the use of imaging techniques such as CT scan or nasal endoscopy. Nasal sinuses were not specifically evaluated and environmental or allergen-related factors were not assessed in detail. In addition, the study did not include a comparator or control group, which limits causal interpretation of the observed symptom improvement following treatment. The short duration of therapy (one week) may also not reflect the full therapeutic effect of intranasal corticosteroids. Future studies should include control groups, multiple centres, objective diagnostic tools, longer follow-up periods and assessment of environmental influences for a more comprehensive evaluation of allergic rhinitis.

CONCLUSION

Inferior turbinate hypertrophy was associated with greater symptom severity. Intranasal beclomethasone dipropionate significantly improved symptoms, and the modified Total Nasal Symptom Score effectively assessed treatment response.

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ORIGINAL ARTICLE

PATTERNS OF LEFT VENTRICULAR HYPERTROPHY AND REMODELLING IN PAKISTANI PATIENTS WITH UNCONTROLLED HYPERTENSION: RELATIONSHIP WITH DURATION OF DISEASE, MEDICATION ADHERENCE, AND SALT INTAKE PROXIES

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Background: Left ventricular (LV) geometric remodelling is a common consequence of uncontrolled hypertension and is associated with adverse cardiovascular outcomes. Various clinical (duration of hypertension) and behavioural (adherence with medication and salt-intake) factors may influence LV geometry patterns. The objectives of this study were to determine the distribution of left ventricular geometry and to assess its association with duration of hypertension, medication adherence, and salt intake among patients with uncontrolled hypertension. **Methods:** A cross-sectional study conducted at Peshawar Institute of Cardiology. A total of 140 patients with uncontrolled hypertension were enrolled through consecutive sampling. Clinical data, duration of hypertension, medication adherence, and salt intake were recorded. Echocardiography was performed to assess left ventricular mass index (LVMI) and relative wall thickness (RWT), and LV geometry was classified into normal geometry, concentric remodelling, concentric hypertrophy, and eccentric hypertrophy. Data were analysed using SPSS-25. Chi-square test was applied to determine associations, and $p \leq 0.05$ was considered statistically significant. **Results:** The mean age of participants was 52.3 ± 10.1 years, with 55.7% males. Concentric hypertrophy was the most prevalent LV geometric pattern (32.9%), followed by normal geometry (24.3%), concentric remodelling (21.4%), and eccentric hypertrophy (21.4%). No statistically significant association was observed between LV geometry and duration of hypertension ($p=0.694$), medication adherence ($p=0.524$), or salt intake ($p=0.585$). **Conclusion:** Concentric hypertrophy was the predominant LV geometric pattern among patients with uncontrolled hypertension. Duration of hypertension, medication adherence, and salt intake were not significantly associated with LV geometry in this study population.

Keywords: Concentric hypertrophy, Hypertension, Left ventricular geometry, Medication adherence, Salt intake

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INTRODUCTION

Hypertension is a chronic cardiovascular disorder characterized by persistently elevated systemic arterial blood pressure and remains one of the leading modifiable risk factors for cardiovascular morbidity and mortality worldwide.¹ Sustained pressure overload primarily affects the left ventricle, leading to structural adaptations collectively referred to as left ventricular hypertrophy (LVH) and ventricular remodelling. LVH represents an increase in left ventricular mass due to myocardial cell enlargement, while remodelling reflects alterations in ventricular geometry, including concentric hypertrophy, eccentric hypertrophy, and concentric remodelling. These geometric patterns have important prognostic implications, particularly in patients with uncontrolled hypertension.²

Globally, hypertension affects more than one billion individuals and contributes substantially to ischemic heart disease, stroke, heart failure, and premature mortality.³ The burden is particularly high in low- and middle-income countries. In South Asia, the prevalence of hypertension ranges from 25 to 35%

among adults, with higher rates reported in urban populations.⁴ Despite the availability of effective pharmacological therapies, blood pressure control remains suboptimal in many patients, accelerating target-organ damage, particularly structural cardiac changes that increase long-term cardiovascular risk.

The development of hypertensive LVH is multifactorial. Persistent elevation of systemic vascular resistance imposes chronic afterload on the left ventricle, stimulating compensatory myocardial hypertrophy. The duration of hypertension plays a key role, as prolonged exposure to elevated blood pressure enhances myocardial stress and structural adaptation. In addition, medication adherence significantly influences disease progression, as poor adherence leads to sustained uncontrolled blood pressure and accelerates cardiac remodelling. High dietary sodium intake, common in South Asian populations, is another important contributor. Other factors such as age, obesity, diabetes mellitus, dyslipidaemia, and genetic susceptibility may further influence the extent and pattern of ventricular hypertrophy.⁵

The pathophysiology of left ventricular remodelling involves complex hemodynamic and neurohormonal mechanisms. Chronic pressure overload increases myocardial wall stress, leading to adaptive myocyte hypertrophy aimed at maintaining wall tension. Activation of the rennin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system promotes myocardial fibrosis and extracellular matrix deposition, resulting in alterations in ventricular geometry.⁶ Concentric hypertrophy develops in response to pressure overload and is characterized by increased wall thickness. Eccentric hypertrophy may occur when volume overload coexists. Over time, these structural changes impair diastolic relaxation and ventricular compliance and may progress to systolic dysfunction and overt heart failure.⁷

Left ventricular hypertrophy often remains asymptomatic in early stages but may eventually lead to symptoms such as exertional dyspnoea, reduced exercise tolerance, palpitations, and angina-like chest discomfort. The presence of LVH significantly increases the risk of atrial fibrillation, ventricular arrhythmias, ischemic heart disease, heart failure, and sudden cardiac death.⁷ Diagnosis primarily relies on assessment of left ventricular mass index (LVMI), wall thickness, and geometric patterns on echocardiography. Management focuses on optimal blood pressure control using antihypertensive therapy along with sodium restriction, weight reduction, and regular physical activity.⁸

Although regression of LVH is associated with improved cardiovascular outcomes, limited local data exist regarding patterns of left ventricular remodelling in Pakistani patients with uncontrolled hypertension and the role of modifiable factors such as disease duration, medication adherence, and salt intake. Understanding these relationships may help improve risk stratification and preventive strategies in this population.

MATERIAL AND METHODS

This cross-sectional analytical study was conducted at the Department of Cardiology, Peshawar Institute of Cardiology over a period of six months from June to November 2025. A total of 140 patients with uncontrolled hypertension were enrolled using non-probability consecutive sampling. Uncontrolled hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on at least two separate readings despite ongoing antihypertensive therapy or documented poor blood pressure control in known hypertensive patients.⁹ Adult patients aged 30–70 years of either gender with a confirmed diagnosis of primary hypertension for at least one year were included. Patients with secondary hypertension, known valvular heart disease, congenital

heart disease, cardiomyopathy unrelated to hypertension, ischemic heart disease with prior myocardial infarction, chronic kidney disease stage IV or above, and pregnant women were excluded to minimize confounding structural cardiac changes.

The sample size was calculated using Daniel's formula (utilized in WHO guidelines for single proportions in cross-sectional studies) taking anticipated frequency of left ventricular hypertrophy as 50%⁴, confidence level of 95%, and a margin of error of 8%. The calculated sample size was 150; however, after accounting for feasibility and expected complete data availability, 140 patients were included in final analysis.

After obtaining approval from the institutional ethical review committee and written informed consent from the participants, demographic and clinical data were recorded using a structured proforma. Information regarding age, gender, duration of hypertension, current antihypertensive medication, and comorbidities was documented. Duration of disease was categorized into ≤ 5 years, 6–10 years, and >10 years based on patient history and medical records. Medication adherence was assessed using a structured self-reported validated adherence questionnaire¹⁰, and patients were categorized as adherent or non-adherent based on standard scoring criteria. Salt intake proxies were evaluated through dietary history, including frequency of adding extra salt to meals, consumption of processed or salted foods, and self-reported high-salt dietary habits.

Blood pressure was measured on a mercury sphygmomanometer with the patient in a seated position. Patients underwent transthoracic echocardiography by an experienced cardiologist using a standardized protocol. Left ventricular mass was calculated using the Devereux formula, and left ventricular mass index (LVMI) was derived by indexing to body surface area. Left ventricular hypertrophy was defined according to established gender-specific cut-off values of LVMI (≥ 115 g/m² for males and ≥ 95 g/m² for females). Relative wall thickness was calculated to determine geometric patterns. Based on LVMI and relative wall thickness, patients were classified into normal geometry, concentric remodelling, concentric hypertrophy, or eccentric hypertrophy.

Data were analysed using SPSS-29. Quantitative variables such as age, duration of hypertension, blood pressure, and LVMI were expressed as Mean $\pm$ SD, while qualitative variables such as gender, adherence status, salt intake category, and remodelling patterns were expressed as frequencies and percentages. The association between patterns of left ventricular remodelling and duration of disease, medication adherence, and salt intake proxies was assessed using Chi-square test, and $p \leq 0.05$ was considered statistically significant.

RESULTS

The study population comprised of 140 patients with a mean age of 52.3 ± 10.1 years. Male participants accounted for 55.7% of the cohort, whereas females constituted 44.3%. Regarding duration of hypertension, 34.3% had hypertension for ≤ 5 years, 40.0% for 6–10 years, and 25.7% for more than 10 years. Most (65.7%) patients were adherent to medications, while 34.3% were non-adherent; and 27.1% had low, 40.0% moderate, and 32.9% had high salt intake (Table-1).

The systolic blood pressure (SBP) ranged from 140 to 180 mmHg (mean 160.97 ± 11.37) and diastolic blood pressure (DBP) from 90 to 110 mmHg (mean 100.01 ± 5.80). Left ventricular mass ranged from 160 to 299 g (236.40 ± 42.16 g), and the left ventricular mass index (LVMI) ranged from 96 to 160 g/m², (129.49 ± 18.54 g/m²). Relative wall thickness (RWT) varied between 0.34 and 0.65 (0.49 ± 0.09).

Overall distribution of left ventricular geometry indicated that 24.3% patients had normal geometry, 21.4% had concentric remodelling, 32.9% had concentric hypertrophy, and 21.4% had eccentric hypertrophy, showing a predominance of concentric hypertrophy among the study population (Table-2).

When stratified by duration of hypertension, patients with hypertension of 6–10 years showed the highest proportion of concentric hypertrophy (47.8%), whereas those with < 5 years of hypertension had a relatively higher proportion of eccentric hypertrophy (43.3%). Normal geometry was more common among patients with 6–10 years of hypertension (41.2%), and concentric remodelling was fairly evenly distributed across all duration categories. There was no statistically significant association between duration of hypertension and left ventricular geometry ($p=0.694$), (Table-3).

Patients adherent to medication had a higher prevalence of concentric hypertrophy (37.0%) compared with non-adherent patients (25.0%). Normal geometry was more common among non-adherent patients (29.2%) than adherent patients (21.7%). Concentric remodelling and eccentric hypertrophy were distributed similarly between the two groups. The Chi-square analysis demonstrated no statistically significant relationship between medication adherence and left ventricular geometry ($p=0.524$), (Table-4).

Concentric hypertrophy was most frequent among patients with moderate salt intake (39.3%), while eccentric hypertrophy was slightly higher among those with high salt intake (21.7%) compared with low intake (21.1%). Normal geometry was most commonly observed in patients with high salt intake (28.3%). Concentric remodelling appeared highest in the low salt intake group (28.9%). No statistically significant association was found between salt intake and left ventricular geometry ($p=0.585$), (Table-5).

Table-1: Demographic and clinical characteristics of study participants (n=140)

Variable	Category	n (%)
Age (Mean age: 52.3 ± 10.1 Years)	30–39	18 (12.9)
	40–49	40 (28.6)
	50–59	44 (31.4)
	60–70	38 (27.1)
Gender	Male	78 (55.7)
	Female	62 (44.3)
Duration of Hypertension	≤ 5 years	48 (34.3)
	6–10 years	56 (40.0)
	> 10 years	36 (25.7)
Medication Adherence	Adherent	92 (65.7)
	Non-Adherent	48 (34.3)
Salt Intake Proxy	Low	38 (27.1)
	Moderate	56 (40.0)
	High	46 (32.9)

Table-2: Distribution of left ventricular geometry among study participants (n=140)

LV Geometry Category	n (%)
Normal	34 (24.3)
Concentric Remodelling	30 (21.4)
Concentric Hypertrophy	46 (32.9)
Eccentric Hypertrophy	30 (21.4)

Table-3: LV geometry stratified by duration of hypertension [n (%)]

Duration of Hypertension	Normal	Concentric Remodelling	Concentric Hypertrophy	Eccentric Hypertrophy
≤ 5 years	11 (32.4)	9 (30.0)	15 (32.6)	13 (43.3)
6–10 years	14 (41.2)	11 (36.7)	22 (47.8)	9 (30.0)
> 10 years	9 (26.5)	10 (33.3)	9 (19.6)	8 (26.7)
Total	34 (24.3)	30 (21.4)	46 (32.9)	30 (21.4)

$$\chi^2=3.873, df=6, p=0.694$$

Table-4: LV Geometry stratified by medication adherence (n=140)

Medication Adherence	Normal	Concentric Remodelling	Concentric Hypertrophy	Eccentric Hypertrophy
Adherent	20 (21.7)	19 (20.7)	34 (37.0)	19 (20.7)
Non-Adherent	14 (29.2)	11 (22.9)	12 (25.0)	11 (22.9)
Total	34 (24.3)	30 (21.4)	46 (32.9)	30 (21.4)

$$\chi^2=2.240, df=3, p=0.524$$

Table-5: LV Geometry stratified by salt intake

Salt Intake	Normal	Concentric Remodelling	Concentric Hypertrophy	Eccentric Hypertrophy
Low	7 (18.4)	11 (28.9)	12 (31.6)	8 (21.1)
Moderate	14 (25.0)	8 (14.3)	22 (39.3)	12 (21.4)
High	13 (28.3)	11 (23.9)	12 (26.1)	10 (21.7)
Total	34 (24.3)	30 (21.4)	46 (32.9)	30 (21.4)

$$\chi^2=4.687, df=6, p=0.585$$

DISCUSSION

Hypertension remains a major global public health challenge and a leading cause of cardiovascular morbidity and mortality. Persistent elevation of blood pressure leads to structural and functional cardiac alterations, particularly changes in left ventricular (LV) geometry, which are recognized predictors of adverse cardiovascular outcomes.^{11–13} In the present study, concentric hypertrophy emerged as the most prevalent LV geometric pattern, followed by normal geometry,

concentric remodelling, and eccentric hypertrophy. These findings indicate a substantial burden of maladaptive myocardial remodelling among patients with persistently uncontrolled blood pressure.

Our results are consistent with those reported by Hahkan *et al*¹⁴ and Khan *et al*¹⁵, who observed high prevalence of LVH among hypertensive patients and significantly higher left ventricular mass (LVM) and left ventricular mass index (LVMI) in uncontrolled compared with controlled hypertensive individuals. Although our study focused on geometric patterns rather than overall LVH prevalence, the predominance of concentric hypertrophy and elevated mean LVMI support the association between uncontrolled hypertension and adverse cardiac remodelling in Pakistani populations.

In contrast, Masood *et al*¹⁶ reported a lower prevalence of LVH among newly diagnosed hypertensive patients. Their cohort included younger individuals with recently diagnosed hypertension, whereas our study involved patients with established and uncontrolled disease. This difference likely explains the higher LVMI and greater prevalence of concentric hypertrophy observed in our population, highlighting the progressive nature of LV remodelling with prolonged hypertension and inadequate blood pressure control.

Although a trend toward increased concentric hypertrophy with longer disease duration was observed, no statistically significant association was identified. This finding differs from the study by Adeseye *et al*¹⁷ who reported larger ventricular dimensions in patients with longer disease duration and identified concentric remodelling as the most common geometric pattern. Differences in treatment status, blood pressure control, and population characteristics may explain these variations, as their cohort included treated hypertensive patients whereas our study focused on individuals with uncontrolled hypertension.

No significant association was found between salt intake and LV geometry. Previous studies using 24-hour urinary sodium measurements, such as those by Cailar *et al*¹⁸ have demonstrated a positive association between sodium intake and LVMI. Other investigations, including those by Nista *et al*¹⁹ and Van der Westhuizen *et al*²⁰ have also reported significant relationships between sodium excretion and increased cardiac mass. Lack of association in our study may be attributed to the use of dietary proxy measures rather than objective sodium assessments, as well as limited statistical power.

Medication adherence also showed no significant relationship with LV geometry, although adherent patients demonstrated a slightly higher proportion of concentric hypertrophy. These findings are consistent with Kamasova *et al*²¹ who reported only a weak inverse correlation between adherence and LVMI.

Overall, the absence of statistically significant associations in our study reflects the multifactorial nature of LV remodelling in hypertension, where hemodynamic load, neurohormonal activation, and genetic factors interact with behavioural determinants such as medication adherence and dietary habits.

A major strength of this study is the echocardiographic evaluation of LV geometry using standardized parameters (LVMI and RWT). However, several limitations should also be acknowledged. The cross-sectional design precludes causal inference, and the moderate sample size may have limited statistical power. Salt intake was assessed indirectly through dietary history rather than objective sodium measurements.

CONCLUSION

Concentric hypertrophy was the most prevalent LV geometric pattern among patients with uncontrolled hypertension. No significant association was found between LV geometry and duration of hypertension, medication adherence, or salt intake. Further large-scale prospective studies are required to clarify determinants of LV remodelling in hypertensive patients.

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MM: Concept, Study design, Data analysis, Manuscript drafting

AR: Supervision, Data interpretation

AW: Study design, Data collection, Data interpretation

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ORIGINAL ARTICLE

IMPACT OF DIGITAL TECHNOLOGY ON THE TEACHING AND LEARNING IN DENTAL EDUCATION

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Background: Incorporation of Digital tools for acquisition of high quality knowledge and skills is dire need of dental education which is quite challenging. **Methods:** Study was conducted at School of Dentistry Shaheed Zulfiqar Ali Bhutto Medical University Islamabad for one month from 2nd October to 2nd November 2025 under the Ethical Approval No. SOD/ERB/2025/95. Qualitative research was conducted where 50 undergraduate 2nd year BDS students participated. Large group interactive session was used as initial mode of knowledge transfer through PowerPoint presentation pertaining to Dental Material Sciences. The learning process of students was investigated through a digital tool 'Kahoot'. Five open ended questions were used for students' interviews to collect generic feedback regarding fun and ease while handling digital technology. This qualitative data was displayed in word codes recorded from software R Studio-24. **Results:** Out of 50 participants, 44 were female. Students depicted that Kahoot was more lesson-understanding, entertaining, beneficial, enjoyable, valuable, helpful, competitive showing effective permanent learning with more grasp on the topic. Digital tool promoted learning with ease and fun. Kahoot enhanced platform for collaborative learning with sense of high scoring achievement thus, confirming that Kahoot is best option for learning purposes in BDS teaching at undergraduate level. **Conclusion:** Digital tool like Kahoot enhanced the learning process of undergraduate 2nd year BDS students pertaining to subject of Dental Material Sciences with ease and fun thus promoting collaborative learning in a friendly environment.

Keywords: Dental Education, Digital tool, Fun, Kahoot, Teaching

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INTRODUCTION

There is dire need of incorporating digital tools in the dental education for acquisition of high quality knowledge and skills which is quite challenging.¹ Digital technology based systems are required for better retention of this subject in order to improve the academic performance. The digitally applicable web based blended learning inducing online Kahoot can be used not only for improving the learning process but also amplifying the understanding and engagement level of students with ease and fun.^{2,3}

According to recent studies, Kahoot has been used in the medical profession attributed to various subjects including pathology, pharmacology, immunology, microbiology, and histology since 2017.⁴ This online learning has become popular among medical professionals during COVID-19 epidemic where physical in-person training was impossible as a result of lockdown worldwide.⁵ The lack of on-campus instruction during this COVID shift has been linked to lower levels of involvement, attention, collaboration, loneliness altogether with mental and general health deterioration. Thus, Kahoot has proven to be a useful and an efficient e-learning platform that has the capacity of increasing enthusiasm and engagement of students with ease and fun.³

Currently, health professional educators are facing the genuine challenge of keeping students engaged during teaching and learning sessions pertaining dental speciality that could be useful in the development of metacognitive skills. Retention of Dental Material Sciences subject matter attributed to dental education is difficult because its curriculum is a true combination of physics, chemistry and biology that needs attention. There is scarcity of data available regarding learning of students with fun and ease at undergraduate level in dentistry. This study aims to gauge the better learning of undergraduate 2nd year BDS students attributed to Dental Material Sciences subject.

METHODOLOGY

This study was conducted at School of Dentistry, Shaheed Zulfiqar Ali Bhutto Medical University for a period of one month (2nd October to 2nd November 2025) with the Institutional Ethical Approval No. SOD/ERB/2025/95. Sample size calculated for the current study was 50 which was supported by Central limit theorem of normal approximation for samples >30.⁶ Purposive sampling technique was used where 50 undergraduate second year BDS students volunteered to participate in this study and informed consent was obtained from them. The study aimed to investigate the

effect of Digital online Kahoot quiz on learning subject of Dental Material Sciences. The initial mode for transfer of knowledge was long group interactive session after which learning of students was gauged through validated open ended questionnaire available in the literature.^{4,5} The digital quiz involved creation of a Kahoot teacher account following free registration on 'https://kahoot.com/'. A Kahoot quiz was generated on 'https://create.kahoot.it', comprising of 20 multiple-choice questions supplemented with images, each question had a time limit of 30 seconds (Figure-1).^{6,7}

The feed back of 2nd year undergraduate BDS students was recorded via interviews for finding the effect of Kahoot on learning of Dental Material Sciences subject. The open ended questionnaire used for the Kahoot led learning feedback pertaining Dental Material Sciences subject is illustrated in Table-1.

R Studio-24 was used for the word codes obtained from the open ended questionnaire responses of the participants. Qualitative data was displayed as frequencies and percentages from SPSS-26.

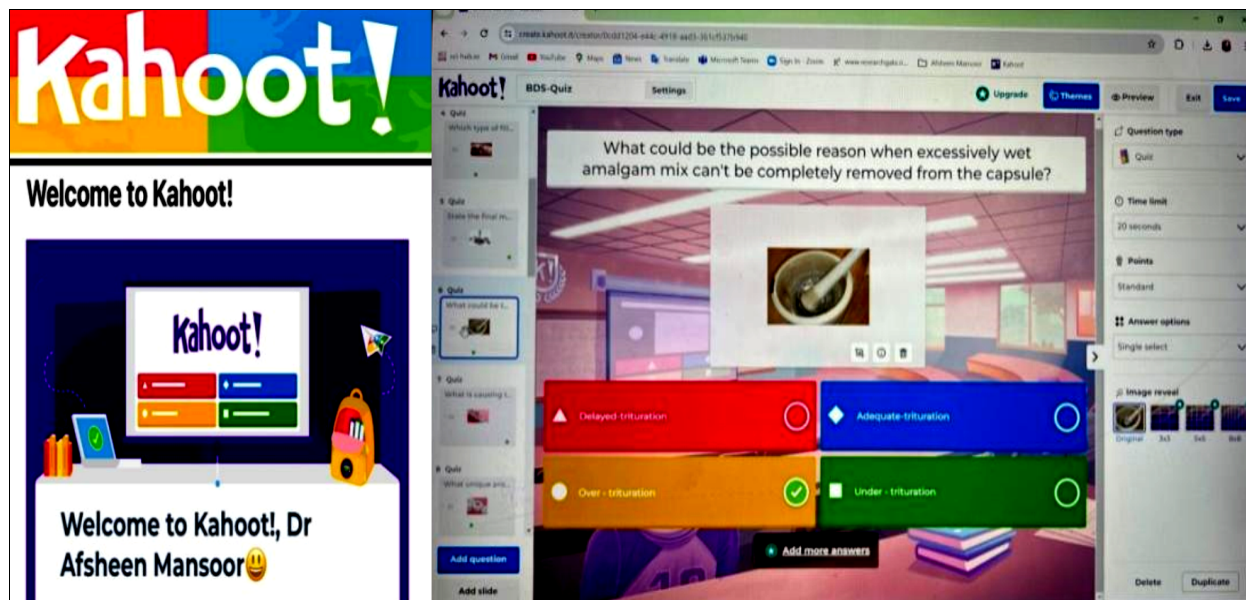


Figure-1: Kahoot pertaining Dental Material Sciences subject for 2nd year BDS students

Table-1: Open-ended questionnaire regarding feedback of students attributed to Kahoot led learning

No.	Questions attributed to Kahoot led learning in Dental Material Sciences subject
1.	What do you think about the game Kahoot! as an in-class activity that you have participated in?
2.	How did you feel while you were playing Kahoot!?
3.	Should the game Kahoot! be used for Dental Material Sciences lessons? Why?
4.	What do you think about learning Dental Material Sciences subject via Kahoot?
5.	Has Kahoot! changed your opinions towards learning Dental Material Sciences subject?

RESULTS

The pictorial version of R Studio displayed verbal responses of students regarding Kahoot is illustrated in the Figure-2.

A total 44 (88.0%) female students and 6 (12.0%) male students participated in this study. The Kahoot Quiz was fully equipped with a mark score sheet tool that checked the grasp of students pertaining Dental Material Sciences subject. The 2nd Year BDS students were actively interacting with their peers and were taking part in the quiz more enthusiastically. The response of the students regarding 5 qualitative questions was recorded through R Studio-24 where frequency and percentage of the highly repeated words from the open-ended questionnaire data was extracted to figure out the

opinion of undergraduate 2nd Year BDS students regarding utilization of Kahoot for learning purposes. The code word responses used excessively by 2nd Year BDS students regarding Kahoot in Q-1 to Q-5 are given in Figure-3.

This study revealed that Kahoot quiz is more lesson-understanding, entertaining, beneficial, enjoyable, valuable, helpful, competitive showing effective learning, more grasp on topic, permanent learning, more effective learning, easy learning with fun. Kahoot enhanced platform for collaborative learning, improving knowledge, proper educational practice, interesting revision tool with broader perspectives, confirming that Kahoot is good option for learning of 2nd Year BDS students at the undergraduate level (Figure-3).



Figure-2: Code word pictorial depiction by R Studio-24 showing various responses of 2nd Year BDS students regarding Kahoot led learning

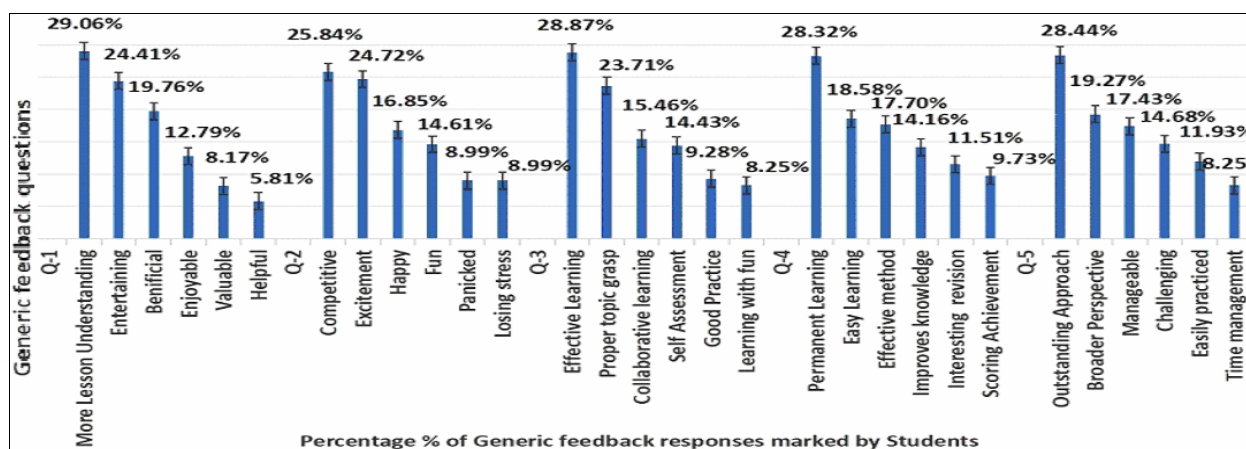


Figure-3: Generic feedback percentages of 2nd year BDS students regarding Kahoot led learning

DISCUSSION

Kahoot is the best tool for learning purposes in BDS teaching at undergraduate level pertaining Dental Material Sciences with sense of high scoring achievement in broader perspectives. Kahoot is more lesson-understanding, entertaining, beneficial, enjoyable, valuable, helpful, competitive promoting effective permanent learning. Kahoot enhanced the grasp on Dental Material Sciences topic in an easy way with fun, thus providing a platform for collaborative learning. The usage of Digital tool in learning is quite challenging but if appropriately managed it could be beneficial for the knowledge retention purposes in the BDS teaching at the undergraduate level.

Learning with Kahoot is appreciated because of its friendly user capabilities, attractive features, and its healthy competition arising properties. Game-based learning is commonly considered as unique follow-up system that truly facilitates the student-centred learning where teachers are facilitators. Kahoot has capacity of delivering high concentration of knowledge through media into brains of the students.⁸ Delivery of academic content through this technology has become a promising avenue for students because of its versatility.

In recent years, combination of digital tools have played a major role in multiple fields such as robotics, and artificial intelligence (AI) machines.⁸ Various studies demonstrated that digital technology based learning engages the matter content more effectively in comparison to the traditional textbooks, written assignments and schooling. These studies have proven the positive effects of blended Kahoot based learning not only on the academic performances of the students but also their brain growth.^{9,10} Kahoot is more competitive, challenging and manageable in the learning process.^{11,12} The 2nd year BDS students in this study were familiar with the content matter that was already taught to them, therefore the Kahoot used in the review process was potent enough for imparting the deeper and permanent learning.

Collaborative learning in Kahoot magnified the competition level of these students for high scoring and they learnt time management in short duration as well. This instrumental tool is quite beneficial for students in overcoming the learning deficiencies in case if the subject matter is quite difficult to understand further, magnifying the smart features of this friendly human user digital technology and its usage in healthcare

systems at larger scale to benefit the general wellbeing, dental issues and mental health of individuals in a community. Future studies are required to employ this innovative digital technology for dental education among healthcare professionals at different levels.

LIMITATION

The limitation of the current study is its small sample size that might pose an impact on the results.

CONCLUSION

Digital tool like Kahoot amplified the learning process of undergraduate BDS students pertaining to Dental Material Sciences with ease and fun thus promoting collaborative learning in a friendly environment. It is difficult to develop such digital technology-based quizzes. Workshops should be carried out to train the teachers for creating proper questionnaires, assignments, discussions, exams and MCQs.

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ORIGINAL ARTICLE

MEDICAL STUDENTS' EXPERIENCE OF FEEDBACK DURING CLINICAL ROTATIONS IN PAKISTAN: A QUALITATIVE STUDY

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Background: Feedback in clinical medical education is crucial to bridge the gap between the learner's performance and competence. This study aimed to investigate the experience and perception of medical students' feedback during clinical training and especially factors that determine effectiveness and educational benefit. **Methods:** The qualitative design was based on semi-structured interviews with undergraduate medical students who completed clinical rotations in a public sector medical school in Northern Pakistan. The sampling technique was purposive and the interviews were conducted until thematic adequacy was attained. Thematic analysis was done with NVivo software. **Results:** Analysis led to the production of three interconnected themes namely characteristics of the feedback delivery, perceived impact of the feedback on the learning processes, and contextual barriers influencing feedback exchange. Students placed a lot of emphasis on timely, specific, and practical oriented feedback. Nevertheless, inconsistency or inarticulate feedback decreased regulatory certainty and clarity. Attendance to effective feedback was further restrained by hierarchical norms and lack of chances of conversation. **Conclusion:** The learning path of medical students involves clinical feedback as one of its major factors. Faculty feedback enhancements and integration of formal feedback mechanisms within the clinical training process can help to enhance the outcomes of the educational process and learner engagement.

Keywords: Clinical, Competence, Feedback, Medical Education, Medical Students, Pakistan, Performance, Undergraduate

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INTRODUCTION

Feedback is an undivided component of clinical medical education that plays the role of perfecting the performance¹, adjusting the career standards and educating clinical judgment among the learners.² Feedback is enabling to both reflective practice and developmental skills in the context of providing it in an effective way.³ Regardless of its identified significance, medical students have often expressed discontent in the quality and utility of feedback that they receive in clinical settings.^{4,5}

The adequate feedback has been characterized as precise, time based, practical, and integrated into a favorable educational context.^{6,7} Available evidence indicates that feedback in clinical environments has been found to be perceived as slow, unclear or not actionable enough to affect education. The opportunities to meaningful feedback interactions can further be limited by structural forces like high workload in the clinical setting and the deep-rooted hierarchical relationships.^{5,8} Under these conditions, the students might be reluctant to request clarification or start open communication with the managers.

Despite the vast amount of literature that has been conducted internationally related to feedback practices, there is scarcity of clinical rotation feedback qualitative research in Pakistan. The perspectives of the students in this context are paramount in explaining the

experiences of feedback in ordinary clinical training and informing educational interventions that are relevant to the specific area. This research thus intends to examine the experience of medical students in the context of feedback in clinical rotations, and also to find out factors that influence the perceived effectiveness of feedback.

METHODOLOGY

This qualitative study was approved by the institutional ethical review board, and all the participants gave informed consent. This study was carried out between May and Sep 2025 at a public sector medical college and its affiliated 500-bedded tertiary care hospital in Pakistan where students do their clinical rotations. Students included in the study rotated through Internal Medicine, General Surgery, Paediatrics, and Obstetrics/Gynaecology.

The purposive sampling strategy was used to ensure that all the clinical disciplines were represented. Semi-structured interviews of 30–45 minutes duration using an interview guide which discussed the experiences in feedback and perception about the feedback were done. Interviews continued until thematic saturation was achieved after 26 interviews; four additional interviews confirmed saturation. This is also in line with qualitative approaches in other clinical feedback studies.⁵ Audio-taped interviews were transcribed word-to-word.

NVivo software was used to perform thematic analysis. The transcripts were coded and the differences discussed. Themes emerged through the patterns of repeated data.

RESULTS

All 30 participants were between 21 and 25 years old, with balanced representation from both genders and clinical disciplines.

Theme 1: Quality and Delivery of Feedback

Participants described feedback as inconsistent, insufficiently specific, and reported receiving general comments rather than detailed feedback that could guide improvement:

"Sometimes I get feedback that just says 'good job' or 'needs improvement' without telling what exactly I should work on." (Participant 15)

Vague feedback was perceived as minimally helpful. Participants also expressed frustration with feedback that focused on minor details rather than core clinical skills:

"Feedback often feels superficial; it doesn't tell me what I need to fix or how to fix it." (Participant 8)

Theme 2: Impact of Feedback on Learning

Students emphasized that high-quality feedback enhances learning and motivation:

"When I get detailed feedback, I know what to do next. It pushes me to work harder." (Participant 18)

Conversely, poorly delivered feedback undermined confidence:

"If feedback is just criticism without guidance, I feel discouraged and unsure what to do next." (Participant 25)

Theme 3: Barriers to Effective Feedback

Barriers included hierarchical culture, limited dedicated time for feedback, and lack of structured mechanisms:

"Approaching seniors for feedback is intimidating. They seem busy and not easily approachable." (Participant 22)

Time constraints were cited as a key issue:

"Supervisors are focused on clinical duties, and feedback often feels like an afterthought." (Participant 19)

The results are elaborated in Table-1.

Table-1: Themes, Subthemes, and Illustrative Quotes

Theme	Subtheme	Illustrative Quote
Feedback quality and delivery	General and non-specific feedback	"Feedback often feels superficial..." (P8)
Feedback quality and delivery	Delayed feedback	"Feedback is often after the rotation..." (P12)
Impact on learning	Motivational value of feedback	"It pushes me to work harder." (P18)
Impact on learning	Negative effects of poor feedback	"I feel discouraged..." (P25)
Barriers to effective feedback	Hierarchical culture	"Approaching seniors is intimidating." (P22)
Barriers to effective feedback	Limited feedback opportunities	"Feedback feels like an afterthought." (P19)

DISCUSSION

This study brings out the fact that medical students appreciate specific, timely, and actionable feedback. These features coincide with the principles of good feedback found in the educational literature.⁹ Specific feedback makes expectations clear and facilitates meaningful reflection, whereas timeliness increases relevance.¹⁰ Diluted feedback, in its turn, can have no effect on improved performance and may even discourage a learner. This suggests that the absence of specificity and timeliness may explain why students viewed feedback as unhelpful for clinical improvement, rather than just a communication gap.

Respondents noted that hierarchical culture in clinical training impeded open feedback conversations, which are in line with the results of studies of both medical and allied health settings.^{4,5} Time constraints associated with clinical practice also impede feedback, which is consistent with the structural issues reported in both qualitative as well as quantitative studies on feedback.¹¹

Moreover, the positive and negative emotional reactions of students to feedback, which are observed in relation to the supportiveness and dismissiveness of feedback, are consistent with the literature that puts an emphasis on the affective aspect of feedback reception.¹² Effective feedback practices can enhance learner motivation, engagement, and commitment to

learning.¹³ This finding highlights that feedback in this context is not a neutral exchange of information but an emotional event that shapes students' professional identity, which may explain why dismissive comments had lasting effects on confidence.

Programs aimed at formalizing structured feedback systems (e.g., periodic feedback meetings and standardized instruments) might increase consistency and quality, as proposed in global medical education studies.¹⁴ However, our findings suggest that formalizing feedback may have limited impact unless hierarchy and seniors' approachability are also addressed.

CONCLUSION

Medical students in clinical settings described feedback as often vague, delayed, and lacking clear guidance, which limited its usefulness for improving clinical skills. Specific and timely feedback increased students' motivation to learn, whereas dismissive or unclear comments reduced confidence. Key barriers included hierarchical culture, insufficient time allocated for feedback, and seniors being perceived as unapproachable. Creating protected time for feedback discussions during rotations could improve the learning experience. Given the single-setting nature of this research, further studies across multiple settings are needed to assess how common these challenges are.

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ORIGINAL ARTICLE

MEDICAL STUDENTS' EXPERIENCES WITH THE INTEGRATED MODULAR CURRICULUM: A QUALITATIVE STUDY AT CENTRAL PARK MEDICAL COLLEGE, LAHORE

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Background: Integrated modular curricula are increasingly adopted in medical education to promote conceptual learning and strengthen basic-clinical science integration. Qualitative evidence from Pakistani private-sector medical colleges remains limited. The objective of this study was to explore the academic and emotional experiences of medical students studying under an integrated modular curriculum at Central Park Medical College, Lahore. **Methods:** A qualitative exploratory study was conducted from Aug to Nov 2025. Second-year MBBS students enrolled in the integrated modular curriculum were recruited through purposive sampling. Data were collected via semi-structured in-depth interviews and analyzed using Braun and Clarke's six-step thematic analysis. Data collection continued until thematic saturation. **Results:** Six themes emerged: curricular perception, learning experience, integration of sciences, assessment and feedback, challenges and support, and clinical readiness. Students reported improved conceptual understanding, motivation, and clinical relevance. Challenges included heavy workload, time-management difficulties, fragmented assessments, and interdepartmental coordination gaps. Continuous assessments promoted regular study but emphasized factual recall over conceptual understanding. Peer, faculty, and institutional support aided adaptation. **Conclusion:** The integrated modular curriculum promoted meaningful learning and clinical relevance but revealed implementation challenges. Improving curriculum organization, faculty development, assessment strategies, and student support may maximize benefits of curriculum integration. **Keywords:** Clinical competence, Integrated curriculum, Medical education, Medical students, Qualitative research

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INTRODUCTION

Globally medical education is undergoing a major transformation from traditional discipline-based teaching to integrated and student-centred approaches.¹ An integrated modular curriculum is designed to link basic sciences such as anatomy, physiology and biochemistry with clinical subjects in a coordinated and meaningful way, allowing students to understand how scientific knowledge is applied to real patient care. Instead of studying individual subjects in isolation, students learn through body systems, clinical scenarios, and thematic modules. This method aims to develop better clinical reasoning, deeper understanding and stronger professional identity from the early years of medical training.² In many countries, including Pakistan, medical education had traditionally followed a subject-based curriculum, where basic sciences were taught separately during the pre-clinical years and clinical subjects were introduced later. Although this approach helped students to acquire strong foundational knowledge, it often created a disconnect between theoretical knowledge and clinical practice.³ Consequently, many students struggle to apply

classroom knowledge to real clinical situations. Students often memorize large volumes of information without full understanding. As a result, graduates may enter clinical training with limited ability to integrate scientific knowledge into clinical decision-making.⁴ To overcome these limitations, many medical schools globally have adopted an integrated modular curriculum. These curricula encourage students to learn through clinical cases, system based modules and problem focused learning, making education more relevant and meaningful. Integration also supports competency based medical education, where the goal is not only to pass examinations but to develop skilled, confident and ethical doctors who can provide safe and effective patient care. Research from many countries has shown that integrated learning can improve student motivation, conceptual understanding and long-term retention of knowledge.⁵

In Pakistan, medical education has also entered a period of reform. The Pakistan Medical and Dental Council and other regulatory bodies have encouraged medical colleges to adopt integrated and outcome based curricula inline with international standards. As a result,

several public and private medical colleges have shifted to modular and integrated systems.⁶ Central Park Medical College, Lahore, is one of the institutions that have adopted an integrated modular curriculum to enhance educational quality and better prepare students for clinical practice. Modules are designed to bring together basic sciences and clinical topics so that students can see the connection between what they study and how it is used in patient care. Continuous assessments are used to keep students engaged throughout the year. In theory, this approach should improve motivation, understanding and readiness for clinical practice.

While the goals of integration are widely supported, the process of implementation is complex. Implementing a new curriculum involves more than revising timetables or course content; it also requires changes in teaching methods, assessment strategies, faculty roles, and student learning approaches. Without careful planning and support, students may struggle to adjust. This is particularly true for medical students who are already facing heavy academic pressure and high expectations.⁷ Several studies conducted in different countries have reported that students may experience confusion, stress, and uncertainty during the transition to an integrated curriculum. Students may experience uncertainty regarding effective study strategies, time management and preparation for unfamiliar assessment formats. Instead of focusing on understanding, they may feel forced to memorize large amounts of information under time pressure. These difficulties can affect not only academic performance but also emotional well-being, motivation and confidence.⁸

Studies in South Asia have shown that lack of coordination between departments, poorly aligned assessments and unclear learning objectives can weaken the benefits of integration. When different subjects are not properly synchronized, students may face overlapping content in some areas and gaps in others. This makes it difficult to build a clear and structured understanding of the curriculum. As a result, the intended purpose of integration may not be achieved, and instead students may perceive learning as more complex and fragmented.⁹ Therefore, students' personal experiences are valuable in evaluating the effectiveness of curriculum reform. Although examination results and curriculum documents provide useful information, students' interviews offer direct insight into how the curriculum functions in everyday practice. Their experiences reveal how teaching methods, assessment policies, workload and support systems affect their daily learning and emotional health. Understanding these experiences is essential for identifying what is working well and what needs improvement.¹⁰

Exploring these experiences is especially important in the Pakistani context, where medical

students face intense competition, high parental expectations and demanding academic environments. A curriculum that increases stress without providing adequate support can negatively affect learning and mental health.¹¹ Conversely, a well-designed integrated curriculum can help students develop confidence, strengthen their professional identity, and foster a greater sense of purpose in their studies. Despite the growing adoption of integrated modular curricula in Pakistan, there is still limited qualitative evidence exploring students' experiences and perceptions, particularly in private-sector medical colleges. Most published studies have focused on academic outcomes or quantitative measures of satisfaction, with relatively little attention given to how students experience curriculum implementation in their daily learning environment. Understanding these experiences is essential because students' perspectives can identify practical challenges and strengths that may not be captured through examination results or survey data alone. This gap in the literature provides the rationale for the present study. The findings of this study are expected to provide valuable insights for curriculum developers, faculty members and policymakers working to improve medical education in Pakistan.

METHODOLOGY

This qualitative exploratory study was conducted using semi-structured interviews to explore the academic and emotional experiences of second-year MBBS students studying under the Integrated Curriculum System (ICS) at Central Park Medical College, Lahore, affiliated with the University of Health Sciences (UHS), from August to November 2025, after ethical approval from Institutional Ethical and Review Board (Ref. No. CPMC/IRB-No/1530).

Twelve, second-year MBBS students who were enrolled in the ICS participated voluntarily. Written informed consent was obtained from all participants. Participants were selected using purposive sampling by thematic saturation and recruitment ceased when no new themes emerged from the interviews. Students who had completed their first academic year under ICS, demonstrated regular attendance, and were fluent in English or Urdu were included. Students who had repeated the year, were on extended leave, or declined participation, were excluded.

Each participant completed a semi-structured interview based on a questionnaire containing open-ended questions designed to obtain detailed reflections on their learning experiences, assessment, integration and support systems. Interviews were conducted in a private room within the academic block and lasted approximately 45–60 minutes. Interviews were conducted in English or Urdu according to participants' preference, and were recorded and transcribed for

analysis. Participant anonymity was ensured using pseudonyms (P1–P12).

Data were analysed using Braun and Clarke's Six-Step Thematic Analysis Framework:¹²

1. Familiarization with the data
2. Generating initial codes
3. Searching for themes
4. Reviewing themes
5. Defining and naming themes
6. Producing the report

Coding was performed using NVivo 12 Pro (QSR International) to organize data, identify patterns and retrieve participant quotes.¹³ Codes were grouped into categories and refined into overarching themes that reflected students' learning experiences, assessment, integration and support systems. Member checking was conducted with three participants to confirm accuracy of interpretations.

RESULTS

Six major themes emerged from the thematic analysis:

Theme-1: Students' View of the Curriculum

Sub-theme: Daily routine, strengths and weaknesses

Participants described their daily academic routine as long, tiring and confusing because different subjects were taught together. Several participants perceived the timetable as intensive and insufficiently organized.

"Long lectures with mixed subjects make the day heavy and scattered." (P5)

"More practical and relevant but overloaded and sometimes poorly organized." (P3)

"I am satisfied by this system but it's kind of bitter and sweet." (P12)

Overall, participants recognized both the strengths and limitations of the curriculum, particularly in relation to workload management and organizational structure.

Theme-2: Change in Learning Style

Sub-theme: From memorizing to understanding

Most participants reported that the integrated curriculum improved their understanding of concepts and made them more motivated to learn.

"The modular curriculum has made me focus more on understanding concepts." (P6)

"Integrated curriculum made me more motivated." (P11)

Participants also described greater engagement and confidence as a result of the more meaningful learning experience.

Theme-3: Linking Basic and Clinical Sciences

Sub-theme: Understanding theory with clinical use

Many participants appreciated the integration of basic sciences with clinical scenarios. They reported that this approach enhanced their understanding of the practical application of medical knowledge. However, some participants expressed concern that the increased workload limited their ability to develop a strong

foundation in the basic sciences.

"It helps me a lot to connect theory with clinical cases." (P3)

"It made it hard to focus on basic subjects." (P8)

Theme-4: Assessment and Feedback

Sub-theme: Continuous testing

Participants had mixed feelings about frequent tests. Although regular assessments encouraged continuous engagement with learning, several participants believed that they emphasized factual recall rather than conceptual understanding.

"Assessments are frequent but feel fragmented." (P3)

Theme-5: Challenges and Support

Sub-theme: Workload and help from others

Participants identified the extensive syllabus and associated workload as major academic challenges. Nevertheless, many participants acknowledged that support from senior students, faculty members, and counselling services helped them cope with these challenges.

"There is a big problem in time management." (P6)

"We have a student counselling service which helps us a lot." (P12)

Theme-6: Clinical Readiness and Future Value

Sub-theme: Purpose and professional growth

Many participants perceived that the integrated curriculum enhanced their preparedness for clinical practice and increased the perceived relevance of their studies.

"It boosts my motivation and makes studying feel purposeful." (P3)

"It enhances my knowledge by integrating the basic and clinical subjects." (P12)

DISCUSSION

This study explored the experiences of medical students studying in an integrated modular curriculum at Central Park Medical College. The findings showed that the integrated system strongly influenced the learning, motivation, workload, emotional well-being and professional identity of students. Six major themes emerged including curricular perception, learning experience, integration of basic and clinical sciences, assessment and feedback, challenges and support and academic performance with clinical relevance. Together, these themes provide important insight into how the integrated curriculum is working in practice and how it is being experienced by students.

Students described their daily academic life as long, tiring and confusing due to mixed-subject lectures and heavy schedules. While they appreciated the clinical relevance of the curriculum but many felt that the syllabus was poorly organized and difficult to manage. These findings showed that although the integrated modular system has clear educational goals, its structure and delivery need improvement. Similar results have been reported in study of Muddassir *et al*¹² and Khurshid

S *et al*¹⁴ where students found integrated schedules exhausting and difficult to follow due to overlapping content and poor coordination.

The ‘bitter and sweet’ description given by students reflects this dual experience. On one hand, integration made learning more meaningful; on the other, it increased mental and physical fatigue. Medical students already face heavy academic demands, and when integration is not carefully planned, instead of reducing the stress it increases it. This suggests that integrated curricula should not only focus on content integration but also on design of timetables, length of lectures and workload balance.¹⁵

One of the most positive findings was that the integrated curriculum changed the learning methods of students. Many students reported that now instead of rote memorization they have moved towards conceptual understanding. They felt more motivated, confident and engaged with their studies. This is one of the core aims of integration, to promote deeper learning rather than surface learning. Students’ comments showed that they were able to see connections between different subjects, which helped them a lot to understand the concepts better. This aligns with the study of Bowen *et al* that integrated curricula support meaningful learning and improve the abilities of students to apply knowledge.¹⁶ When students understand why they are learning something and how it connects to clinical practice, they are more likely to remain motivated.¹⁷ However, motivation alone is not enough. If workload and organizations are poor, even motivated students can become overwhelmed. Therefore, if the learning approach is improved, the weaknesses in structural and administrative policies can reduce its full benefits.¹⁸

Students strongly valued the link between basic sciences and clinical practice. Many felt that connecting theory to real clinical cases made learning more relevant and helped them to understand medical concepts more clearly. This supports the core philosophy of integrated education that learning should be meaningful and clinically oriented from the start.¹⁹

However, not all students had the same experience. Some reported that the heavy workload and lack of coordination made it difficult to build strong basic knowledge. This is an important issue. Integration should strengthen, not weaken the basic sciences. If departments do not align their teaching or if students are overburdened, integration may actually harm foundational learning. This finding is in agreement to the study of Meng *et al*²⁰ who demonstrated the importance of proper sequencing and departmental coordination. Anatomy, physiology, pathology and clinical subjects must be carefully synchronized so that students can build knowledge step by step. Without this, integration becomes confusing rather than helpful.

Students had mixed opinions about continuous

assessment. While frequent tests kept them involved and prevented from the chaos of last minute but many felt that assessments focused more on recall than understanding. This suggests a mismatch between teaching goals and assessment design. This is in accordance with the study of Jensen *et al*²¹ who demonstrated that integrated curricula aim to promote higher order thinking, but if exams only test memorization, students will continue to use surface learning strategies. Assessment drives learning. If students know they will be tested on facts rather than concepts, they will study accordingly. This reduces the benefit of integration.

Students also reported that assessments felt fragmented and poorly coordinated. This again points to the need for interdepartmental collaboration. Integrated teaching requires integrated assessment tests that should reflect the connections between subjects and assess clinical reasoning, not isolated facts.²²

Students faced major challenges related to time management and syllabus overload. The merged curriculum made it difficult to organize study time, leading to stress and fatigue. However, strong support from seniors, teachers and counselling services helped many students to cope. These findings are similar to the study of Putri GA, who described that support systems are essential in education. When students are challenged academically, emotional, social and academic support can protect them from burnout. Institutions must invest in mentoring, counselling and peer-support programs to help students to manage the demands of integrated learning.²³ Some students expressed dissatisfaction to faculty support, especially when teachers moved too quickly to clinical topics without ensuring strong basic understanding. This highlights the need for faculty training. Teachers must understand how to support students in an integrated environment.²⁴

Despite of challenges, many students felt that the integrated curriculum improved their clinical readiness and gave meaning to their studies. They felt motivated because their learning was clearly connected to patient care. This is a powerful outcome. When students see the purpose of their education, they develop stronger professional identity and long term commitment to medicine.²⁵ This shows that integration can support lifelong learning and national educational goals by producing doctors who think clinically and work across disciplines. However, for this to happen, the system must be properly designed and supported.

CONCLUSION

The integrated modular curriculum at Central Park Medical College offers several educational advantages, including improved conceptual understanding, enhanced motivation, and stronger appreciation of the relationship between basic and clinical sciences. Students also

identified important challenges, particularly related to heavy workload, time management, fragmented assessments, and inadequate coordination between departments. Despite these concerns, institutional support systems and the perceived clinical relevance of the curriculum contributed positively to students' learning experiences. The effectiveness of an integrated curriculum depends not only on its design but also on its implementation. Strengthening departmental coordination, faculty development, assessment strategies, and student support mechanisms may help maximize the benefits of curriculum integration while minimizing the challenges experienced by learners.

LIMITATIONS AND RECOMMENDATIONS

This study was a single centre study and relied on self-reported interview data, which may limit generalizability and introduce personal bias. The findings reflect students' experiences rather than statistical representation. Future research should include multiple institutions by using longitudinal or mixed-method approaches and incorporate faculty perspectives too to gain a more comprehensive understanding of implementation of integrated curriculum.

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ORIGINAL ARTICLE

ASSOCIATION OF BREASTFEEDING WITH THE RISK OF
RETINOPATHY OF PREMATURITYNaseer Ahmad Memon, Azizullah Langah, Ameer Ali Jamali, Munawar Ali Siyal, Arshad
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Background: Premature neonates are at risk of various health complications. The objective of this study was to find out the association of breastfeeding in development of retinopathy of prematurity (ROP). **Methodology:** This descriptive cross-sectional study was conducted at Paediatric Unit of Institute of Mother and Child Health (IMCH), Nawabshah. The study participants were divided into two groups based on their feeding type as breastfed group (exclusively breastfed infants) and formula fed group (>60% per day formula milk feed). Ophthalmoscopy was done with a binocular indirect ophthalmoscope for evidence of retinopathy. Data was analysed on SPSS-20. **Results:** The baseline characteristics among both groups were same with almost no significant association except the stage of ROP and weight at discharge. The frequency of developing ROP was more among infants who were on formula feed (38.3%) as compared to infants on breastfeed (31.2%) but the results were non-significant. Most of the infants developed stage 2 or stage 3 ROP among formula feed group (23.3%) in comparison to breastfed infants (8.8%). The severity of ROP reported strong significant association among the groups ($p < 0.05$). The multivariate logistic regression analysis reported that the type of feeding was a strong predictor of severity of ROP (stage 2 or 3). **Conclusion:** Development of ROP is more frequent among formula fed infants as compared to infants on breastfeed, but no significant association was found. However, the severity of ROP had significant association with type of feeding.

Keywords: Breastfeed, Formula feed, Prematurity, Retinopathy of prematurity

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INTRODUCTION

Prematurity refers to the birth of an infant before completing 37 weeks of gestation.¹ The rate of preterm births varies across countries, with estimates ranging from 5% in European nations to 18% in Malawi. In Pakistan, the preterm birth rate is reported as 18.89%.² Premature neonates are at risk of various health complications, including respiratory distress syndrome, bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular haemorrhage, hyperbilirubinemia, patent ductus arteriosus, and retinopathy of prematurity (ROP).³

ROP is a vascular disorder that affects the immature retina of preterm infants. While it is both preventable and treatable, several factors contribute to its development, such as low birth weight, oxygen therapy, and inadequate nutritional support.^{4,5} Infants diagnosed with ROP may experience vision-related issues, including refractive errors, blindness, strabismus, visual field defects, and impaired colour vision.⁶ The frequency of ROP varies depending on healthcare resources, with rates between 5% to 8% in developed nations and up to 30% in developing countries.⁷ Research conducted in Pakistan has reported an ROP incidence of 10.5% among premature infants⁸, with urban Punjab showing a higher incidence of 24.6%.⁹ Although the exact causes of ROP are not fully known, prematurity, low birth weight, and retinal immaturity are recognized as primary risk factors. Additional

contributing factors include oxygen supplementation, congenital heart disease, metabolic imbalances, anaemia, infections, and blood transfusions.^{10,11}

Breast milk is believed to offer protective benefits against ROP because of its antioxidant and immune-boosting properties.¹² It contains essential nutrients, including vitamins C and E and beta-carotene, which provide stronger antioxidant effects compared to formula milk.¹³ Breast milk has immunomodulatory components such as immunoglobulin A in secretions, lactoferrin, cytokines, lysozymes, and various cellular elements that support the infant's immune system.¹⁴ These protective factors may reduce the risk of conditions like necrotizing enterocolitis (NEC) and sepsis, which in turn lowers the likelihood of ROP development.¹⁵

In Pakistan, the absence of large-scale studies, make it difficult to determine the exact incidence of the condition. Potential protective factors, such as breast milk, remain underexplored. The current study aimed to find out the association of breastfeeding in development of retinopathy of prematurity.

MATERIAL AND METHODS

A descriptive cross-sectional study was conducted at the paediatric unit of Institute of Mother and Child Health (IMCH), Nawabshah from Jul 2024 to Jan 2025. The study got ethical approval from the Institutional Review Board. Informed consent was taken from the parents.

The neonates having birth weight of less than 2.5 Kg and gestational age of less than 37 weeks were included. Infants either having any congenital malformation or congenital cataract or parents refused to give assent were excluded. Sample size was calculated to be 140 using the OpenEpi calculator.

Feeding type of the neonates, including formula feed or breastfeed, was noted while the initial retinal examination for ROP was done after completing neonatal period. Date of last menstrual period and antenatal ultrasound reports were used to calculate the gestational age. The study participants were divided into two groups based on their feeding type as breastfeed group including exclusively breastfeed infants and formula feed group including more than 60% per day feed was on formula milk. Indirect ophthalmoscopy was done by a binocular indirect ophthalmoscope. Demographic data and the examination findings were recorded on preformed proforma. Severity of ROP was classified into five stages including demarcation line, visible ridge, blood vessel in the ridge. Sub-total retinal detachment and total retinal detachment in stage I to stage V respectively.

Statistical Package for Social Science (SPSS) version 20 was used to analyze the data. Mean $\pm$ SD were calculated for numerical variables. Categorical variables were presented as frequency and percentage. Chi-square test was used to see association of categorical variables with occurrence of ROP while after adjusting the confounding factors, multivariate logistic regression analysis was performed and odd ratios were calculated for associated factors, keeping 95% confidence interval, and $p \leq 0.05$ considered statistically significant.

RESULTS

Current study included a total of 140 premature infants, out of which 80 infants were exclusively on breastfeed while 60 infants were on formula feed. The baseline characteristics among both groups were same with almost no significant association except the stage of ROP and weight at discharge. Majority of the study participants were female, belonging to lower socioeconomic status, among both groups, with no significant association. The gestational age of most infants was 32 to 34 weeks (66.2% and 70% respectively) and the mode of delivery was spontaneous vaginal delivery (SVD) (67.5% and 61.7% respectively) with birth weight 1.5 to 2 Kg (43.8% and 40% respectively) but all these having no significant association among the groups.

The frequency of developing ROP was more among infants who were on formula feed (38.3%) as compared to infants on breastfeed (31.2%) but the differences were non-significant. Most of the infants developed stage 2 or stage 3 ROP among formula feed group (23.3%) in comparison to breastfeed infants

(8.8%), none of the case with stage 4 or stage 5 was diagnosed. The severity of ROP reported strong significant association among the groups ($p < 0.05$). Breastfed infants were having more weight at discharge than formula fed infants and strong significant association was noted ($p < 0.05$). The detailed characteristics of study participants among both groups are presented in Table-1.

Table-1: Characteristics of study participants (n=140)

Variables	Breastfeed n=80 [n (%)]	Formula milk n=60 [n (%)]	p
Gender			
Male	37 (46.2)	26 (43.3)	0.82
Female	43 (53.8)	34 (56.7)	
Socioeconomic status			
Lower	37 (46.2)	24 (40.0)	0.54
Middle	29 (36.3)	20 (33.3)	
Upper	14 (17.5)	16 (26.7)	
Gestational age			
≤32 weeks	27 (33.8)	18 (30.0)	0.27
32–34 weeks	53 (66.2)	42 (70.0)	
Mode of delivery			
SVD	54 (67.5)	37 (61.7)	0.69
C-Section	26 (32.5)	23 (38.3)	
Birth weight			
≤1.5 Kg	29 (36.2)	20 (33.3)	0.43
1.5–2 Kg	35 (43.8)	24 (40.0)	
≥2 Kg	16 (20)	16 (26.7)	
ROP	25 (31.2)	23 (38.3)	0.35
Severity of ROP (Stage 2 or 3)	7 (8.8)	14 (23.3)	0.003*
Weight at discharge (Kg)	2.57±1.5	2.19±1.3	0.01*

Gestational age and the birth weight were the two most important confounding factors in developing stage 2 or 3 ROP. The multivariate logistic regression analysis was performed, and the results reported that the type of feeding was a strong predictor of severity of ROP (stage 2 or 3), after adjusting the two important confounding factors. The odd ratios calculated for associated factors, keeping 95% confidence interval, are presented in Table-2.

Table-2: Multivariate regression analysis of associated factors in Stage 2 or 3 ROP

Parameters	OR	95% CI	p
Gestational age	0.91	0.857–0.952	0.003*
Birth weight	0.95	0.91–0.99	0.000*
Breastfeeding	0.23	0.074–0.48	0.005*

DISCUSSION

ROP is a multifactorial disease and the presence of prooxidant metabolite is one of the main contributing factor as it stimulates the retinal endothelial growth factor leading to excessive growth of retinal vasculature that is why studies stated that early neonatal nutrition can balance the oxidative stress, in turn decreasing the risk of development of ROP.¹¹ Human milk contains multiple antioxidants including inositol, vitamin E, catalase, glutathione peroxidase, taurine and carotenoids which counter the free radicals in preventing oxidative

stress. Notably the antioxidant carotenoid is only present in human milk but not in formula feed, it down regulates the endothelial growth factor which is an important predictor in the pathogenesis of ROP.¹⁶ ROP is a complex disease influenced by multiple factors, with prematurity, low birth weight, and oxygen therapy being key contributors to its development. Our study found female predominance but no significant association with ROP. Similar findings were observed by other studies^{8,17} reporting equal incidence of ROP among both genders.

Gestational age and the birth weight were the two most important factors, significantly associated with the occurrence of ROP in the current study. Worldwide studies reported strong significant association of ROP with the prematurity and the weight at the time of delivery.^{17,18} On the other hand, a study conducted in China reported contradictory findings as there was no significant association of birth weight between ROP and non-ROP groups.¹⁹

Current study reported that the frequency of developing ROP was more among infants who were on formula feed as compared to infants on breastfeed but the result was non-significant. Research by Manzoni *et al*²⁰ and Ginovart *et al*²¹ found that the frequency of ROP is lowest among those infants who were exclusively on breastfeed. Study by Metzger *et al*²² reported that the preterm infants born between 24 and 28 weeks and were on breastfeeding, had lower rate of development of ROP. However, the study did not observe significant differences among those born before 32 weeks of gestational period.²² On the other hand, Keraan *et al*²³ conducted a study and noted that a higher incidence of ROP among breastfeeding infants, though the authors did not provide a clear explanation for this outcome.

More infants developed stage 2 or stage 3 ROP among formula fed group (23.3%) in comparison to breastfed infants (8.8%), while the severity of ROP reported strong significant association among the groups. Current results align with a meta-analysis conducted by Zhou *et al*²⁴ which suggests that breastfeeding significantly reduces the risk of ROP at any stage, including severe cases. Porcelli *et al*²⁵ noted that those neonates who have higher intake of breastfeed during initial two weeks of life, are less likely to develop ROP, but there is no significant association of breastfeed and ROP on 4th week of life.

CONCLUSION

Development of ROP is more frequent among formula fed infants as compared to infants on breastfeed, but no significant association was found. The severity of ROP had strongly significant association with the type of feeding as stage 2 or stage 3 ROP cases were more among formula fed group in comparison to breastfed infants.

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ORIGINAL ARTICLE

TRANSLATION AND CULTURAL ADAPTATION OF THE DEPRESSION AND SUBSTANCE USE MODULE FOR PATIENTS WITH SUBSTANCE USE DISORDERS AND DEPRESSION IN PAKISTAN

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Background: Depression and substance use disorders (SUDs) frequently co-occur in Pakistan, with co-morbidity rates reported between 30–60% among treatment-seeking patients. The study aimed to translate and culturally adapt the DSU-M into Urdu for use in local clinical and research settings. **Methods:** A cross-sectional methodological design was conducted in Pakistan following Breslin’s back-to-back translation model and expert committee validation. Two bilingual mental-health professionals performed independent forward translations, which were reconciled into a single version. Two independent translators, blinded to the original, conducted back translation. An expert committee comprising of two clinical psychologists, one psychiatrist, and one linguist reviewed both versions to ensure semantic, conceptual, and cultural equivalence. Content-validity indices were computed (CVI= 0.91), indicating excellent agreement among experts. **Results:** The Urdu DSU-M showed a high level of linguistic congruence with the original version. Only minor cultural adaptations were required, such as replacing idiomatic expressions (‘feeling low’) with culturally meaningful alternatives (دل نہ چاہا۔ پیسہ نہیں کما)۔ Expert committee validation confirmed semantic accuracy, cultural relevance, and clinical applicability of the final Urdu version. **Conclusion:** The Urdu DSU-M is a linguistically accurate and culturally appropriate adaptation of the original English module. It holds potential to enhance diagnostic precision, patient engagement, and clinical management of co-morbid depression and SUDs in Pakistan. Future research should include psychometric testing and field validation to establish reliability and clinical utility.

Keywords: Cultural Adaptation, Depression, Pakistan, Substance Use Disorders, Translation, Urdu

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INTRODUCTION

Depression and substance use disorders (SUDs) are among leading causes of disability worldwide, often occurring together as co-morbid conditions. It is estimated that nearly one-third of individuals with SUDs globally also experience clinically significant depressive symptoms that cause psychosocial impairment and poorer treatment outcomes than patients with a single disorder.¹ The co-occurrence of depression and SUD is associated with increased risk of relapse, suicide attempts, and chronic medical illnesses, creating a major public-health burden in high- and low-income settings.²

In South Asia, dual burden of depression and SUD is of particular concern due to limited mental health resources and pervasive social stigma. Pakistan, with an estimated 6.45 million people using illicit substances, faces rising rates of psychiatric comorbidities.^{3,4} Recent hospital-based studies from Pakistan report that 30–60% of treatment-seeking patients with SUDs also meet criteria for depression, emphasizing urgent need for integrated interventions.⁵

Despite the magnitude of this issue, culturally adapted diagnostic and therapeutic tools remain insufficient in Pakistan. Most interventions

are borrowed from Western contexts and are often not fully applicable due to differences in language, cultural perceptions of mental illness, and health-seeking behaviours.^{6,7} Consequently, many patients face diagnostic delays, low adherence, and diminished treatment efficacy.

The DSU-M is an evidence-based module providing structured guidance for clinicians addressing overlapping symptoms of depression and SUD. High-income countries and neighbouring regions show improved patient engagement, reduced depressive symptoms, and better substance-use outcomes.^{8,9} However, its potential remains untapped in Pakistan because no validated Urdu version exists.

Although several screening and therapeutic modules exist internationally, few have been culturally adapted for Pakistan. The concept of *cultural adaptation* in this study refers to ‘the systematic modification of content, idioms, and expressions of a psychological intervention so that it becomes semantically, conceptually, and contextually equivalent to the target culture’. The present study aimed to translate and culturally adapt the DSU-M into Urdu through a structured methodological design ensuring conceptual integrity and clinical relevance for Pakistani patients with dual diagnoses.

METHODOLOGY

This cross-sectional methodological design was used to translate and culturally adapt the Depression and Substance Use Module (DSU-M) into Urdu. The study was carried out in Pakistan in clinical settings where mental-health professionals provide services for patients with depression and substance-use disorders. The translation process was conducted in multiple phases following Brislin's back-to-back translation model¹⁰ and incorporated expert-committee validation to ensure conceptual and cultural equivalence. (Figure-1).

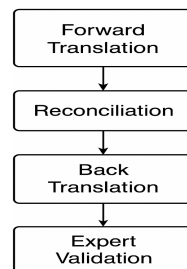


Figure-1: Brislin's back-to-back translation model¹⁰

The translation process commenced with forward translation, in which two bilingual mental health professionals independently translated the original English version of the Depression and Substance Use Module (DSU-M) into Urdu. Both translators were proficient in English and Urdu and possessed clinical experience in psychology, ensuring that technical and psychological terminology was accurately conveyed. Their familiarity with clinical practice was instrumental in maintaining the precision of psychological concepts while simultaneously rendering the text accessible to Urdu-speaking patients and practitioners. Independent translations also reduces individual bias and provided a broader linguistic basis for reconciliation.¹¹ Forward translation was performed by two bilingual mental-health professionals with ≥ 5 years of clinical experience. Their independent Urdu drafts were reconciled into one version.

This procedure is considered a gold standard in cross-cultural adaptation studies. It allows for the identification of semantic inconsistencies, conceptual ambiguities, and unintentional distortions introduced during the initial translation phase.¹² Back translation was then conducted by two independent translators, blinded to the original text, to identify any semantic or conceptual inconsistencies. By comparing the back-translated text with the original module, the research team was able to assess the fidelity of meaning and ensure consistency across versions.

The expert-validation committee comprised two clinical psychologists, one psychiatrist, and one linguist, each with at least 10 years of professional experience. The panel compared the back-translated

version with the original DSU-M to determine semantic and conceptual equivalence. Discrepancies were discussed until full consensus was achieved. Each item was rated for relevance and clarity on a 4-point scale, and a Content Validity Index (CVI) of 0.91 was obtained, demonstrating excellent expert agreement.

In a brief pilot assessment, mental-health practitioners confirmed clarity and comprehension of adapted Urdu terms. The committee systematically compared the back-translated version with the original DSU-M to determine semantic equivalence, conceptual accuracy, and overall content validity. Discrepancies were discussed in detail, and revisions were made through consensus, thereby enhancing the reliability of the final Urdu version. The committee incorporated cultural and contextual adjustments to ensure that the translated module was not only linguistically accurate but also relevant and comprehensible within the Pakistani sociocultural context. Expressions and idiomatic phrases that might otherwise impede patient understanding were replaced with culturally appropriate alternatives, while preserving the clinical intent of the original text. Through this rigorous translation and validation process, the Urdu version of the DSU-M was produced as a linguistically precise, culturally sensitive, and clinically relevant tool, intended to support the assessment and treatment of patients with co-morbid depression and substance use disorders in Pakistan. No further linguistic modifications were required.

The study was approved by the Institutional Review Board (IRB) of the Islamic International University Islamabad (IIUI/PSY-2025-07). All procedures complied with the Declaration of Helsinki revision.

RESULTS

The translation and validation process was completed in sequential phases; forward translation, back translation, expert review, and quantitative validation. Each stage was systematically assessed to ensure linguistic accuracy, semantic equivalence, and cultural relevance. The findings are presented under 3 domains: linguistic equivalence, cultural adaptation, and expert validation.

High congruence was observed between the forward- and back-translated versions. Minor phrase variations did not change meaning. Inter-rater agreement among translators was 0.89 (Cohen's κ). The expert committee confirmed that the core concepts and clinical terminologies were preserved, ensuring semantic accuracy across versions. No major discrepancies were identified that could compromise the validity of the Urdu translation.

During the expert review, certain linguistic and cultural adaptations were required to enhance clarity and

acceptability for the Pakistani population. For example, idiomatic expressions in English were revised into culturally understandable Urdu equivalents that better conveyed the intended meaning to patients. These adjustments ensured that the language remained clinically precise yet sensitive to local cultural interpretations of emotional states.

The expert committee confirmed the Urdu DSU-M was semantically accurate and culturally suitable with mean item-rating 3.72 ± 0.21 out of 4. Experts agreed the adaptation would improve clinician-patient communication and patient engagement in psychiatric settings. The final Urdu version was therefore validated for future clinical and research use in Pakistan.

Table-1: Examples of cultural and linguistic adaptations in Urdu translation of DSU-M

Original English Term/Phrase	Initial literal Urdu translation	Final adapted Urdu equivalent	Rationale for adaptation
Feeling Low	نیچے محسوس کرنا	دل نہجھ جانا۔ مایوسی محسوس کرنا	Improved cultural resonance
Loss of interest	دلچسپی کا کھو جانا	دلچسپی ختم ہونا	Simpler daily language
Craving	خواہش	شدید طلب	More precise clinical term
Hopelessness	نا اُمیدی	اُمید کھو دینا	Culturally stronger expression
Guilt feeling	قصور کا احساس	ذمہ داری یا شرمندگی کا احساس	Reflects socially nuanced concept
Anxious thoughts	بے چین خیالات	فکر، یا گھبراہٹ کے خیالات	Idiomatic localization

DISCUSSION

The present study achieved the successful translation and cultural adaptation of the Depression and Substance Use Module (DSU-M) into Urdu, establishing its semantic and conceptual equivalence with the original English version. The process ensured that the Urdu DSU-M retained clinical accuracy while incorporating culturally appropriate terminology and idioms that are more easily understood by Pakistani patients. These findings indicate that the adapted DSU-M module is both linguistically reliable and contextually relevant for use in clinical and research settings across Pakistan. The findings of the current study are consistent with prior cross-cultural adaptation studies conducted in South Asia and the Middle East, which demonstrated that translation of psychological modules significantly improves accessibility and patient engagement. For example, Kudla¹³ validated the validation of the Hindi version of the schedule for meaning in life evaluation, reporting enhanced clinical applicability. Similarly, Azar *et al*¹⁴ highlighted the benefits of culturally adapted treatment modules in Iran, while Turkish scholars Akbaba, Özyürek, and Dinç have emphasized that translation increases acceptability without compromising psychometric validity.¹⁵⁻¹⁷ Overall, these studies highlight the importance of contextual adaptation in improving diagnostic accuracy and treatment outcomes, supporting the relevance of the Urdu DSM.

From Berry's acculturation theory and linguistic relativity perspective, cultural adaptation influences how emotional states are expressed and interpreted. Therefore, modifying idioms such as 'feeling low' to 'دل نہجھ جانا' not only improves semantic fit but may also enhance therapeutic resonance and patient

empathy. A significant strength of this study lies in its rigorous methodology. According to Kowal¹⁸, the Brislin back-to-back translation model provided a structured framework to ensure linguistic fidelity, while the inclusion of expert committee (psychologists) enhanced the validity of the adapted version. The systematic approach of Brislin¹⁰, minimized semantic drift and allowed cultural nuances to be addressed effectively. Although patient pilot testing was not conducted in the present study, expert-led validation provides a strong foundation for future clinical implementation and empirical evaluation. The current study has certain limitations, this study's main limitation is absence of large-scale patient validation, which precludes psychometric generalization. Potential translation bias may have occurred where culturally stigmatized idioms required paraphrasing. Limiting adaptation to Urdu excludes Pakistan's regional languages.

Despite these limitations, the current study has important implications. The availability of an Urdu version of the DSU-M has the potential to improve the quality of mental healthcare by enhancing communication between clinicians and patients, reducing diagnostic barriers, and promoting culturally sensitive treatment approaches. The translated module provides researchers in Pakistan with a standardized tool to study the complex relationship between depression and substance use, thereby contributing to global evidence on dual diagnoses. Future studies should focus on validating the Urdu DSU-M through psychometric testing and assessing its clinical effectiveness in diverse patient populations. Future validation should employ confirmatory factor analysis and reliability testing (Cronbach $\alpha \geq 0.80$ target) with diverse patient samples to ensure psychometric robustness.

CONCLUSION

The Urdu DSU-M was translated and culturally adapted using a rigorous, multi-stage methodological process. The final version demonstrated linguistic accuracy, conceptual fidelity, and cultural relevance. Its validation indices indicate strong expert consensus. The module provides clinicians and researchers with a standardized tool to enhance diagnostic precision, patient engagement, and culturally responsive care for co-morbid depression and SUD patients in Pakistan. Large-scale clinical validation is strongly recommended for nationwide implementation.

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Book reference: Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Bremner BM, (Editors). Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: McGraw Hill; 1995. pp.465-78.

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