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EDITORIAL

PHYSIOLOGY OF AFFERENT AND CENTRAL PARTS OF AUTONOMIC NERVOUS SYSTEM

Tehseen Iqbal
RYK Medical College, Rahim Yar Khan

The Autonomic Nervous System (ANS) and the endocrine system control the internal environment of the body. The organization of the ANS is on the basis of the reflex arc. Changes in chemical composition, blood pressure, osmotic pressure, stretch in viscera, and temperature are detected by autonomic receptors. The visceral afferent fibres are myelinated and they accompany the visceral motor fibres. The sensory autonomic neurons are pseudo-unipolar cells located in the dorsal root ganglia of somatic spinal nerves. Once the afferent fibres gain entrance to the spinal cord or the brainstem, they are thought to travel alongside the somatic afferent fibres to the autonomic centres in different parts of the brain. Information reaches the higher autonomic centres from viscera through an ascending system that involves the nucleus tractus solitarius, the parabrachial nucleus, the periaqueductal gray matter, and the hypothalamus. The hypothalamic paraventricular nucleus, pontine A5 cell group, rostral ventrolateral medulla, and medullary raphe nuclei send direct output to the preganglionic autonomic neurons. The amygdala, mesencephalic periaqueductal gray, caudal ventrolateral medulla, nucleus of the tractus solitarius, and medullary lateral tegmental field feed into these direct pathways.

Keywords: Autonomic stimuli, autonomic receptors, nucleus tractus solitarius, hypothalamus

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The new integrated modular curriculum of University of Health Sciences (UHS) has included the autonomic nervous system (ANS) in the foundation module of the 1st Year class while anatomy of the nervous system and physiology of the somatic nervous system is placed in the 2nd Year MBBS. All senior physiologists agree that ANS is to be taught after the discussion of the somatic nervous system. This is a natural progression of developing a clear concept of the nervous system. Many physiology books describe only the efferent part of the ANS or the autonomic outflows only, and so students cannot comprehend the overall architecture of the autonomic nervous system. It is advantageous to describe our nervous system (including ANS) on the basis of a reflex arc[1], as reflex arc is usually discussed in the premedical classes.

The ANS and endocrine system control the internal environment of the body (homeostasis) and behaviour. The ANS has an afferent limb, efferent limb, and a central integrating system. The afferent component of the autonomic nervous system is identical to the afferent component of the somatic sensory system, and it forms part of the general afferent segment of the entire nervous system. A modern definition of the ANS takes into account visceral afferent pathways, several forebrain and brainstem regions as well as the descending pathways that activate the preganglionic sympathetic and parasympathetic neurons.[2] Because much of the actions of ANS relate to control of the viscera, it is sometimes called the visceral nervous system. The enteric nervous system is also considered part of the ANS.[3] For convenience of our students and teachers, physiological and anatomical aspects of afferent and central parts of the ANS are discussed here.

Stimuli and Autonomic sensory receptors

Chemical changes like arterial oxygen concentration, blood carbon dioxide concentration are detected by chemoreceptors in aortic and carotid bodies. For blood glucose, amino acids, fatty acids, chemoreceptors are in the hypothalamus. Blood pressure changes are detected by baroreceptors present in arch of aorta and carotid sinus. Stretch or mechanical distension in viscera is detected by mechanoreceptors or stretch receptors, e.g., in the urinary bladder or intestines etc. Temperature change in the body is detected by thermoreceptors present in the skin and hypothalamus. Change in osmolality of extracellular fluid is detected by osmoreceptors present in the hypothalamus. Change in H^+ concentration is detected by chemoreceptors present in carotid bodies and medulla oblongata. Although the brain receives such information and utilizes this information for regulatory purposes, we are not consciously aware of these stimuli.[2,3,5] These autonomic sensory receptors should not be confused with the autonomic receptors on the autonomic effectors which are called adrenergic and cholinergic receptors.

Autonomic afferent pathways

General visceral afferent fibres from viscera and blood vessels accompany their efferent counterparts, and are the peripheral processes of neuronal cell bodies located in the sensory ganglia of some cranial nerves and in spinal dorsal root ganglia.[4] The visceral afferent fibres are myelinated fibres and they supply information that originates from autonomic sensory receptors in the viscera. Their peripheral axonal branch extends to one of the viscera and a central axonal branch enters the CNS.[3] Sympathetic (Thoracolumbar) afferent myelinated nerve fibres travel from the viscera through

the sympathetic ganglia without synapsing. They pass to spinal nerve via white rami communicantes and reach their cell bodies in dorsal root ganglia of corresponding spinal nerves. The central axons then enter the spinal cord and may form afferent component of a local reflex arc and ascend in spinothalamic tracts to higher centers, such as hypothalamus. Parasympathetic (Craniosacral) afferent myelinated nerve fibres travel from viscera in the head and neck region to their cell bodies, located in the sensory ganglia of the cranial nerves III, VII, IX and X and so to the brain stem. From the pelvic organs to the posterior root ganglia of the Sacro-spinal S2, S3, and S4 nerves. The central axons then enter the CNS and take part in the formation of local reflex arcs, and pass through spinothalamic tracts to higher centers of the ANS, such as the hypothalamus. Once the afferent fibres gain entrance to spinal cord or brainstem, they are thought to travel alongside, or mixed with somatic afferent fibres to autonomic centers in different parts of the brain. Information reaches the higher autonomic centres from viscera through an ascending system that involves the nucleus tractus solitarius, parabrachial nucleus, periaqueductal gray matter, and hypothalamus.[5]

Autonomic control centres in CNS

The hypothalamic paraventricular nucleus, pontine A5 cell group, rostral ventrolateral medulla, and medullary raphe nuclei send direct output to preganglionic autonomic neurons. The amygdala, mesencephalic periaqueductal gray, caudal ventrolateral medulla, nucleus of tractus solitarius, and medullary lateral tegmental field feed into these direct pathways. The rostral ventrolateral medulla is generally considered the major source of excitatory input to preganglionic sympathetic neurons in intermediolateral nuclei of spinal cord.[2,3]

Descending Autonomic Pathways

The pathways that influence preganglionic autonomic neuronal activity include spinal cord and brainstem reflex pathways, as well as descending control systems originating at higher levels of nervous system, such as hypothalamus. The hypothalamus and its closely allied structures send output signals to brain stem, mainly into reticular areas of mesencephalon, pons, and medulla, and from these areas into peripheral nerves of ANS.[6] Pathways that control preganglionic neurons in the intermediolateral nuclei of spinal cord include direct projections from hypothalamic paraventricular nucleus, pontine catecholaminergic A5 cell group, rostral ventrolateral medulla, and medullary raphe nuclei. Many brain regions feed into these direct pathways which include amygdala, mesencephalic periaqueductal gray, caudal ventrolateral medulla, nucleus of tractus solitarius, and medullary lateral tegmental field. The rostral ventrolateral medulla is generally considered the major source of excitatory input to preganglionic sympathetic neurons.[2–5]

Autonomic Reflexes

Visceral sensory and autonomic neurons participate in visceral reflex arcs. These reflexes are pupillary light reflexes (Direct and Consensual), sneeze and cough reflexes, baroreceptor and chemoreceptor reflexes, micturition and defecation reflexes, etc. In some peripheral reflexes, branches from visceral sensory fibres synapse with postganglionic motor neurons within sympathetic ganglia. Complete three neuron reflex arcs (with small sensory, motor, and intrinsic neurons) exist entirely within the wall of digestive tube; these neurons are part of enteric nervous system.[2,3,6]

Can we consciously control our ANS?

Although autonomic nervous system mostly acts at subconscious level, two examples of perceived visceral sensations are pain sensations from damaged viscera and angina pectoris from inadequate blood flow to heart.[2] Though the ANS is not considered to be under direct voluntary control, some people can exert some conscious control over some autonomic functions by developing control over their thoughts and emotions. For example, feelings of extreme calm achieved during meditation[7] are associated with cerebral cortex influence on parasympathetic centres in hypothalamus via various limbic structures. Voluntary sympathetic activation can occur when people decide to recall a frightful experience; in this case the cerebral cortex acts through the amygdala.

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ORIGINAL ARTICLE

REFERENCE VALUES FOR HAEMOGLOBIN LEVEL AND RED CELL COUNT FOR ADULT MALE POPULATION OF MUZAFFARABAD

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Background: For each population, its own normal reference values should be established. Reference values for haemoglobin concentration (Hb con) and red blood cells count (RBC#) have been worked out for different populations. This study was conducted to determine normal reference values for Hb con and RBC# for adult male population in district Muzaffarabad. **Methods:** This cross-sectional study was conducted in district Muzaffarabad from Jul 2019 to Feb 2020. A total of 384 healthy adult local males, aged 18–50 years, were enrolled through stratified random sampling. Collection of information and blood sampling were carried out in the community. Levels of Hb con and RBC# were assessed using Sysmex Haematology Analyzer. Comparison of determined reference values was made between different groups of study population and with reference values already being used. **Results:** Mean age of study population was 29.11±9.26 years with a range of 18–50 years. Mean value of Hb was 13.05 g/dL (9.73–16.37 g/dl) and RBC# 4.58 million/µL (3.4–5.76 million/µL) respectively. Determined values were compared between different groups of study population and with the reference values being used. **Conclusion:** Normal reference values for Hb con and RBC# for adult male population in district Muzaffarabad were different from values which are being used.

Keywords: Reference values, Haematological indices, Haemoglobin, Red blood cell count, Male, Muzaffarabad

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INTRODUCTION

Haemoglobin (Hb) is the iron containing metalloprotein in red blood cells (RBCs). Hb transports oxygen from the lungs to the body tissues. Aerobic metabolism provides energy and functions of the cells are powered. Hb also transports carbon dioxide (CO_2) from the tissues to the lungs. It transports about 20–25% of CO_2 as carbaminohaemoglobin. It also transports nitric oxide which binds with globin protein, released simultaneously with O_2.[1] Hb concentration is expressed as g/dL.[2] Reference range for Hb con being used for adult male Pakistani population is 13–17 g/dL.[3]

RBCs are the principal means of O_2 delivery to the tissues. O_2 is taken up in the lungs by RBCs and delivered to the tissues while passing through the capillaries. In human adults, about 2.4 million new RBCs are produced each second. Mature RBCs are elliptical biconcave disks. Most organelles and nuclei are absent in RBCs in adults and maximum space is occupied by Hb, which is responsible for the red colour of blood. In adult life RBCs undergo development in the bone marrow. They circulate in the body for 100–120 days, before they are engulfed by macrophages and their components are recycled. RBCs are most numerous among blood cells and body as well. About 70–84% of the cells in the human body are RBCs.[4]

Red Blood Cell count (RBC#) is tested as a part of complete blood count. RBC# is expressed in million/µL. Hb con is affected by number of RBC#.[2] Reference range for RBC# being used for adult male Pakistani population is 4.5–5.5 million/Cmm.[3]

Studies conducted in different populations of the world[5–12] have worked out the reference ranges for haematological indices in adults and children. Many factors affect the values of haematological indices even in healthy populations and these factors include sex, age, body build, ethnic background, altitude, nutrition, environment and social conditions. The reference values for haematological indices are different for different populations in the world. Therefore, establishment of its own reference values have been stressed for each population.[5–12]

Reference values for haematological indices used for Pakistani population are the reference values derived from populations of western countries.[3,13] Previous studies on Pakistani population groups[3,13] have determined that the reference values derived for these populations are different from the values which are being used. The objectives of this study were to determine the reference values for Hb con and RBC# for adult male population in district Muzaffarabad.

MATERIAL AND METHODS

This cross-sectional study was conducted based on the blood samples of adult males in the age range from 18–50 years, residing in urban and rural areas of district Muzaffarabad, from July 2019 to February 2020. Approval was obtained from Ethical Review Committee of Khyber Girls Medical College, Peshawar and

Executive Director, Abbas Institute of Medical Sciences, Muzaffarabad. Sample size was 384, which was calculated with population proportion sample size formula[14]. Stratified random sampling technique[15] was used. Target population was 165,460 (21% of total population of district Muzaffarabad). Percentage of target population in each of 28 union councils of district Muzaffarabad was calculated using optimum allocation (disproportionate allocation) stratified random sampling strategy[15].

Written informed consent was obtained from all participants. Healthy adult males were included in this study. Exclusion criteria were high altitude (>8,000 feet[16]) dwelling, acute or chronic diseases, use of drugs which interfere with Hb con or RBC#, blood loss during last 3 months, blood transfusion during last 12 months, blood donation during last 3 months, surgery during last 3 months, tobacco smoking, family history of haematological disorders and exposure to hazardous chemicals.

Data were collected using an objectively structured questionnaire. Blood samples were obtained by trained team members. Detailed medical history was taken and general physical, systemic examination was performed on each subject.

Four (4) mL venous blood was withdrawn from each subject in EDTA vials and analysed within 4 hours of sampling[8] at AIMS, Muzaffarabad.

Sysmex Hematology Analyzer XP-100 (Serial No. A–4847) and Sysmex specified reagents were used. Procedure was performed strictly in accordance with manufacturer's instructions, while observing strict quality control of the machine.[2,17]

Data were analyzed using SPSS-22. Means and standard deviations were calculated. Independent sample Student's *t*-test was used to see the mean differences, and $p<0.05$ was considered statistically significant.

RESULTS

Mean age of study population was 29.11±9.26 years with a range of 18–50 years. Majority (276, 71.87%) of the study population belonged to rural areas and 108 (28.13%) lived in the urban areas. Majority of study population (170, 44.27%) belonged to lower socioeconomic class, followed by lower middle class (148, 38.54%), upper middle class (51, 13.28%) and upper class (15, 3.91%) (Table-1).

Mean values of Hb con was 13.05 (range: 9.73–16.37) g/dL, and RBC# was 4.58 (range: 3.4–5.76) million/µL. (Table-2).

No significant difference was found on Student's *t*-test between different groups of study population except, in Hb con mean values of lower and lower middle class ($p=0.00$). (Table-3).

Hb con and RBC# in this study were different from the reference values currently being used. Determined values of Hb con and RBC# are lower and have wider range than the normal reference values in use. (Table-4).

Table-1: Demographics of study population (n=384)

Variables	Frequency	Percentage
Area of residence		
Rural	276	71.87
Urban	108	28.13
Socioeconomic status		
Lower class	170	44.27
Lower middle class	148	38.54
Upper middle class	51	13.28
Upper class	15	3.91

Table-2: Hb conc and RBC# in study population

Variable	Mean±SD	Mean±2 SDs	Range
Hb con (g/dL)	13.05±1.66	13.05±3.32	9.73–16.37
RBC# (million/µL)	4.58±0.59	4.58±1.18	3.40–5.76

Table-3: Comparison of Hb con and RBC# values in age, residence, education and socioeconomic groups

Variables	Hb con (g/dL)	RBC# (million/µL)
Age group		
Up to 34 years	12.96±1.65	4.56±0.60
>34 years	13.28±1.68	4.62±0.56
p	0.767	0.452
Residence		
Rural	12.94±1.69	4.55±0.61
Urban	13.33±1.57	4.66±0.56
p	0.306	0.15
Educational Status		
Up to HSSC	12.58±1.47	4.48±0.60
More than HSSC	13.97±1.63	4.77±0.52
p	0.146	0.33
Socioeconomic Status		
Lower class	11.75±0.82	4.55±0.61
Lower middle class	13.46±1.13	4.66±0.56
p	0.000	0.71

Table-4: Comparison between measured range values and reference values in use

Variable	Measured values	Reference values in use
Hb con (g/dL)	9.73–16.37	13–17
RBC# (million/µL)	3.4–5.76	4.5–5.5

DISCUSSION

It is necessary to establish normal reference values for haematological indices in a population for screening, diagnosis, and monitoring of associated pathological conditions. The normal reference values for haematological indices are influenced by many factors, e.g., ethnicity, environmental factors, age, gender, nutritional factors, social factors, and genetic influences necessitating the establishment of normal reference values for each population.[3,5–13]

Reference values for haematological parameters have been determined in different populations of the world. Studies conducted by Addai-Mensah O *et al*[5] in three regions of Ghana, Mulu W *et al*[6] in Gojjam zones in Amhara region, Ethiopia,

Shaheen NA *et al*[7] in Saudi Arabia, Siraj N *et al*[8] in Asmara, Omarine Nlinwe N *et al*[9] in Bamenda, North West Region of Cameroon, Rosenfeld LG *et al*[10] in Brazil, and Iftikhar R *et al*[11] in Nyala, Darfur determined the values of haematological indices in healthy adult populations. Study by Ouma JO *et al*[12] in Kombewa Sub-County, Kisumu, Western Kenya, determined the reference values of haematological parameters among infants aged 1 to 17 months. Reference values for haematological indices for Pakistani population are derived from the populations of western countries. Reference values from different Pakistani populations were determined in a very small number of studies.[3,13]

Study by Shaikh MS *et al*[3] determined reference intervals for routine and special haematological parameters for adult population in Karachi. They concluded that determined values of the parameters were different from the values in practice. Reference values of haematological indices for healthy adult population determined by Mazhar N *et al*[13] from Lahore, Karachi, Quetta, Rawalpindi and Abbottabad were found different from international reference values in use. Measured reference values of Hb con and RBC# in this study are different from the reference values currently in use for adult male population in district Muzaffarabad. Results of studies in Pakistani populations[3,13] and different populations of the rest of the world[5–12] favour the results of this study.

CONCLUSION

The reference values for Hb con and RBC# for adult male population in district Muzaffarabad are different from the values already in use. Determined values of Hb con and RBC# are lower and have wider range than the normal reference values currently in use.

LIMITATIONS

This study was conducted in district Muzaffarabad only and cannot be generalized for whole adult population of Kashmir. This study reflects reference range for male population only and lacks information about females. This study is focused on people 18–50 years old. Studies with larger sample size including female population, all age groups and parameters will further clear the picture.

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ORIGINAL ARTICLE

PHYSIOLOGICAL AND SOCIO-ECONOMIC SATISFACTION LEVEL OF PATIENTS FOR ACRYLIC AND CAST ALLOY DENTURES

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Background: The ultimate loss of dentition creates lot of oral problems for edentulous patients which can be prevented with the provision of acrylic or cast alloy denture but patient satisfaction level attributed to these dentures is still unknown. We evaluated patient satisfaction level regarding aesthetics, pain, cost, retention, comfort and speech between acrylic and cast alloy denture wearers. **Methods:** Freshly edentulous patients wearing complete dentures with acrylic resin denture (AD) (n=65) and Co-Cr cast alloy denture (CD) (n=65) took part in study. Smart Patient Satisfaction Questionnaire was used to investigate satisfaction of these patients after one month (AD-1 and CD-1) and then after 3 months (AD-3 and CD-3). Scoring system 0=Not-Satisfied, 1=Satisfied and 2=Well Satisfied was used to evaluate general satisfaction of patients in both groups regarding speech, taste, pain, aesthetics, comfort, cost, and retention. **Results:** Patient satisfaction level between AD and CD wearers displayed insignificant differences with respect to aesthetics (p=0.614), pain (p=0.842), retention (p=0.852), comfort (p=0.842), speech (p=0.943), and taste (p=0.753). Patient satisfaction level between AD and CD users related to cost was significant (p=0.001) depicting that AD group was more satisfied with cost as compared to CD users. **Conclusions:** Both groups were satisfied with their aesthetics, pain control, retention, comfort, speech, and taste but patients using AD were found to be more satisfied with cost as compared to CD users who found these dentures quite expensive.

Keywords: Acrylic Denture, Cast alloy, Cost effective, Pakistan, Patient satisfaction

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INTRODUCTION

The main purpose of the restorative dentistry is to preserve natural teeth and their masticatory ability for maintaining both facial aesthetics and oral functions, in addition to get relief from pain.[1,2] The WHO global oral health status 2022 has reported that a total of 3.50 billion population worldwide is influenced by oral diseases out of which, 3/4 persons residing in middle income or low income countries are more adversely affected other than high income countries. Complete loss of teeth during adulthood is referred as edentulism that gives sound information about health status of any individual. Internationally, incidence of edentulism has been reported between 6–69% by WHO.[3] There is a huge prevalence of tooth loss in about 23% of the population belonging to age group above 60 years while 7% belonging to age group above 20 years worldwide.[4] Previously, reported prevalence of edentulism in different countries has been 21.70% in Mexico, 3.0% in Ghana, 9.0% in China, 58.0% in Canada, and 16.30% in France[5], whereas 51.40% and 48.60% in urban and rural areas especially involving the aged people. Furthermore, it has been narrated that this problem of edentulism would increase more because of the increased population of the aged people.[6] Complete loss of tooth due to any reason might adversely affects the food selection type of an individual resulting in the poor nutritional status[7], that could become the possible reason of certain diseases including coronary heart disease and chronic kidney disease.[8]

Dental prosthesis is the only solution to replace missing teeth/edentulism for the patients in order to improve their quality of life by enhancing their mastication, functions, tissue preservation and phonetics.[9,10] The dental prosthesis used to replace the complete missing teeth in the oral cavity are known complete dentures (CDs). There are two types of conventional materials used most commonly for the fabrication of dentures (CDs) such as metal alloys and methyl polymethacryls. The materials used for this purpose are cobalt-chromium alloys and acrylic resins.[11] The impairments in masticatory ability and satisfaction level have also been reported by the patients after using these prosthesis for some time which has most probably compromised their dietary habits in turn leading to the downfall of the healthy status of the edentulous patients.[10,12] Therefore, currently it has become essential to evaluate the patient's self-satisfaction before confirming the future efficacy of the prosthesis.

The effectiveness of dental prosthesis in terms of patient's satisfaction towards various factors can be calculated via subjective and objective methodology.[12] The subjective method is dependent on the patient's perception and ability about satisfaction level while objective method relies on the patient's experimentation of masticating and biting the test food.[13] The subjective

method is based on the oral health related quality of life and satisfaction through a patient's oriented questionnaire which is cost, resource and time effective in many ways.[10,12] On the other hand, objective method provides tools and equipment to check the chewing abilities but it is more expensive, time and resource consuming.[13] This method might not be possible in patients who received dentures from private clinics and hospitals especially in low-income countries like Pakistan that requires an easy and accurate way to assess the patient's satisfaction. Currently, subjective method including Smart Patient satisfaction level via Questionnaire has been developed which is quite authentic and valid.[14] This Smart Patient Questionnaire could easily identify the patient's satisfaction towards aesthetics, speech, retention, stability, taste, pain, and cost in a much smarter and practical manner. This latest smart Questionnaire have not been incorporated in the Pakistani population in the clinical practice to evaluate the comparison of patient's satisfaction between acrylic resin denture (AD) wearers and Co-Cr cast alloy denture (CD) wearers. Our study focused to compare the patient's satisfaction level between AD wearers and CD wearers in order to find out the more feasible prosthesis for the edentulous patients.

MATERIAL AND METHODS

This Questionnaire oriented interventional study was conducted after the ethical approval from School of Dentistry, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad Pakistan with ERB Reference letter no: SOD/ERB/2023/22-05. Total 130 freshly edentulous patients, 60–70 years old, wearing complete dentures were selected for this study. These patients were medically fit and did not use any other medication that might adversely affect their ridge, bone and gums.

Freshly edentulous patients wearing complete dentures less than 1 month were included in study. These patients were divided into two groups of 65 each named as AD (n=65) and CD (n=65). The AD was allocated to the patients using acrylic resin complete denture while CD to the patients using the Co-Cr cast alloy complete denture. The Smart Patient Satisfaction Questionnaire was used in this study to evaluate the personal satisfaction of patients using AD and CD. This Questionnaire was filled by patients of both groups initially after one month (AD-1 and CD-1) and then finally, after 3 months of utilizing these dentures again (AD-3 and CD-3).

The score system was used to evaluate the general satisfaction of the patient in both groups regarding speech, taste, pain, aesthetics, comfort, cost, and retention where scoring was evaluated through three digits showing 0 (Not-Satisfied), 1 (Satisfied) and 2 (Well Satisfied).[15] These data were analysed using SPSS-22 with confidence interval at 95%, and $p \leq 00.05$ was taken as statistically significant.

RESULTS

The mean values of patient satisfaction level in AD wearers for aesthetics were AD1=1.37±0.77 and AD3=1.40±0.79, for Pain AD1=0.47±0.71 and AD3=1.66±0.65, for cost AD1=1.81±0.50, and AD3=1.81±0.50, for Retention AD1=1.27±0.75 and AD3=1.56±0.69, for Comfort AD1=0.27±0.57 and AD3=1.76±0.56, for Speech AD1=0.37±0.70 and AD3=1.56±0.71, for Taste AD1=0.50±0.76 and AD3=1.89±0.40.

The Patient satisfaction level towards acrylic denture in all aspects increased after three months. On the other hand, the mean values of patient satisfaction level in CD wearers for Aesthetics were CD1=1.40±0.79 and CD3=1.48±0.73; for Pain CD1=0.52±0.73, and CD3=1.65±0.65; for Cost CD1=0.22±0.60 and CD3=0.22±0.60; for Retention CD1=1.29±0.75 and CD3=1.59±0.66; for Comfort CD1=0.33±0.62 and CD3=1.75±0.56; for Speech CD1=0.40±0.73 and CD3=1.56±0.71; and for Taste CD1=0.54±0.767 and AD3=1.92±0.32. The Patient satisfaction level towards cast alloy denture increased in all the aspects after three months except cost (Figure-1).

The patient satisfaction level among AD and CD wearers increased after three months of utilization confirming the enhanced patient satisfaction level for Pain, Retention, Comfort, Speech, and Taste which was statistically significant (p=0.001). Patient satisfaction for Aesthetics was found to be insignificant in both groups AD (p=0.484) and CD (p=0.526). On the other hand, inter-group patient satisfaction level for cost remained insignificant among AD (p=0.577) and CD wearers (p=0.589) even after three months of usage (Table-1).

The mean value of patient satisfaction in AD and CD wearers respectively was 1.39±0.78 and 1.44±0.76 for Aesthetics, 1.06±0.90 and 1.09±0.89 for Pain, 1.81±0.50 and 0.22±0.60 for Cost, 1.42±0.73 and 1.44±0.72 for Retention, 1.02±0.93 and 1.04±0.92 for Comfort, 0.97±0.92 and 0.98±0.92 for Speech, and 1.19±0.92 and 1.23±0.91 for Taste (Figure-2).

The variables investigated for the patient satisfaction level between AD and CD wearers displayed insignificant differences after three months with respect to Aesthetics (p=0.614), Pain (p=0.842), Retention (p=0.852), Comfort (p=0.842), Speech (p=0.943), and Taste (p=0.753). On the other hand, after three months the differences in patient satisfaction level between AD and CD wearers related to cost were significant (p=0.001). Patients using AD were found to be more satisfied with the cost of this prosthesis as compared to the CD users (Table-2).

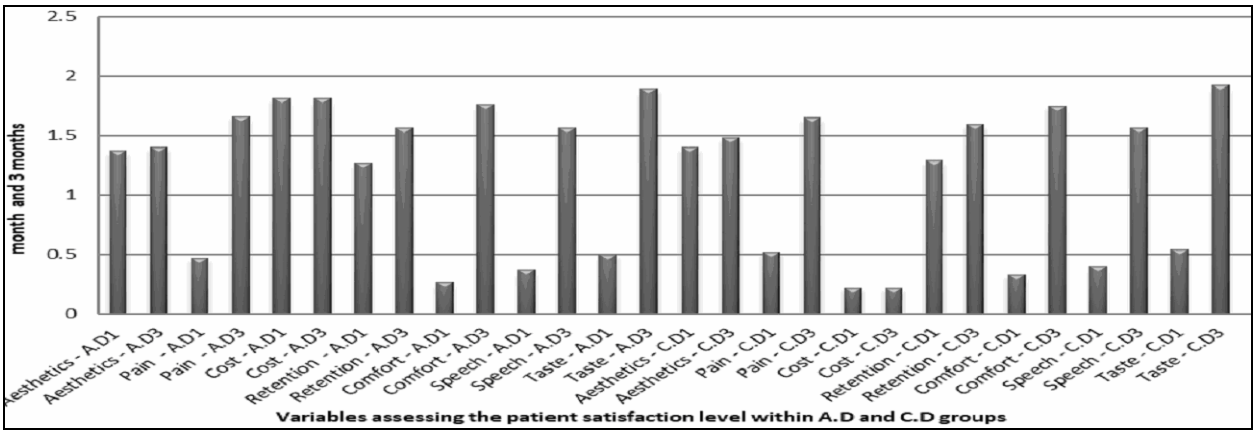

Figure-1: Patient satisfaction level among acrylic denture wearers (AD1 and AD3) and cast alloy denture wearers (CD1 and CD3) after one and three months

Table-1: Inter-group comparisons in patient satisfaction between AD and CD wearers

Comparing groups for AD and CD wearers	Comparison of patient satisfaction level between AD1-AD3 and CD1-CD3 wearers	Mean difference with SD	95% Confidence Interval of the Difference		*p*
			Lower limit	Upper limit	
AD for Aesthetics	Comparison of Aesthetics	-0.03±0.36	-0.12	0.05	0.484
AD for Pain	Comparison of Pain	-1.19±0.95	-1.43	-0.95	0.001
AD for Cost	Comparison of Cost	-0.05±0.67	-0.13	0.07	0.577
AD for Retention	Comparison of Retention	-0.29±0.61	-0.44	-0.13	0.001
AD for Comfort	Comparison of Comfort	-1.48±0.93	-1.72	-1.24	0.001
AD for Speech	Comparison of Speech	-1.19±1.09	-1.47	-0.91	0.001
AD for Taste	Comparison of Taste	-1.38±0.89	-1.61	-1.16	0.001
CD for Aesthetics	Comparison of Aesthetics	-0.07±0.98	-0.32	0.17	0.526
CD for Pain	Comparison of Pain	-1.12±0.90	-1.35	-0.89	0.001
CD for Cost	Comparison of Cost	-.07±0.79	-0.14	0.09	0.589
CD for Retention	Comparison of Retention	-0.30±1.10	-0.57	-0.02	0.034
CD for Comfort	Comparison of Comfort	-1.41±0.81	-1.61	-1.20	0.001
CD for Speech	Comparison of Speech	-1.15±0.97	-1.40	-0.91	0.001
CD for Taste	Comparison of Taste	-1.38±0.83	-1.59	-1.17	0.001

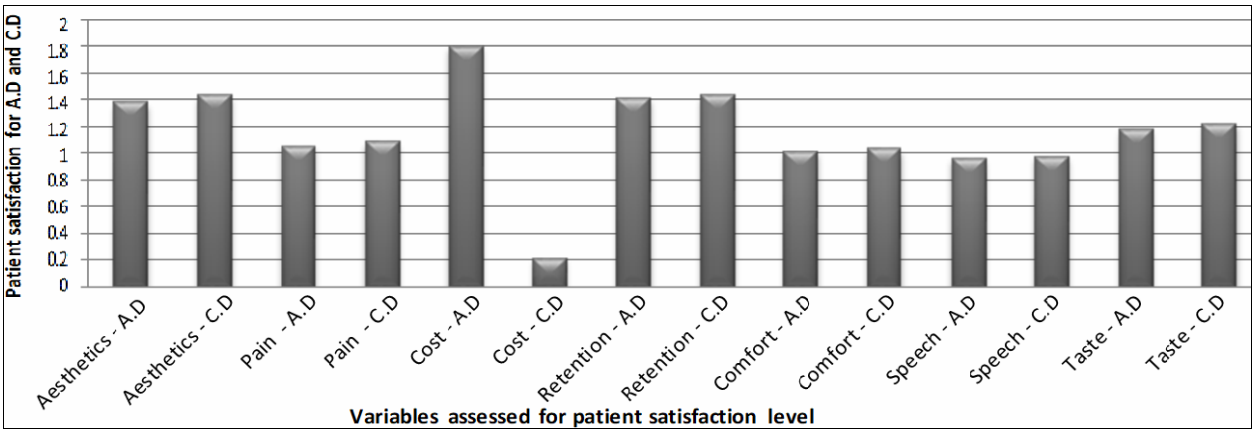

Figure-2: Mean patient satisfaction level between acrylic denture wearers and cast alloy denture wearers

Table-2: Comparison of patient satisfaction between AD and CD wearers

Variables	Mean difference	95% CI of the Differences		*p*
		Lower limit	Upper limit	
Aesthetics	-0.049	-0.242	0.143	0.614
Pain	-0.049	-0.247	0.202	0.842
Cost	-1.58	1.44	1.72	0.001
Retention	-0.017	-0.198	0.164	0.852
Comfort	-0.024	-0.255	0.208	0.842
Speech	-0.008	-0.239	0.222	0.943
Taste	-0.037	-0.266	0.193	0.753

DISCUSSION

Various subjective methods have been employed to assess the patient satisfaction level while using the removable prosthesis either partial or full dentures. This methodology is valid enough to evaluate the 'Oral Health Related Quality of Life' (OHR-QoL) with respect to the patient satisfaction level in terms of aesthetics, pain, cost, retention, comfort and speech.[10,12] Multiple questionnaires have been developed and used

in distinct countries depending upon the evident differences in their ethnicity, culture, and socio-economic status. These questionnaires were formulated to measure the patient satisfaction level regarding general aspects and masticatory abilities in elderly people[14], complete and partial denture wearing individuals[16]. Currently, latest validated questionnaires[14,17] are utilized to investigate the subjective aspects of the patient satisfaction level because this method is more easy and reliable. Secondly, this methodology saves time and cost when patients give their feedback about the specific treatment of partial or complete denture quite feasibly.[13,18]

Pakistan is a low income country where subjective method to calculate the patient satisfaction level regarding aesthetics, pain, cost, retention, comfort and speech could be more appropriate and easy to conduct. The present study compared the effects of patient satisfaction level between acrylic denture and cast alloy denture wearers initially after one month of usage and then finally after three months. The patient satisfaction level enhanced within both AD wearer and CD wearer groups regarding pain control, retention, comfort, speech, and taste after three months. Patient satisfaction level regarding aesthetics and cost reduced within both AD (AD1 and AD3) wearer and CD (CD1 and CD3) wearer groups after three months of usage. Patient satisfaction level while comparing AD and CD revealed that both groups were satisfied with its aesthetics, pain control, retention, comfort, speech, and taste after three months. On the other hand, patients using AD were found to be more satisfied with the cost of this prosthesis as compared to CD users who found these dentures quite expensive. The findings of this study were different from some other researches conducted in the past, despite the fact that validated subjective tools were used.[14,19,20]

The difference in the results of our study might be due to alterations in the socio-economic status and lifestyles where AD wearers and CD wearers both were satisfied regarding their aesthetics, pain control, retention, comfort, speech, and taste in the same manner. On the other hand, AD wearers were more satisfied about the cost of this prosthesis in comparison to the CD wearers who were not very well satisfied about the cost of their prosthesis where cost of CD was comparatively more. Our study was found to be better than another study because in our study various factors contributing in the patient's satisfaction level were investigated separately in comparison to the ultimate impact observed previously which gave little clue about the patient satisfaction level using a prosthesis.[14,19,20] The complete denture prosthesis is the basic need of the edentulous patients who have lost their teeth entirely in the old age[21] that has become a global problem[6]. Factors found in close association with edentulism are diabetes, smoking, education, hypertension, arthritis, asthma, quality of life especially low income, and old age. These major factors induced the edentulism in about one-third of the aged people ≥65 years[22] because of direct relationship between the aging process and health demand which is important. Moreover, increasingly shifted demographic status in Pakistan has contributed to the declined health indices, enhanced poverty rate and fast population growth rate.[23] Thus, acrylic denture was more cost-effective as compared to the cast alloy denture which was statistically significant (p=0.001).

The unaffordable cost could be a big challenge in meeting the required healthcare demand of the society. The economic status of the individual is responsible for the provision of the adequate healthcare.[24] Other factors responsible for determining the health include lifestyle, socio-economic, and environmental conditions.[25] Some researchers also confirmed that lower socio-economic status is the main cause responsible for the dental caries prevalence eventually leading to the edentulism[26,27], and endodontic/restorative procedures are among most commonly practiced procedures in a dental setup.[28] Tooth retention is still considered a vital indicator of oral health of the population.[29] Poor control for dispensing regulations, cost and medicine availability has been confirmed by many developing and underdeveloped countries.[30] There is a definitive need to improve the socio-economic demographics and health status by ensuring the cost-effective dental treatment to the population.

CONCLUSIONS

Patient satisfaction level while comparing AD wearer and CD wearer revealed that both groups were satisfied with their Aesthetics, Pain control, Retention, Comfort, Speech, and Taste, but Patients using AD were found to be more satisfied with the cost of this prosthesis as compared to the CD users who found their dentures quite expensive. The unaffordable cost could be a big challenge in meeting the required healthcare demand of the Pakistani society. There is need to improve the socioeconomic demographics and health status by ensuring the provision of cost-effective dental treatment.

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AM: Substantial, data collection, data analysis, manuscript writing, interpretation, critical review
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ORIGINAL ARTICLE

MOXIFLOXACIN INDUCED QT INTERVAL PROLONGATION: A RISK TO TORSADE DE POINTES IN ELDERLY PATIENTS

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Background: Quinolones are notorious for QT interval prolongation and sometimes carry risks for development of Torsade de Pointes. Objective of this study was to determine the effect of moxifloxacin on QT interval prolongation on electrocardiogram. **Methods:** It was a cross-sectional study, conducted in Medical Department of Mardan, Medical Complex, Mardan, from January to December 2021. Moxifloxacin was given for treatment of different ailments to 57 patients after approval of study protocols from Ethical Committee of Gajju Khan Medical College/Bacha Khan Medical Complex Swabi. Their baseline ECGs, second ECG on its T_{max} and third set of ECGs were recorded, in triplicates, on 48 hours of treatment. QTc was calculated using Bazett's formula either using lead II or alternatively AVR, AVF, V_5, V_6, or V_4, leads. Moxifloxacin was administered in recommended doses. **Results:** Of the 57 patients, 24 patients (42%) showed QTC prolongation (prolonged QTc: For male >450 ms, and for female >470 ms); and 19 patients (33%) reached to the limits for a risk (Patients with QT_c >500 ms or QTc change over baseline >60 ms) for development of Torsade de pointes. Remaining 14 patients (25%) faced no complications. Statistically significant changes were observed for both male and female patients (p<0.05). However, QT prolongation was sustained for 48 hours in female only. **Conclusion:** Moxifloxacin produced significant changes in QTc particularly in elderly patients. Mean changes in QTc on 48 hours were prolonged in females than males.

Keywords: Moxifloxacin, QT interval, Torsade de Pointes, Bazett's Formula, ECG

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INTRODUCTION

Safe and effective uses of drugs are basics for pharmacotherapeutics. Fluoroquinolones are used for treatment of different infections like skin and soft tissues infections, respiratory tract infections, gastroenteritis and genitourinary tract infections. Most frequent adverse effects of quinolones are connective tissues damage, headache, oral thrush, skin rash and photosensitivity and prolongation of QT interval.[1,2]

QT interval consists of time for QRS complex and JT interval. QRS complex represents time for ventricular depolarization. JT interval reflects ventricular repolarization time.[3] More than 120 ms value for QRS Complex indicates widening of QRS complex which is sometimes attributed to blockade of sodium channels, Class IA and IC anti arrhythmic drugs, local anaesthetics, tricyclic antidepressants and $5HT_3$, antagonists have been reported for QT interval prolongation along with widening of QRS complex.[4,5] Prolongation of the QT interval may lead to reflex ventricular tachycardia and Torsade de Pointes (TdP), If not dealt promptly, it may lead to syncope,[6] ventricular fibrillation and sudden cardiac death.[7] It has been reported that most of QT interval prolonging drugs block rapid component of the delayed rectifier Potassium K_{ir} or IRK.[8,9] The term 'Torsade de Pointes' which is continuous twisting of QRS complex around isoelectric line was coined by French physician Francois Dessertenne in 1966 that occurred in an old lady with heart block.[10] In previous decades, QT interval prolongation associated with TdP was the only parameter which became the cause of withdrawal of many drugs in post-marketing surveillance.[11] Drugs are withdrawn during post-marketing surveillance period as information about prolongation of QT interval are usually missed in preclinical studies.[12]

Predisposing factors for QT interval prolongation and TdP include old age, female sex, decreased left ventricular ejection fraction, bradycardia, left ventricular hypertrophy, ischemia and electrolytes imbalance, especially hypokalemia, hypomagnesaemia, hypocalcaemia, genetic polymorphism and heart block.[13,14]

The measured QT interval is transformed by heart rate as reported by Bazett's, Fridericia, and Framingham. Bazett's correcting formula has got popularity and is commonly used because of its simplicity. Thus, QT interval is an important tool for clinicians to predict serious adverse effects like TdP and ventricular fibrillation and even in preclinical phase of new drug development. Though, the risk of TdP is not a linear function of QT interval, yet QT interval of 500 ms or more is considered an increased risk.[15] According to Pratt *et al*, minimal changes in QT interval (5–10 ms) in population study should be taken seriously.[16]

Withdrawal of grepafloxacin and sparfloxacin

from market has raised questions on quinolones. New generation fluoroquinolones are commonly used in variety of community acquired infections and nosocomial infections. Moxifloxacin is frequently used these days. It is studied for QT interval prolongation in different populations.[17–19] Current work is an attempt to study the effects of moxifloxacin on QT interval in our set-up.

MATERIAL AND METHODS

Fully informed consents were obtained from patients who participated in the study. The Ethical Committee of Gajju Khan Medical College/Bacha Khan Medical Complex, Swabi approved the protocols. All protocols were carried out in light of Helsinki declaration for ethical procedures.

Twelve-lead ECGs were recorded using conventional 12-lead ECG machine. Stable patients, 57 of either sex or age, to whom moxifloxacin was prescribed, were followed for changes in QT interval. Baseline ECGs were recorded in triplicate. Second set of ECGs were recorded after the administration of first dose on respective T_{max} 1–2 hours of administration of drugs. The third set of ECGs were obtained in 48 hours as most of patients were discharged on day 3rd. An additional ECG was also recorded when patients complained of possible adverse effects, syncope, TdP or arrhythmic episodes during the therapy.

Stable patients of either sex who required quinolones for treatment of their illnesses were enrolled in the study using purposive sampling technique. Patients with normal serum electrolytes levels for sodium, potassium and calcium were included in the study. Patients already taking quinolones or other pro arrhythmogenic drugs, hypertensive drugs, comatose patients and patients with ongoing baseline ECG changes of ischemia, infarction or arrhythmia were excluded from the study.

Lead II of 12-lead ECG was selected for measuring possible changes in QT interval and QRS complex in pre-dose and post-dose states. When Lead II was not readable, then Leads AVR, AVF, V_5, V_6, or V_4 were selected for analysis.[20] QRS complex was measured from the beginning of Q wave to the end of S-wave. QRS complex values equal to less than 120 ms were considered normal. QT interval was measured from the beginning of Q wave to the end of T wave.

Bazett's formula was used for determination of QTc.[21] Bazett's formula for: $QTc=QT/\sqrt{RR}$, where R-R is preceding risk for TdP the QT interval.

Patients were declared to be at risk for development of TdP whence their QTc values were more than 500 ms, or difference in their QTc values were more than 60 ms versus baseline QTc values.[3,22] QTc was considered prolonged if its value in males and females were respectively >450 ms and >470 ms.[7]

Data was expressed in tables using SPSS-21. One way ANOVA was used for testing the significance of differences at 95% CI and $p<0.05$.

RESULTS

Mean age of the patients (n=57) was 64.71±15.65. Frequencies of patients who reached the limits for (i) prolongation of QTC interval, and (ii) for reaching limits for possible risks of TdP were expressed. There were 24 cases of prolonged QTc, and 19 cases reaching limits for risks for development of possible TdP (Table-1).

Remaining 14 patients in the study faced no known and related complications that are inferred in this study protocol.

Table-1: Effects of Moxifloxacin on QTc and reaching limit for TdP

	Number of patients
Patients with QTc prolongation	24
Patients at risk to TdP	19
Patients with no related ECG changes	14

Prolonged QTc= for male >450 ms and for female >470 ms + patient with QTc >500 ms or QTc change over base line >60 ms.

Cases that reached the limits for QTc (500 ms or above) were subdivided on the basis of gender. Mean changes in QTc on 1–2 hours and 48 hours were recorded against baseline QTc values. Only those cases are presented here where changes were more than 500 ms (Table-2).

Table-2: Effects of Moxifloxacin on QTc. Mean changes in QTc at baseline, after 1–2 hours and after 48 hours are shown ($p<0.05$)

Parameter	Males	Females
Mean Basline QTc	439.2	470.2
QTc After 1–2 hours	518.4	534.4
QTc after 48 hours	487.8	508.4

DISCUSSION

Moxifloxacin is one of the current antibiotics that are frequently prescribed for treatment of respiratory tract infections, urinary tract infections, skin and soft tissues infections and gastrointestinal tract infections. Their spectrum against atypical pathogens gives them an edge over some Cephalosporins in addition to cover typical microorganisms. Therefore, nowadays fluoroquinolones are used as broad-spectrum antibiotics similarly and emergence of resistance to cephalosporins and penicillins makes quinolones the priority drugs. Since very long, it is evident that quinolones and some anti-malarials prolong the QT interval. All the quinolones, as a class, have been implicated to prolong QTc.[23] But the potential to prolong QT interval is not the same for all fluoroquinolones. The preclinical and clinical studies suggest that there are significant differences in potencies to prolong QT interval and develop risk for arrhythmia

among the fluoroquinolones. All quinolones block voltage gated potassium channels especially the K_{ir} or IRK a rapid component of delayed rectifier potassium current. However, the degree of K_{ir} or IRK blockage is not the same for all quinolones. Our findings are consistent with the reports of Owen[23] and Tsikouris[24] as moxifloxacin has shown highest mean QTc changes both in males and females.

Nevertheless, it is imperative to keep in mind the associated risk factors in addition to drugs that may have direct effect on heart. Like studies have shown that even non cardiac drugs in the presence of associated risk factors like female gender, heart disease, electrolyte disturbances, excessive dosing, drug interactions, and history of familial long QT syndrome have led to the precipitation of *Torsade de Pointes*. Therefore, a deliberate approach is necessary while opting for a drug which is notorious for QT interval prolongation especially when two of associated risk factors co-exist.[25–27]

More reports say that any changes more than 35 ms in QTc while taking a drug is considered as drug effect.[28] Hence, these changes in the QTc cannot be ignored and requires further work to answer the concerns been raised in our findings. Our findings show that moxifloxacin significantly changes QTc in elderly patients. Hence the prescribers shall be conscious about the use of moxifloxacin particularly in elderly patients especially with mean age more than 64 years.

CONCLUSION

Moxifloxacin produced significant changes in QTc particularly in elderly patients. Mean changes in QTc on 48 hours were prolonged in females than males.

LIMITATIONS AND RECOMMENDATIONS

It was a single centre study in limited number of patients, detailed randomized controlled studies are recommended to establish safety of fluoroquinolones particularly of moxifloxacin in elderly patients.

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ORIGINAL ARTICLE

WORKPLACE BASED CHALLENGES FOR POSTGRADUATE TRAINEE DOCTORS WORKING IN A PUBLIC SECTOR HOSPITAL

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Background: Workplace-based challenges are experiences that are seen as inappropriate by the person experiencing or observing the challenge. These challenges may arise every day in different situations or may be a one off incident that is disturbing and affects one's productivity. The study aims to identify and analyse the major hurdles that healthcare professionals encounter in their daily practice. **Methods:** A qualitative approach was employed to collect data from a diverse group of doctors at a public sector hospital in Sialkot. Semi-structured interviews were conducted in groups from different departments of the hospital in 2023. The consenting participants were interviewed regarding the challenges they face day to day working in government setup. Themes were extracted and data was tabulated to draw results. **Results:** We interviewed 21 consenting doctors from different departments mainly, Medicine, Surgery, Paediatrics and Gynaecology and identified six main themes which were high workload, security threats, financial Issues, resource constraints, time constraints, and inadequate work-life and personal-life balance. Amongst the 21 doctors, (47.62%) were females and (52.38%) were males. the challenges of high workload was stated by all (100%) of the participants, followed by security threats (91.5%), resource constraints (85.7%), financial issues (76.1%), time constraints (71%) and work and personal life imbalance (71.4%). **Conclusion:** Doctors reported significant levels of work-related stress, poor work-life balance, inadequate work capacity, and about one-third of them burned out, a sign of unfavourable working conditions.

Keywords: work based challenges, post graduate trainees, public sector hospital

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INTRODUCTION

The healthcare system of Pakistan witnessed a significant development in recent years but it continues to face numerous challenges. Among the key stakeholders in the healthcare system, doctors play a pivotal role in delivering quality medical care to patients.[1] The country's emphasis on producing more doctors has resulted in significant gains in the doctor-to-population ratio; nonetheless, issues of quality and capacity, as well as the effective and equitable deployment of health-related human resources, remain significant.[1] However, the workplace environment for doctors in hospitals across Pakistan presents various obstacles that may impact their performance, job satisfaction, and overall well-being.[2] During their medical training, trainee doctors in Pakistan, like in many other developed and under developed countries, experience a variety of workplace-based problems. Trainee doctors are frequently required to work long and arduous hours, often surpassing the accepted limits for safe and successful medical practice. This can result in weariness, burnout, and a decrease in learning ability.[3] The patient load at hospitals and medical institutions can be burdensome, particularly in public hospitals with a high patient-to-doctor ratio.[4] Trainees may have difficulty balancing patient care, learning, and personal well-being. In Pakistan, trainee doctors may have restricted access to current medical resources, textbooks, and research materials. This can make it difficult for them to keep up with medical advances.[5] Some medical institutions may lack enough infrastructure, equipment, and technology, which can impede good patient care and training.[5] Due to the high expense of education and training, trainee doctors sometimes suffer financial difficulties. Low stipends or incomes during training may not be sufficient to cover their costs.[6] Medical training can be rigorous, making it difficult for trainees to maintain a healthy work-life balance. This can lead to burnout and have a negative impact on their general well-being. Dealing with patients, especially in urgent or difficult situations, can be emotionally draining for trainee doctors. They may not have enough psychological assistance to deal with the stress and emotions involved. Some trainee doctors may not be exposed to a wide range of medical situations and procedures, limiting their exposure to various medical problems and treatments.[7] This study aims to identify and analyze the challenges that healthcare professionals encounter in their daily practice in our locality.

METHODOLOGY

It was a qualitative descriptive study where Semi-Structured Interviews were conducted of volunteer post graduate trainee doctors in groups. The study was

carried out at a local government sector teaching hospital. Ethical approval was taken from to carry out the interviews. The consenting participants from the major disciplines, i.e., Medicine, Surgery, Obs/Gyn, and Paediatrics who were currently working at the hospital were invited for focused group interviews at a calm and comfortable setting. The participants were post graduate trainees and were included in the study based on their availability and willingness to contribute to the research. In-depth interviews were conducted with a subset of doctors from each department to obtain qualitative insights into their experiences. We interviewed them with open ended questions regarding the challenges they face while at work. The interviews aimed to explore the reasons behind the challenges and how they impacted the doctors' professional and personal lives. Their responses were recorded in writing and weren't voice recorded to assure them safety and anonymity. After the interviews, themes were extracted from the data. Thematic analysis was utilized to identify recurring themes and patterns related to workplace challenges.

RESULTS

We interviewed a total of 21 doctors in departmental groups, out of which 10 (47.62%) were females and 11 (52.38%) were males.

Table-1: Basic details of participants

Items	Number	Percentage
Gender		
Females	10	47.62
Males	11	52.38
Departments of postgraduate trainees		
Gynaecology and obstetrics	6	28.57
General surgery	4	19.05
General medicine	6	28.57
Paediatrics	5	23.81
Working Experience after graduation		
2 yrs	3	14.29
2.5 yrs	2	9.52
3 yrs	5	23.81
4 yrs	5	23.81
5 yrs and above	6	28.57
Year of Training		
1st year	9	42.86
2nd year	8	38.09
3rd year	3	14.29
4th year	1	4.76
Marital Status		
Married	12	57.14
Unmarried	9	42.86

The interview responses revealed the following major themes:

a) High Workload: All the participants (21) 100% reported that they faced an excessive workload when one individual has far too much work to handle on his own, leading to increased stress and fatigue. One of the participants said, 'Sometimes I have to take anti-depressants and painkillers to ease my stress and body aches after long duty hours'.

b) Security threats: The majority of the participants (19) 90.47% felt insecurity in their working environment in the form of violence by attendants of patients especially if a patient passes away, theft and harassment by media persons. 'I left my bag at the reception counter of the Emergency ward to see a patient when I returned my phone and cash were not in the bag', a trainee doctor from the participants said. One other participant said, 'Attendants of patients start shouting and even fighting if something goes wrong'.

c) Financial Issues: Most of the participants (16) 76.19% were not satisfied with their pay scale as due to inflation they could hardly meet their needs, especially as some of them had big families to take care of. A doctor said, 'My wife tells me that her family married her to a doctor as they thought doctors earn good, but her concept changed after two years of marriage with me as I can hardly meet our needs'.

d) Resource Constraints: Majority of doctors (18) 85.71% cited inadequate space, medical equipment and shortages of essential supplies as significant challenges affecting patient care. A Participant said, 'We have to see even two patients on same bed due to lesser number of beds in medical emergency'. Another participant said, 'We don't have proper rest rooms sometimes we have to use public rest rooms'.

e) Time Constraints: One of the participants from Surgery Department said, "I don't get time for studying books or doing research". Many of the respondents (15) 71.42% expressed dissatisfaction with the limited opportunities for career advancement and professional development in the healthcare system. They could not get time for self-study. One participant said, 'We have to teach juniors, see patients, do ward rounds and report to seniors, it's difficult to manage all in limited time'.

f) Work-Life and personal-life Imbalance: Many doctors (15) 71.42% struggled with maintaining a healthy work-life balance due to long working hours and demanding schedules. Due to this they must compromise in their personal life too. A trainee doctor said, 'I can't see my two-year-old son for long periods'. 36 hours of calls at hospitals and part time jobs make very hard situations for some to manage their personal lives.

The interviews with 21 doctors further emphasized the impact of these challenges on their morale and job satisfaction. (Table-2).

Table-2: Identified themes from interviews of participants.

Identified challenges	Number	Percentage
High Workload	21	100
Security Threats	19	90.47
Financial Issues	16	76.19
Resource Constraints	18	85.71
Time Constraints	15	71.42
Work-Life and personal-life imbalance	15	71.42

DISCUSSION

The identified challenges include high workload, security threats, financial issues, resource constraints, time constraints, and inadequate work-life balance. These findings resonate with existing literature and highlight the urgent need for systemic improvements and policy changes to enhance the working conditions for doctors in the country. The challenge of high workload is a consistent issue faced by doctors in many healthcare systems worldwide. The study's findings align with the research conducted by Azam *et al* which highlights the excessive workload as a major factor contributing to burnout and decreased job satisfaction among doctors in Pakistan's hospitals.[8] This issue also resonates with global research, as studies from different countries have demonstrated the negative impact of heavy workloads on physician well-being and patient care.[9] Security threats are another significant concern identified in this study. The fear of violence, theft, and harassment faced by doctors is consistent with the research by Shiraz Shaikh, which documented the increasing incidents of violence against healthcare professionals in Pakistan.[10] Similar findings have been reported in studies from other countries, indicating a global problem that can compromise the safety and well-being of medical practitioners.[11] Financial challenges were reported by a substantial number of participants in the study. The dissatisfaction with pay scales and financial struggles experienced by doctors' echoes findings from studies conducted in other countries. For instance, research by Friedberg MW *et al*, in 2014,[12] has shown that inadequate compensation and financial concerns contribute to stress and dissatisfaction among doctors. This highlights the importance of addressing financial well-being as a crucial aspect of healthcare workforce satisfaction and retention. Inadequate resources, including space, medical equipment, and essential supplies, are reported challenges that affect patient care. Similar findings are documented in studies conducted in low-resource settings globally, including Sub-Saharan Africa.[13] Resource shortages can compromise the quality of care delivered by healthcare professionals and hinder their ability to provide optimal treatment and services. Time constraints and limited opportunities for career advancement were prevalent challenges in our study. Research by Abdulghani *et al*[14], in Saudi Arabia also emphasized the challenges related to time management and professional development for healthcare professionals. Limited time for continuing education, research, and personal development can hinder doctors' ability to stay updated with medical advancements and provide high-quality care. The struggle to maintain a healthy work-life balance is a universal challenge in the medical field. The study's findings align with research conducted by Shanafelt *et al*[15], which identified a high prevalence of burnout among medical students, residents, and practicing physicians in the United States. This issue emphasizes the importance of addressing work-life balance to prevent burnout and support the overall well-being of doctors.

Limitations: While this study offers valuable insights into the challenges faced by trainee doctors in Pakistan's healthcare system, there are limitations that need to be acknowledged. The study's focus on a single teaching hospital and its qualitative nature might limit the generalizability of findings. Future research could expand the scope to include a wider range of healthcare institutions and explore potential solutions to these challenges in greater detail.

By addressing these challenges, Pakistan can foster a more conducive and supportive environment for its healthcare professionals, ultimately leading to enhanced patient outcomes and a stronger healthcare system.

CONCLUSION

Doctors reported significant levels of work-related stress, poor work-life balance, inadequate work capacity, and about one-third of them burned out, a sign of unfavourable working conditions. Still, the majority were really motivated to practice. Hospitals should start measuring these indices to evaluate their quality, and studies should concentrate on how well various organizational and individual therapies for occupational stress and burnout work.

RECOMMENDATIONS

Efforts to mitigate these challenges could include: Improving Work Conditions: Addressing issues such as workload and resource constraints through proper staffing and investment in infrastructure. Enhancing Compensation: Providing competitive salaries and benefits to attract and retain skilled medical professionals. Safety Measures: Implementing security measures to protect healthcare workers from violence and harassment. Support Programs: Offering psychological support and counselling services to address stress and burnout. Career Development: Creating opportunities for continuous medical education and professional growth. By addressing these challenges, Pakistan can foster a more conducive and supportive environment for its healthcare professionals, ultimately leading to enhanced patient outcomes and a stronger healthcare system.

LIMITATIONS AND FUTURE RESEARCH

While this study offers valuable insights into the challenges faced by trainee doctors in Pakistan's healthcare system, there are limitations that need to be

acknowledged. The study's focus on a single teaching hospital and its qualitative nature might limit the generalizability of findings. Future research could expand the scope to include a wider range of healthcare institutions and explore potential solutions to these challenges in greater detail.

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ORIGINAL ARTICLE

CYTOLOGICAL AND BIOCHEMICAL IMPACT OF ARSENIC EXPOSURE ON THE ENDOCRINE SYSTEM AND OESTROUS CYCLE OF FEMALE RATS

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Background: Rising concentration of arsenic in drinking water is severely damaging the reproductive health of both humans and animals. This study was thus designed to evaluate the deleterious effects of sodium arsenite at a minimum dose on the endocrine system and oestrus cycle of female Sprague Dawley rats. **Methods:** A randomized control trial was conducted at College of Physicians & Surgeons Pakistan, Regional Centre, Islamabad. Sixty healthy female Sprague Dawley rats were randomly divided into group 1 (control) and group 2 (experimental) with 30 rats in each group. After one week of acclimatization, the control group was administered 10 ml of distilled water daily via oral gavage, and the experimental group was administered 4 µg of sodium arsenite dissolved in 10 ml of distilled water daily via oral gavage. After one week of habituation, vaginal smears were taken daily to study the oestrus cycle. Whereas, serum oestrogen and progesterone levels were assessed using ELISA after 14 days of intervention. Biochemical parameters (oestrogen and progesterone) were analyzed on SPSS-22. Comparison of means of these hormones was evaluated by the Student's *t*-test. **Results:** After exposure to sodium arsenite, the oestrus cycle of the experimental group was prolonged and halted in the diestrus phase along with significant reduction of serum estradiol and progesterone levels. **Conclusion:** Low dose of arsenic delays and disturbs regulation of oestrus cycle and disrupts the hormonal levels in female rats.

Keywords: Arsenic, Estradiol, Oestrus cycle, Progesterone

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INTRODUCTION

Arsenic is a constituent of earth's crust where it exists in various organic and inorganic forms. The inorganic forms of arsenic are readily absorbable in living bodies and hence regarded as the most lethal.[1]. Arsenic is widely used in agriculture as a pesticide and in various industries like wood preservative and glass manufacturing. WHO has declared that the mean concentration of arsenic in potable water should not exceed 10 µg/L.[2] Due to the lack of water filtration systems in under developed and developing countries, arsenic in our earth crust percolates down into the underground water tables and gets entry into the living bodies.[3] Mean concentration of arsenic in various regions of Pakistan is above 40 µg/L which is an alarming situation.[4,5] Its toxic effects have been studied to various organs and systems of animal and human bodies. So far, arsenic has been proved to be neurotoxic, hepatotoxic, nephrotoxic and cardio-toxic. Arsenic is now under discussion as an endocrine disrupter also.[6]

One of the major components of the endocrine system in female rats is oestrous cycle which is controlled by the fluctuations in the serum levels of oestrogen and progesterone. This cycle enables the female rats to reproduce offspring again and again and is similar to the menstrual cycle of human females. This cycle has 4 phases, e.g., pro-oestrus, oestrus, met-oestrus and di-oestrus and it lasts for ~ 4-5 days. There is rapid development of follicles with a rise in estradiol levels in pro-oestrus phase. Ovulation occurs in the oestrus phase with a decline in estradiol levels. Whereas, the met-oestrus and di-oestrus phases are characterized by rise in progesterone levels.[7] These phases are identified by observing the types of cells in the vaginal smear of female rats.

There are certain environmental chemicals and pollutants that disrupt the endocrine system and the oestrous cycle of female rats. WHO in the year 2010, declared the endocrine disrupting chemicals as a high research priority.[8] One of these toxins is arsenic that leads to various adverse effects on the female reproductive tract, e.g., ovarian failure, low weight of ovaries and uterus and dys-steroidogenesis that lead to spontaneous abortions, teratogenesis, and still birth etc.[9,10] Hazardous effects of low dose of arsenic for a brief period of time is still largely under-discovered. This study was designed to evaluate the effects of arsenic on the oestrous cycle of female Sprague dawley rats.

MATERIAL AND METHODS

It was a laboratory based randomized controlled trial conducted at the animal house of College of Physicians and Surgeons Pakistan, Islamabad for one year (1 Jan 2019 to 4 Jan 2020). Ethical approval was obtained from Research Ethical Committee of CPSP, Islamabad according to the National Institute of Health Guide for

Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985). Sixty healthy and non-diseased female Sprague Dawley rats were included in the study. Rats with any visible physical deformity and disabilities were excluded from the study. Animals with body weight of 220–300 g and age 15–16 weeks were selected by non-probability convenient sampling method. All animals were acclimatized for one week under room temperature 25±2 °C, ~60% humidity and 12-hr day and night cycle. During this period, they were provided with distilled water and standard rat diet *ad libitum*.

Animals were randomly allocated into 2 groups, i.e., group 1 (healthy control group) and group 2 (experimental group). After one week of habituation, the intervention period started that lasted for 2 weeks. Animals of group 1 were continued with standard rat diet and distilled water *ad libitum* along with additional 10 ml of distilled water given once daily by oral gavages. The animals of group 2 were given standard rat diet and distilled water *ad libitum* along with additional 10 ml of distilled water mixed with 4 µg of sodium arsenite once daily by oral gavage.

The vaginal smear of all the animals were collected early morning daily for 14 days and visualized under microscope[9]. A blunt plastic pipette was used to collect vaginal secretions. The pipette was rotated clock-wise in the vaginal wall up to 1 Cm and removed immediately to prevent cervical stimulation in the animal.[11] Secretions were placed on the glass slides and left to dry in air. Slides were stained with Papanicolaou stain and studied under 40× of light microscope.[12]

On basis of cytological results, the phases along with duration of oestrus cycle were compared between control and experimental animals. Each cycle was identified by the types of desquamated vaginal epithelial cells in the vaginal smear, e.g., pro-oestrous phase had abundance of nucleated epithelial cells, oestrus phase had cornified cells, met-oestrus and diestrus had leukocytes. Normally the oestrous cycle lasts for 4–5 days and cycle duration beyond these days was considered as prolonged.[13]

Rats were deeply anaesthetized by chloroform inhalation and exsanguinated by single intra-cardiac puncture. Blood was stored in clot activator vials at temperature 4–8 °C. Serum was extracted by centrifugation at 3,000 g for 15 minutes and stored in disposable and sterile Eppendorf tubes at -80 °C till further hormonal analysis. Serum estradiol (E2) and progesterone (P4) were assessed by commercially prepared rat ELISA kits[14].

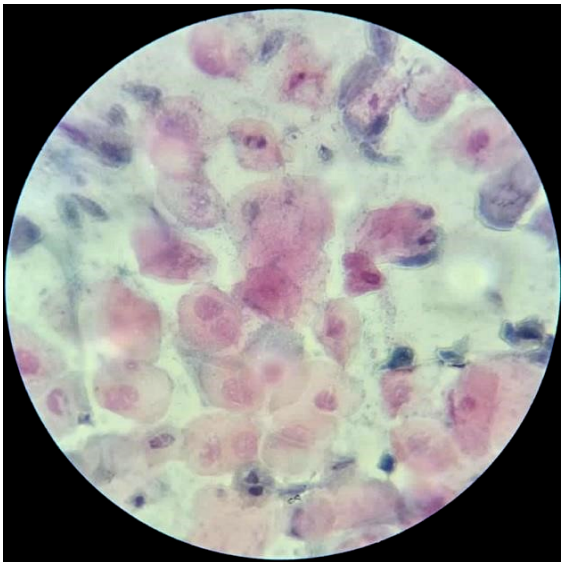
Mean±SD of serum estradiol (E2) and progesterone (P4) levels of both control and experimental groups were estimated with SPSS-22. Comparison of means of hormonal levels between two groups was done on Student's *t*-test, taking $p \leq 0.05$ as significant.

RESULTS

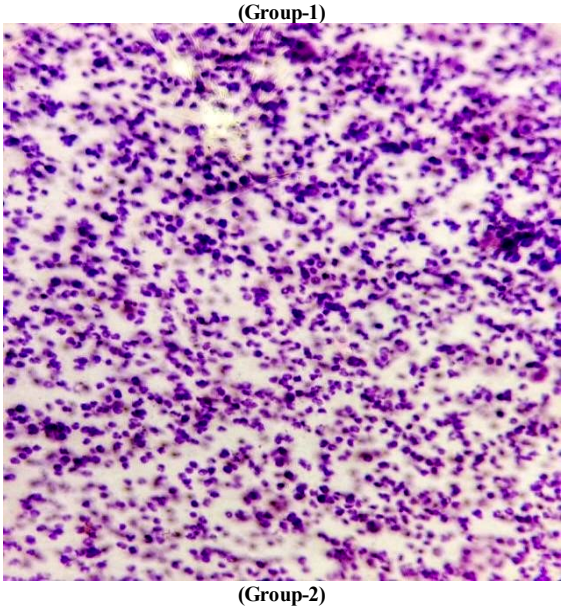
The cytology of vaginal smear of control group showed normal and regular phases of oestrus cycle. In the rats of experimental group the oestrous cycle was prolonged and remarkably hindered in diestrus phase till the end of experiment ($p<0.05$). Serum estradiol and progesterone were significantly reduced after arsenic exposure in group 2 as compared to group 1 ($p<0.05$). (Table-1 and Figure-1).

Table-1: Serum values of estradiol and progesterone of control and experimental groups

Variables	Group 1 (n=30)	Group 2 (n=30)	*p*
Estradiol (pg/ml)	92.0±14.3	35.7±8.8	<0.01
Progesterone (ng/ml)	11.5±2.4	2.1±0.4	<0.05



(Group-1)



(Group-2)

Figure-2: Comparison between the vaginal cytology of both group 1 and group 2 at 40×

DISCUSSION

Epidemiological data suggests that millions of people across the world are exposed to arsenic contaminated drinking water. Arsenic is causing numerous negative health effects, e.g., nervous system diseases, dermatological lesions, malignancies of various organs and cardiovascular problems. Arsenic has been proven as an endocrine disrupter.[15] Our study has evaluated the hazardous effects of low dose of arsenic, given for a short period of time on the female rats reproductive tract and hormonal profile. To evaluate these effects, vaginal smear visualization method by microscope was used which is cheapest, fastest and least harmful to the animals.[16] The results of our study showed that exposure of arsenic prolonged the normal length of oestrus cycle (4–5 days) and normal duration of diestrus phase (48–72 hours). The oestrus cycle of all female rats of experimental group was halted in diestrus phase till the end of experiment. These results are in accordance to the results of Esqueda *et al*[17] and Panpan Chen *et al*[18]. Their studies highlighted that exposure of various doses of arsenic in the pubertal age rats significantly disturbed the oestrus cycle. Relevant studies have also proven that disruption of oestrus cycle is related to the delayed onset of puberty and enhanced the possibility of sub-fertility and infertility in female rats.[19]

Our study has related the disruptive effects of arsenic with the levels of reproductive hormones, e.g., estradiol (E2) and progesterone (P4)[20]. These hormones are responsible for the regulation of oestrus cycle and reproductive cycle homeostasis. The results of our study showed that exposure of 4 µg of sodium arsenite dissolved in 10 ml of distilled water given for 14 days to the female rats significantly reduced the serum levels of estradiol and progesterone. Data of a recent studies by Panpan Chen *et al*[18] and F-Souza *et al*[19] showed similar results indicating arsenic as an endocrine disrupter. These reduced levels of estradiol and progesterone may be due to under stimulation by the pituitary hormones. Arsenic releases free radicals and induces oxidative stress in the body. These cytological and biochemical effects of arsenic could be due to oxidative imbalance and disturbance of reactive oxygen species (ROS) homeostasis in the reproductive tract of female rats.[21] It is, thus plausible that in our study, arsenic has been proven to be reproductive tract toxin even in lower doses.

Our study was animal-based and faced financial limitations. Managing a potent toxin like arsenic demanded a heightened level of vigilance.

CONCLUSIONS

Disruption of oestrus cycle phases and regularity along with disturbance of female hormonal profile after exposure of low dose of arsenic given for a brief period of time concludes that arsenic is a potent reproductive tract toxin and an endocrine disrupter.

IMPACT OF THE STUDY

Given the widespread presence of arsenic in our drinking water, the findings from this study undoubtedly hold substantial importance for public health.

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The authors duly acknowledge the intellectual guidance from (Late) Prof Muhammad Yunus Khan, and thank CPSP, Islamabad, and National University of Medical Sciences for facilitation to complete this study.

RECOMMENDATIONS

Since the dosage utilized in this study is significantly lower than doses relevant to the environment, it is imperative to further assess the connection between exposure to arsenic and reproductive abnormalities in humans.

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AM: Study design, sampling of vaginal smear, and evaluation of cytological changes
MY: Animal handling, and vaginal smear processing
FI: Data processing on SPSS
ZM: Write up, and referencing
SU: Blood sampling, and processing of serum

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ORIGINAL ARTICLE

EFFECT OF HIGH FAT AND CAGED CHICKEN DIET ON OVARIAN HISTOMORPHOLOGY IN FEMALE ALBINO RATS

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Background: Consumption of high fat diet, caged chicken meat and sedentary lifestyle have seriously increased the risks of hyperlipidema that leads to increased ovarian weight as well as ovarian stromal changes associated with difficulties in reproduction. This study is designed to compare the effects of high fat and caged chicken diet on histomorphology of ovaries of female albino rats. **Methods:** This study was conducted in collaboration with National Institute of Health and Anatomy Department of Islamic International Medical College, Islamabad after approval from Ethics Review Committee. The study duration was 12 months from Sep 2021 to Sep 2022, and was performed on 30 albino rats. Control group A was given standard rat diet. Experimental group B was given High Fat Diet (HFD) of 60% fat. Experimental group C was given cubes of caged chicken meat in the raw form. At the end of experiment, animals' ovaries were collected and weighed. The samples were processed, sectioned in 5 µm thickness, stained with H&E and observed under light microscope for stromal vascular changes and congestion. **Results:** The ovarian weight and stromal vascularity significantly increased in caged chicken diet group C compared to control group A and experimental group B. **Conclusion:** Caged chicken diet is more harmful than HFD in causing ovarian weight gain and ovarian stromal hypervascularity.

Keywords: Caged chicken, High fat diet, Ovary, Histomorphology, Stroma, Stromal hypervascularity, Polycystic ovaries, Steroid sex hormones, Hyperlipidemia

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INTRODUCTION

Human ovaries are paired organs, oval shaped, that lie bilaterally in ovarian fossa. Grossly human ovaries are attached with the uterus at its inferior pole by means of ovarian ligament. Each ovary is attached to the posterior surface of the broad ligament by a peritoneal fold that is known as mesovarium.[1,2] Ovaries has two important functions, i.e., gametogenesis and steroidogenesis (the production of oestrogen and progesterone). At puberty under the influence of hormones, folliculogenesis occurs during various phases of ovarian cycle.[3]

Factors like sedentary lifestyle and diet influence the ovarian folliculogenesis. Diet plays a major role in the health of an individual. Food containing excess of oils and fats trigger the emergence of excessive deposition of adipose tissue leads to weight gain in ovaries.[5,6]

With the change in the eating habits, intake of chicken meat has markedly increased now a days. Chicken meat is rich in cholesterol and fats.[6] The increased cholesterol consumed through meat is absorbed in the intestine, where it is packaged as triacylglycerol-rich particles known as chylomicrons.[7] The deleterious effects of high fat diet and caged chicken meat consumption is leading to changes in ovarian weight.[8]

The present study was designed to compare weight changes and microscopic ovarian stromal vascular congestion in ovaries of female albino rats fed on High Fat Diet (HFD) and caged chicken meat.

MATERIAL AND METHODS

This randomized control trial was conducted in collaboration with National Institute of Health (NIH) and Anatomy Department of Islamic International Medical College, Islamabad after approval from Ethics Review Committee (Appl #Riphah/IRC/20/242). The duration of the study was 12 months from Sep 2021 to Sep 2022.

Thirty (30) albino Sprague Dawley adult female rats were included in the study. The animals were divided into 3 equal groups randomly after allotting animal numbers to all. Group A was given standard pellet animal diet for rats (20 gm per rat). Group B was given 60% High Fat Diet (12-gram *ghee* mixed with standard rat diet per rat). Group C was given caged chicken cubes 20 gm per rat as diet replacement.

After completion of 9 weeks, all animals were sacrificed and dissected. Removed right ovaries were cleaned from fatty tissues and washed with normal saline. Tissue paper was used to remove the excess fluid and weighed using a digital scale with precision of 0.001 gm.

Data was entered and analysed using SPSS-21. Mean and standard error of mean were calculated for quantitative variables. One-way analysis of variance (ANOVA) was applied for the mean comparison of quantitative variables. The results were expressed as Mean±SD. Post hoc Tukey's test was applied for the multiple comparisons among groups.

RESULTS

Mean weight of ovary was 0.05 gm in control group A, and it was 0.07 and 0.08 gm in group B and group C respectively. A significant increase in ovary weight was found in experimental group C compared to group B and A (p=0.000) (Table-1, 2).

Control group A showed normal stroma in 100% of rats. Fifty (50%) of rats in experimental group B showed severe (grade 4) vascular congestion and 40% of rats showed moderate (grade3) vascular congestion, and 10% showed a minimum degree of vascular congestion. In experimental group C 60% of rats showed severe (grade 4) vascular congestion, and 40% showed moderate (grade 3) vascular congestion. Severe degree of stromal vascular congestion was found around the follicles in experimental group C compared to groups B and A (Table-3, Figure-1).

Table-1: Comparison of mean weight (gm) of ovary in control and experimental groups

Groups	A (Control)	B (HFD)	C (Caged chicken diet)
Mean	0.05	0.07	0.08
SEM	0.0013	0.0014	0.0010
p	0.000*		

*Significant

Table-2: Post hoc Tukey's test for mean differences in ovarian weight (gm) among study groups

Groups	Mean difference	*p*
A *vs* B	0.018	0.000*
A *vs* C	0.028	0.000*
B *vs* A	0.010	0.000*

*Significant

Table-3: Group-wise distribution of stromal vascular congestion in ovarian cortex among control and experimental groups of Sprague Dawley rats (N=30)

Groups	Negligible (Grade 0)	Minimal (Grade 1)	Mild (Grade 2)	Moderate (Grade 3)	Severe (Grade 4)	*p*
A (Control)	10 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.000*
B (HFD)	0 (0%)	0 (0%)	2 (20%)	4 (40%)	4 (40%)	
C (Caged chicken diet)	0 (0%)	0 (0%)	0 (0%)	4 (40%)	6 (60%)	

*Significant

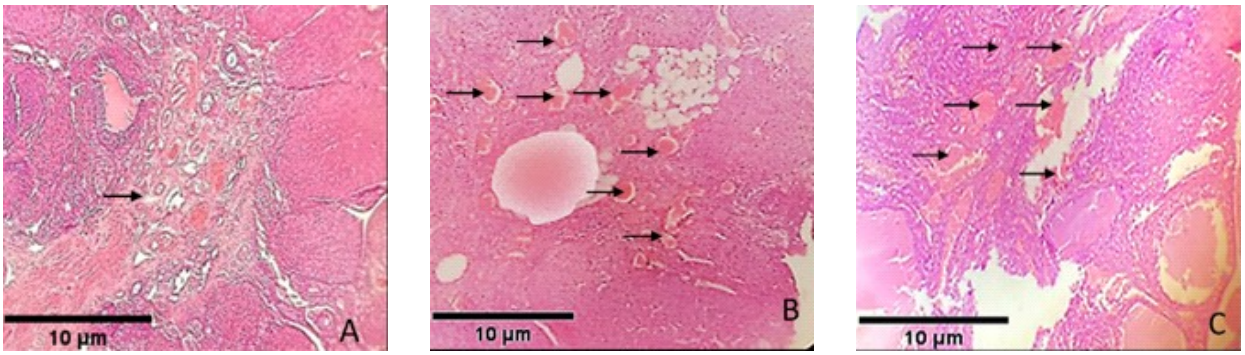

Figure-1: Photomicrographs of ovaries of Sprague Dawley rats

Photomicrographs showing normal stroma in control group A, moderate to severe (grade=3–4) stromal vascular congestion in experimental group B, and severe (Grade=4) stromal vascular congestions in experimental group C. H&E stain, 100×

DISCUSSION

In Pakistan, the most favourable consumption in meat nowadays is chicken. The inclination of the dietary pattern to chicken meat more than red meat may be because of its better taste, easy availability and low cost.[9]

Excessive consumption of high fat diet, caged chicken meat and sedentary lifestyle have seriously increased the weight gain in developed countries.[10] Weight gain is associated with abiogenesis, metabolic syndrome and abnormal accumulation of abdominal fat, triggering the emergence of various ovarian histomorphological changes associated with reproductive problems in female young ones, as reported by Paouli A.[11]

The present study examined a histomorphological comparison in ovaries of the female Sprague Dawley rats fed with HFD and caged chicken diet for 9 weeks[12]. The current study may be the first one providing a comparison that shows feeding of rats with HFD and caged chicken meat bringing changes in ovarian weight[13], causing ovarian stromal hyper vascularity and also deranging hormonal profile. Female albino rats in caged chicken diet group C gained more body weight due to hyperlipidemia and imbalance[14] in the steroidal sex hormones as compared to control group A and high fat diet group B. This showed that increased ovarian weight is associated with the increased animal body weight. These results are consistent with a study by Ahmad S *et al*[15]. Similarly in another study done by Gul S *et al*[16], the results showed that excessive consumption of caged chicken meat in diet leads to increased ovarian weight in female rats which are in favour of current findings.

Regarding the histological features, control group A conserved the normal stroma of the ovarian cortex while in experimental group B and C, marked disturbances in ovarian stroma[17] were observed. Ovarian cortical stroma showed severe to moderate congested blood vessels surrounding the follicles at different developmental stages.[18] Limited studies are available regarding the effect of caged chicken diet on the cortical stromal vascular congestion. Mild to moderate congested blood vessels were observed in cortical stroma of high fat diet group B. These results are consistent with study of Wang MX[19].

CONCLUSION

There is significant increase in weight of ovaries and ovarian stromal vascularity in caged chicken diet group compared to high fat diet group. Consumption of caged chicken diet proved to be more harmful than the high fat diet due to its effects on histomorphology of ovaries in albino rats.

RECOMMENDATIONS

Current study has considered the effect of caged chicken meat as a replacement diet for 9 weeks only. The effects of caged chicken meat consumption can be compared at different intervals like once or twice a week and then evaluated for ovarian as well as other systemic parameters.

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AH: Data collection, literature review
HB: Data collection, literature review
TSH: Data collection and analysis, revision
MSh: Literature search and review, statistical analysis

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ORIGINAL ARTICLE

EFFECTS OF WALNUT LEAVES EXTRACT ON EFFICACY OF DAPAGLIFLOZIN IN TYPE II DIABETIC MICE

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Background: With a rising prevalence of type 2 diabetes mellitus its becoming more important than ever to find new strategies to prevent and cure the disease. Objective of this study was to assess the effects of walnut leaves extract on the efficacy of dapagliflozin in type 2 diabetic mice. **Methods:** It was experimental, randomized control study. A total of 50 male Balb/c mice were included in this study and randomly divided into two groups: Group 1 (Normal Control) consisting of 10 mice and Group 2 (experimental group) of 40 mice. The experimental group was further divided into 4 groups of 10 mice each following induction of type 2 diabetes: Group 2 (Disease Control), Group 3 (Ethanolic walnut leaves extract treated), Group 4 (Dapagliflozin treated) and Group 5 (Combination of dapagliflozin and ethanolic walnut leaves extract treated) for a duration of 45 days. Statistical analysis was done using SPSS-27. One-way ANOVA (post hoc Tukey test) was used to compare the means of HbA1c among groups, and $p<0.05$ was considered significant. **Results:** Mice treated with walnut leaves extract (Group 3), dapagliflozin (Group 4), and the combination of walnut leaves extract and dapagliflozin (Group 5) exhibited significantly reduced serum HbA1c levels compared to those observed in the diabetic control group ($p<0.05$). **Conclusions:** The combined administration of walnut leaves extract and dapagliflozin leads to a significant decrease in serum HbA1c levels in diabetic mice, as compared to mice treated with walnut leaves extract or dapagliflozin alone.

Keywords: Diabetes Mellitus, Walnut leaf, Dapagliflozin, HbA1c

Pak J Physiol 2013;19(4):26–8

INTRODUCTION

Diabetes mellitus (DM), a metabolic disorder, is an important issue for global health that affects many people.[1] In DM, the body's capacity to regulate glucose in the blood is compromised, marked by elevated blood glucose levels. Insulin contributes in control of blood glucose level. Type 1 Diabetes mellitus (T1DM) is caused by insufficient insulin production whereas resistance to insulin leads to type 2 diabetes mellitus (T2DM).[2]

Obesity, lack of physical exercise, genetic susceptibility, and advancing age are the primary risk factors for T2DM. According to the International Diabetes Federation (IDF), prevalence DM has reached alarming levels throughout the world as it has affected roughly 463 million people aged 20–79 years in 2019. T2DM accounts for over 90% of all these diabetic cases. If certain precautionary measures are not taken the current trends might continue to rise and number of the patients might reach 700 million by the year 2045.[3] DM has become a significant public health concern in Pakistan, affecting 19.4 million individuals. According to recent estimates by IDF, over 33,000,000 people in Pakistan have T2DM. This illness affects around 26.8% of adults, emphasizing the critical need for effective preventative and management techniques. The estimated number of people in the nation with T2DM will be 26.1 million by 2030 showing a considerable increase in disease prevalence.[4] Due to its complex metabolic makeup, DM demands thorough and detailed medical care and attention. Despite the medical treatment, patients must actively seek healthy diet and exercise plans to deal with this disease. Therefore, diabetes therapy must include oral hypoglycaemic medicines and lifestyle changes.[5] Pharmaceutical treatment options now accessible for T2DM include metformin, sulfonylureas, thiazolidinediones, and sodium-glucose cotransporter-2 (SGLT2) inhibitors.[6] In recent years, there has been a notable increase in interest surrounding using SGLT2 inhibitors within the realm of oral hypoglycaemic medications.[7]

Dapagliflozin, a selective SGLT2 inhibitor, functions by inhibiting the activity of SGLT2 receptors located in the renal tubules, thereby leading to augmented renal glucose excretion. This approach is associated with the reduction of blood glucose levels and the promotion of weight loss. Dapagliflozin exhibits notable benefits, including its capacity to decrease HbA1c levels, enhance cardiovascular well-being and operate through an insulin-independent mechanism.[8]

There has been a notable increase in scholarly attention toward utilizing botanical substances for managing diabetes. Ayurveda and traditional Chinese medicine have acknowledged the potential of herbs in

managing diabetes. The glucose lowering effects of walnut leaves (*Juglans Regia L.*) have been the subject of scientific investigation. These leaves possess bioactive compounds that have the potential to enhance glucose metabolism and increase insulin sensitivity.[9] Use of walnut leaves as a potential therapeutic intervention for diabetes has been documented in the scientific literature.[10] The polyphenols and flavonoids found in walnut leaves have been shown to increase insulin sensitivity, stimulate glucose absorption by cells, and inhibit carbohydrate metabolizing enzymes.[11]

Both walnut leaves extract and dapagliflozin have established hypoglycaemic properties, but their combined and comparative effects have not been explored yet. This study was designed to observe these two aspects of walnut leaves extract. Adding walnut leave extract as an adjuvant with dapagliflozin may increase efficacy of this drug.

MATERIAL AND METHODS

This comparative experimental investigation was conducted at Animal House, Multidisciplinary Research Laboratory, and Pharmacology Laboratory of Islamic International Medical College (IIMC), Islamabad (Ref.#: Riphah/IRC/22/2081) after approval from the Ethical Review Committee. The duration of the study was 45 days from 1st April 2023 to 20th May2023. The study involved 50 healthy male albino Balb/c mice, aged 6–8 weeks and weighing 30–50 g. The mice were allowed free access to tap water. The standard feed was prepared at IIDC. The light and dark cycle followed a 12-hour pattern.

Walnut (*J. Regia*) leaves, sourced from the vicinity of Muzaffarabad, Azad Kashmir, dried in shade, and were grinded into powder. The 1,000 g of powdered *J. Regia* leaves were soaked in 70% ethanol for 24 hours, and extracted three times using new 96% ethanol for a total of 24 hours at room temperature.[12] The resultant solution was evaporated in a rotary evaporator at 55 °C after filtration through Whatmann #1 paper. The extracted material was kept in airtight glass bottle, shielded from light, and refrigerated at 2–8 °C.[13]

Following a week of acclimation, the mice were split into two groups at random: 10 mice in control Group 1 and 40 mice in experimental group. Group-1 was fed regular food for 5 days. The experimental group received a normal meal with intraperitoneal injections of streptozotocin (40 mg/Kg/day) for 5 days in a row.[14] The fasting blood glucose levels of Group-1 and experimental group were measured using Accuchek® instant glucometer, and compared confirming diabetes in the experimental group.

The experimental group was then split into Groups 2, 3, 4, and 5. The mice in group-2 were designated as Disease Control and were fed only standard chow diet. For 40 days, Group-3 mice were fed a standard chow diet enriched with 200 mg/Kg of ethanolic walnut leaf extract (WLE) each day.[15] The mice in Group-4 were given a regular chow diet combined with an oral dose of the medication Dapagliflozin (1 mg/Kg/day) in drinking water.[16] Group-5 mice were given a standard chow diet supplemented with 200 mg/Kg of ethanolic walnut leaf extract and 1 mg/Kg of dapagliflozin medication added into their drinking water. The final blood samples were completed after 40 days of treatment.

SPSS-27 was used for statistical analysis. The results were reported as Mean±SD. The quantitative parameters between the 5 groups were compared using one-way ANOVA (Post-hoc Tukey test), and $p<0.05$ was considered as significant.

RESULTS

The mean HbA1c (%) in Group-1 was 4.59±0.4122, and in Group-2 it was 7.87±0.34, and was considerably higher than Group-1 ($p<0.001$). In Group-3 the mean HbA1c was 5.20±0.63, it was (5.00±0.54) in Group-4, and 4.66±0.44 in Group-5. Mean of HbA1c (%) was considerably lower than that of Group-2 ($p<0.001$) in Group-3, 4, and 5. Table-1 presents a comparison of Mean±SD of HbA1c (%) in each group.

Table-1: HbA1c levels in all groups (Mean±SD)

Groups	HbA1c (%)	*p*
Group-1 (Normal control)	4.59±0.4122	<0.001*
Group-2 (Disease control)	7.87±0.3498	
Group-3 (WLE treated)	5.20±0.6394	
Group-4 (DAPA treated)	5.00±0.5466	
Group-5 (WLE+DAPA)	4.66±0.4458	

*Significant

DISCUSSION

Findings of the current study support the notion that all experimental drugs significantly reduce the hyperglycaemia caused by streptozotocin; nevertheless, the combined effects of dapagliflozin and walnut leaf extract show very promising outcomes.

In the present study T2DM was induced in all experimental mice by using streptozotocin (STZ) for 5 days intraperitoneally with resultant increase in fasting blood glucose levels. These findings are similar with results of Arulmozhi DK *et al*[14], Rato L, *et al*[17] and Wang J *et al*[18] also used same dose of STZ intraperitoneally in experimental animals for induction of T2DM and observed marked changes in insulin and blood glucose levels.

Group-3 in our study received WLE and the results revealed significant improvement in FBS levels and HbA1c in comparison to disease control group. Our findings are in agreement with Asgary S *et al*[19]. Outcomes of present study are in promise with the facts reported by Nasiry D *et al*[15] who performed a study on protective effects of methanolic WLE on STZ-induced

diabetic peripheral neuropathy in rats. In Group-4 marked reduction was observed in FBS levels and HbA1c in comparison to disease control group. Chang DY *et al*[20] had similar findings, who investigated the antidiabetic effects of dapagliflozin in type 2 diabetic mice and observed that dapagliflozin significantly decreased blood glucose levels and HbA1c. It was also Findings in Group-4 are supported by study of Wei R *et al*[16] who investigated the antidiabetic effects of dapagliflozin in type 2 diabetic mice and reported that dapagliflozin significantly decreased blood glucose and upregulated plasma insulin and GLP-1 levels by promoting beta cell regeneration, enhancing beta cell self-replication.

We observed that the antidiabetic effect was more marked in Group-5 compared to Group-3 and 4. Abdel-Wahab AF *et al*[21] demonstrated that dapagliflozin and irbesartan caused significant reduction in blood glucose levels and HbA1c levels when used alone and combination therapy also has remarkable protective effects on renal function and structure.

CONCLUSIONS

The antidiabetic effects of dapagliflozin were more marked compared to ethanolic walnut leaf extract in diabetic mice. The combined effect of walnut leaf extract and dapagliflozin was more pronounced as compared to using dapagliflozin or walnut leaf extract alone in managing high blood sugar in diabetic mice. Further work is recommended on the active ingredients of walnut leaves and their interactions with other drugs.

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ORIGINAL ARTICLE

INCIDENCE OF OCULAR TRAUMA AMONG THE PATIENTS HOSPITALIZED IN THE OPHTHALMOLOGY DEPARTMENT OF AYUB TEACHING HOSPITAL

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Background: Ocular trauma is leading cause of mono or binocular vision deterioration. This study was conducted to determine the incidence of ocular trauma in patients in our set-up. **Methods:** A retrospective observational study was done from Nov 2021 to Jan 2022 on all admitted patients for age, gender, occupation and activity at the time of injury, nature of injury, and traumatic agent. Data were classified into 5 groups on basis of trauma setting. Injuries were grouped in accordance with Birmingham Eye Trauma Terminology System. **Results:** The total number of patients admitted to the Ophthalmology Department was 458. Out of these, 61 (13.31%) patients were admitted with Ocular trauma. Ocular trauma was highest in age group of 1–20 years (59%), followed by age group 21–40 years (31.1%). Ocular trauma was very frequent (39.34%) in 1st decade of life. Males were most affected (80.3%). The most common setting for ocular injuries was sports/playtime (44.26%) followed by work-related injuries (27.86%) and household/indoor injuries (16.39%). Blunt objects accounted for most trauma (50.81%) followed by sharp objects (45.9%). Wood (39.34%) was the most common traumatic agent followed by stone (24.59%). Cornea (43.47%) was the most frequently damaged tissue followed by eyelids (41.30%). **Conclusion:** Ocular trauma was highest during sports/playtime, especially in the first decade of life. There is a need for parents' education regarding the risk of ocular trauma with trivial objects such as toys and utensils and the impact of ocular trauma on vision.

Keywords: Ocular trauma, Ocular injury, Intraocular foreign body, Eyelids laceration
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INTRODUCTION

Ocular Trauma is a significant cause of monocular blindness all over the world.[1] The epidemiological data for ocular injuries is quite deficient unlike other blinding conditions, hence effects of ocular trauma are very often underestimated.[2] Around 55 million ocular injuries occur annually, limiting daily activities for more than a day.[3] There are around 19 million people with monocular blindness or low vision, and around 2.3 million people with bilaterally low vision due to ocular insults.[4] It has been suggested that 90% of all ocular trauma is preventable.[5] Hence prevention forms the foundation of long-term management.

The demographic pattern concluded from previous studies in Pakistan suggests that ocular trauma occurs most frequently in the first 2 decades of life with a second peak in the elderly.[6] Incidence of ocular trauma is high in males, usually occupation-related and wood being a major traumatic agent, while children suffer during sports and games.[7]

This retrospective study was carried out to see the prevalence and pattern of ocular trauma and common traumatic agents among the admitted patients from northern parts of Pakistan to the Department of Ophthalmology, Ayub Teaching Hospital, Abbottabad.

MATERIAL AND METHODS

This retrospective observational study was carried out for patients admitted with ocular trauma in the Ophthalmology Department of Ayub Teaching Hospital from Nov 2021 to Jan 2022. Detailed history was taken from all the patients included in this study for the date, age, gender, occupation and activity at the time of injury, nature of the injury and traumatic agent. Thorough ophthalmological examination of the patients was carried out including visual acuity with Snellen Chart where possible, anterior segment examination using Slit Lamp to document size of the tear, its location, involvement of visual axis, intraocular foreign body (IOFB), and posterior segment examination using direct and indirect ophthalmoscope. X-ray Orbit (Anterio-posterior and lateral views) and B-scan Ultrasonography were done when and where required to rule out any intraocular foreign body.

Data were categorized in five groups on the basis of trauma setting: injuries that happened at home, injuries that happened outdoor while working (occupational), injuries that took place during sports/playing, injuries related to animals, and others (Road Traffic Accidents, assault injuries, and other outdoor activities).

Injuries were grouped in accordance with Birmingham Eye Trauma Terminology System. Data

collection contained details like age, gender, tissues damaged during trauma, i.e., lids, cornea, sclera, the frequency distribution of form of the traumatic agent, visual acuity where required.

RESULTS

Total number of patients admitted to the Ophthalmology Department of Ayub Teaching Hospital during the sturdy period was 458. Out of these, 61 patients (13.31%) including 49 (80.3%) males and 12 (19.6%) females were admitted due to Ocular Trauma. Mean age of patients was 20.3±16.8 years. There were 36 (59%) patients in 1–20 years age group, while 19 (31.1%) patients were in 21–40 years age group, and 06 (9.8%) in >40 years age group (Table-1).

Table-1: Distribution of age and gender groups

Age groups	Male	Female	Total
1–20 years	28	8	36
21–40 years	16	3	19
>40 years	5	1	6
Total	49	12	61

Out of 61 patients, 19 had eyelid lacerations (13 being simple tears, 2 involved lid margins, and 4 involved canaliculi), while 42 patients had globe injuries. Under injury classification of globe injuries (in accordance with Birmingham Eye Trauma Terminology System), 27 (64.28%) were open globe injuries, and 15 (35.71%) were closed globe injuries. Amongst closed globe injuries, contusions were 8 (53.33%) and 7 (46.66%) were lamellar lacerations. Amongst open globe injuries, lacerations were 21 (77.77%) and 6 (22.22%) were ruptures. Amongst lacerating wounds, 15 (71.42%) were penetrating lacerations, while 6 (28.57%) were IOFB. No patient presented with perforation (Table-2).

Table-2: Type of Tissue damage

Type of Tissue	Frequency	Percentage
Corneal Lacerations	20	32.78
Eyelids Lacerations	19	31.14
Conjunctival Lacerations	6	9.83
Corneal Ulcers	5	8.19
Scleral Lacerations	4	6.55
Corneoscleral Lacerations	3	4.91
Hyphaema	3	4.91
Traumatic Cataract	1	1.63
Total	61	100

Intraocular foreign bodies were found in 8 patients, 14 patients had iris prolapse associated with corneal/scleral lacerations. Visual axis was involved in 13 patients and traumatic cataract was found in 11 patients. In 2 patients, scleral laceration was at least 4 mm away from limbus. Regarding types of traumatic agents, 28 (45.9%) patients had trauma with sharp objects (wood, needle, nails, glass), 31 (50.81%) had trauma due to blunt objects (stone, ball, rod), and 2 (3.27%) due to liquid (acid, hot water) (Table-3).

Table-3: Frequency distribution of traumatic agents

Traumatic Agent	Frequency	Percentage
Wood	24	39.34
Stone	15	24.9
Metallic	5	8.19
Firecrackers	5	8.19
Animals	4	6.55
Glass	2	3.27
Ball	2	3.27
Acid/Hot water	2	3.27
Needle	1	1.63
Fingernails	1	1.63
Total	61	100

The ocular trauma most commonly occurred during sports/playing (44.26%). This was followed by occupational injuries (27.86%). Household/indoor injuries were (16.39%) of the total ocular trauma. Animal-related injuries were (6.55%) and others/ miscellaneous (Fights, RTA) were (4.91%) of all cases (Table-4).

Table-4: Distribution of place of trauma setting

Place of Trauma	Frequency	Percentage
Sports/playing	27	44.26
Occupational	17	27.86
Indoor	10	16.39
Animal-Related	4	6.55
Others/Miscellaneous	3	4.91
Total	61	100

Out of 61 patients, 24 had a visual acuity of 6/60 or higher, 13 patients were underage and unable to cooperate, 8 patients were at counting fingers between 1 foot to 3 meters, 5 patients could acknowledge only hand movements, 7 patients could perceive the light while 4 patients had no perception of light (Table-5).

Table-5: Frequency distribution for presenting visual acuity of patients

Visual Acuity	Frequency	Percentage
6/60 or higher	24	39.34
Counting Fingers	8	13.11
Hand Movement	5	8.19
Light Perception	7	11.47
No Light Perception	4	6.55
Underage	13	21.31
Total	61	100

DISCUSSION

Ocular Trauma is an important cause of monocular visual loss, especially in underdeveloped countries.[8] This study indicates the incidence of ocular trauma among hospitalized patients as 13.31% which is slightly higher compared to the results (11.2%) of a study conducted in Menoufia University Hospitals, Egypt.[9]

This study found the incidence of ocular injuries higher in males as compared to females which is consistent with the other studies done in Pakistan[10–12] and globally.[13–15] It was observed that ocular injuries frequently occur in the first 2 decades with the mean age

of 20 years which is almost the same as previous studies conducted in Pakistan[6] and abroad[16].

According to our study, ocular trauma was most frequent in the first decade of life thus encouraging the need for better awareness programs for young parents regarding the visual prognosis following ocular trauma and prevention of childhood injuries within home during playtime.[15,17] Blunt objects were the most frequent cause of ocular trauma, consistent with the results of some previous studies.[10,18] Wood was the most common traumatic agent followed by stone. The most common setting for ocular trauma found in our study was recreational/sports activities followed by work-related trauma.

Our study found cornea to be the most frequently damaged tissue in ocular trauma followed by the eyelids. This is in agreement with the previous studies from Pakistan.[10,12] Penetrating injuries were highest among the Open Globe Injuries. These injuries, having presenting visual acuity of NPL, PL +, or HM, were associated with poor visual prognosis and more likely to develop monocular blindness as compared to closed globe injuries.[16]

This was not a population-based study and though Ayub Teaching Hospital is a major Tertiary Care Hospital of the region, some patients might have been treated in other healthcare centres, so it does not give exact incidence and prevalence of ocular injuries in the population of Hazara Region. Some cases of ocular trauma might have not reported to healthcare centres either because of lack of education, awareness, or financial resources which may also explain the out-of-proportion male:female ratio in ocular trauma across different studies.[19]

CONCLUSION

Ocular trauma was highest in males and in first decade of life. This calls for better awareness programs and education regarding the use of protective glasses during working and parental supervision of children during playtime. Parents need education regarding risk of ocular trauma with objects like toys and utensils etc. and impact of ocular trauma on vision to decrease the incidence of ocular trauma and blindness.

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ORIGINAL ARTICLE

PREVALENCE OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS ASSOCIATION WITH DISEASE SEVERITY

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Background: Rheumatoid arthritis (RA) is an auto-immune inflammatory arthritis globally affecting 1% of the population. This study was conducted to see prevalence of carpal tunnel syndrome in patients of RA and its association with disease severity. **Methods:** One-hundred-fifty-four patients aged 21–80 years, of both gender, with RA were enrolled using non-probability consecutive sampling technique. Patients were divided into two groups of 77 each: active disease group (DAS-28 score >3.2) and LDA/remission group (DAS-28 score ≤3.2). RA was defined according to the 2010 ACR Diagnostic Criteria for Rheumatoid Arthritis. Disease severity of RA was determined according to DAS-28 score. Carpal tunnel syndrome (CTS) was diagnosed clinically by specific symptoms and clinical signs. Data were analysed using SPSS-25. **Results:** Mean age of the patients was 43.6±13.7 years, 102 (66.3%) were female. Mean disease duration was 8.3±6.1 years, and mean DAS-28 score was 4.3±2.1. RA factor was positive in 98 (63.7%) and Anti-CCP antibody in 79 (51.3%). CTS was present in 49 (31.8%) patients. On stratification, CTS was seen in 32 (41.5%) patients with active disease compared with 17 (22.1%) patients with LDA/remission. No statistical association of CTS was seen with age, gender, disease duration, RA factor positivity, Anti-CCP antibody positivity and disease severity. **Conclusion:** Carpal Tunnel Syndrome was seen in about one-third patients with RA but no statistically significant association was seen with age, gender, disease duration, RA factor or Anti-CCP positivity and disease activity.

Keywords: Rheumatoid Arthritis, DAS-28 Score, Carpal Tunnel Syndrome, Tinel Sign, Phalen Sign

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INTRODUCTION

Rheumatoid arthritis (RA) is a commonly seen auto-immune inflammatory arthritis globally occurring in up to 1% of the population.[1] RA is primarily a joint disease but can have extra-articular features and abnormal immune responses. Due to chronic inflammation, abnormalities in composition and quality of circulating blood cells can cause lymphopenia with raised neutrophils, thrombocytosis and normochromic anaemia, which are useful as markers of inflammation.[2] The plethora of cytokines, auto-antibodies and immune complexes production, deficiencies of growth factors, reduced life span, deficiency of platelet functions and complications of medicine toxicity can help to explain the changes in blood components in longstanding systemic inflammation.[2] Components of circulating blood cells are often employed in evaluating severity of inflammation. To estimate presence and severity of inflammatory conditions ESR and CRP are usually used but their use is restricted due to limitations such as low specificity and reflection of short-term inflammation only. Various non-inflammatory factors such as gender, anaemia, fibrinogen levels, plasma viscosity and hypergammaglobulinemia, confound the use of these markers.[3]

Disease severity in RA is generally assessed by the DAS-28 score at baseline and follow up, which is calculated by the swollen joint count, tender joint count, patient global assessment on VAS and ESR.[4,5] RA is heralded by infiltration of inflammatory cells in the synovium leading to continuous destruction of joints, cartilage and bone.[6] Various cytokines that affect granulopoiesis, anaemia and neutrophil homeostasis including granulocyte colony-stimulating factor, IL-17 and IL-23 are raised in active RA and correlate with disease activity.[7] Many active RA patients have leucocytosis and thrombocytosis.

Carpal tunnel syndrome (CTS) is a common entrapment neuropathy involving upper limb. In the United States, CTS is seen in up to 19% of the population.[8] Risk factors of CTS include diabetes mellitus, thyroid dysfunction, industrial workers, chronic alcoholism, increasing age, pregnancy, malignancy, female sex, and inflammatory conditions.[8,9] It has been postulated that 1 in every 5 patients who have symptoms of pain, tingling and numbness in the hands have CTS on clinical examination and nerve conduction studies. The most characteristic finding of CTS is non-inflammatory fibrosis and thickening of sub-synovial connective tissue.[9,10] Age and movement associated trauma to the synovium and the flexor tendons in the carpal tunnel

leads to degeneration and increase in volume which in turn cause compression of median nerve resulting in CTS.[10] Inflammatory conditions such as RA can cause CTS by teno-synovitis of the flexor tendons and synovitis of the radio-carpal joint which leads to median nerve compression.[11]

Smerilli *et al*[12] reported CTS to be present in 26.3% and Subasi *et al*[13] reported CTS in 13.2% of RA patients. Karadag *et al*[14] reported CTS in RA as 17.0%. RA patients who had CTS had increasing age, disease duration, diabetes mellitus, worse HAQ-DI score, worse CTS patient global score, severe Boston symptom severity and poor functional status scores.[14] However there was no difference in prevalence of CTS depending on disease severity of RA.[14] Data regarding prevalence of CTS in Pakistan is scare. The link of CTS and disease severity in chronic arthritis is not strongly established. The aim of this study was to document the prevalence of CTS in RA and its association with disease.

MATERIAL AND METHODS

This cross-sectional study was done at Department of Medicine, Jinnah Hospital, Allama Iqbal Medical College Lahore, Pakistan from January to December 2022. Approval from Institutional Ethical Review Board was obtained. RA was defined according to the 2010 ACR diagnostic criteria for rheumatoid arthritis.[15] Disease severity of RA was determined according to DAS-28 score.[16] Active disease was labelled as DAS-28 score >3.2 and low disease activity/remission as DAS-28 score ≤3.2. Carpal tunnel syndrome was diagnosed clinically as the presence of specific symptoms on history (pain, numbness, burning and tingling primarily in the thumb and index, middle and ring fingers) and presence of clinical signs on examination (Tinel sign and Phalen Sign). Tinel sign was performed by percussing over the Median nerve and considered positive when a sensation of tingling or 'pins and needles' was elicited in the distribution of the nerve over thumb and index, middle and ring fingers.[17] Phalen's sign involves flexing the wrist to 90 degrees for 1 minute while maintaining the shoulder in neutral and elbow in extension; and symptoms are elicited in the median nerve distribution to indicate CTS.[18] Keeping margin of error as 5% and confidence interval of 95% a sample size of 154 was required keeping expected frequency as 17.0%.[14]

Patients currently or in last 12 weeks on steroids and biologic DMARDS, chronic diseases including hypertension, diabetes mellitus, coronary artery disease, chronic renal failure, chronic obstructive pulmonary disease, haematologic diseases and malignancy, and patients with pregnancy or breast feeding were excluded from the study.

A total of 154 patients aged 21 to 80 years, of both gender, with Rheumatoid Arthritis were enrolled using non-probability consecutive sampling technique. After informed consent, demographic information, e.g., age, sex, socioeconomic status, duration of disease, educational status, along with medical history to ask for symptoms of CTS (pain, numbness, burning and tingling primarily in the thumb and index, middle and ring fingers) was obtained from each participant. Patients were then divided into two groups with 77 participants each. In active disease group, patients having DAS-28 score >3.2 were included who were either treatment naïve or had stopped taking conventional DMARDs for more than 12 weeks. In low disease activity/remission group, patients taking conventional DMARDs with DAS-28 score ≤3.2 were included. All clinical parameters of DAS-28 were assessed and each patient was then examined for CTS (Tinel Sign and Phalen Sign). Standard treatment as per hospital protocol was given to all patients.

SPSS-25 was used for data entry and analysis. For numerical quantitative variables, mean and standard deviation were calculated. For qualitative variables, frequency and percentage were calculated. Chi-square test was applied and $p \leq 0.05$ was considered as statistically significant.

RESULTS

Out of the 154 patients enrolled in our study, 102 (66.3%) were females and 52 (33.7%) were male having mean age 43.6±13.7 years. Seventy-three (47.4%) patients were younger than 40 years old, 51 (33.1%) were aged 41–60 years and 30 (19.5%) were older than 61 years. Mean duration of disease was 8.3±6.1 years with 89 (57.5%) having duration of disease greater than 3 years. Mean ESR was 33.1±24.2 mm/1st hr. Mean VAS score, tender joint count, swollen joint count and DAS-28 score were 3.5±3.2, 4.6±5.1, 2.4±2.7 and 4.3±2.1 respectively. RA Factor was positive in 98 (63.7%) and Anti-CCP antibody was seen in 79 (51.3%). Carpal Tunnel Syndrome was present in 49 (31.8%) patients. Comparison of clinical parameters with regards to disease severity group of Rheumatoid Arthritis is shown in Table-1 and no statistically significant association of disease severity was seen with age (p=0.102), gender (p=0.981), duration of disease (p=0.253) and RA factor positivity (p=0.432) and Anti-CCP antibody positivity (p=0.096).

On stratification, Carpal Tunnel Syndrome was seen in 32 (41.5%) patients with active disease compared with 17 (22.1%) patients with LDA/remission. No statistically significant association of Carpal Tunnel Syndrome was seen with age (p=0.709), gender (p=0.118), duration of disease (p=0.580), RA factor positivity (p=0.431), Anti-CCP antibody positivity (p=0.402) and disease severity (p=0.107) as shown in Table-2. Among the 77 patients with active disease, 43 (55.8%) were females and 34 (44.2%) male having mean age 42.3±14.3 years. Thirty-

nine (50.7%) patients were younger than 40 years old, 25 (32.5%) were aged 41–60 years and 13 (16.8%) were older than 60 years. Mean duration of disease was 8.3±5.2 years with 42 (54.5%) patients having duration of disease greater than 3 years. Mean ESR was 46.3±21.3 mm/1st hr. Mean VAS score, tender joint count, swollen joint count and DAS-28 score were 7.1±1.8, 6.9±3.9, 4.7±2.8 and 5.8±1.4 respectively. RA Factor was positive in 47 (61.1%) and Anti-CCP antibody was seen in 34 (44.2%).

Among the 77 patients with LDA/remission, 59 (76.7%) were females and 18 (23.3%) male having mean age 46.5±13.7 years. Thirty-four (44.2%) patients were younger than 40 years old, 26 (33.7%) were aged 41–60 years and 17 (22.1%) were older than 60 years. Mean duration of disease in years was 8.2±6.4 with 47 (61.0%) patients having duration of disease more than 3 years. Mean ESR was 12.4±4.4 mm/1st hr. Mean VAS score, tender joint count, swollen joint count and DAS-28 score were 1.1±1.3, 1.0±1.4, 0.5±1.0 and 2.8±0.9 respectively. RA Factor was positive in 41 (61.0%) and Anti-CCP antibody was seen in 34 (44.2%).

In the LDA/Remission group, 25 (32.5%) patients were being treated with methotrexate alone, 18 (23.4%) with leflunomide alone, 12 (15.6%) with methotrexate and hydroxychloroquine combination, 10 (13.0%) with methotrexate and leflunomide combination, 7 (9.0%) with sulfsalazine alone and 05 (6.5%) with methotrexare and sulfasalazine combination.

Table-1: Comparison of clinical parameters according to disease activity of rheumatoid arthritis

Clinical parameters	Disease activity	
	LDA/Remission	Active disease
Mean age (Years)	46.5±13.7	42.3±14.3
Mean Duration of disease (Years)	8.2±6.4	8.3±5.2
Mean ESR (mm/Hr)	12.4±4.4	46.3±21.3
Mean VAS score	1.1±1.3	7.1±1.8
Mean Tender joint count	1.0±1.4	6.9±3.9
Mean Swollen joint count	0.5±1.0	4.7±2.8
Mean DAS-28 score	2.8±0.9	5.8±1.4
Age groups		
<40 Years	34 (44.2%)	39 (50.7%)
40–60 Years	26 (33.7%)	25 (32.5%)
>60 Years	17 (22.1%)	13 (16.8%)
Gender		
Female	59 (76.7%)	43 (55.8%)
Male	18 (23.3%)	34 (44.2%)
Duration of disease		
≤3 years	30 (39.0%)	35 (45.5%)
>3 years	47 (61.0%)	42 (54.5%)
RA Factor status		
Positive	51 (66.2%)	47 (61.0%)
Negative	26 (33.8%)	30 (39.0%)
Anti-CCP antibody status		
Positive	45 (58.5%)	34 (44.2%)
Negative	32 (41.5%)	43 (55.8%)
Carpal tunnel syndrome		
Present	17 (22.1%)	32 (41.5%)
Absent	60 (77.9%)	45 (58.5%)

Table-2: Comparison of qualitative clinical parameters according to Carpal Tunnel Syndrome

Clinical Parameters	Carpal Tunnel Syndrome		*p*
	Present	Absent	
Gender			
Female	38 (37.2%)	64 (62.8%)	0.118
Male	11 (21.2%)	41 (78.8%)	
Age			
≤40 years	27 (37.0%)	46 (63.0%)	0.709
41–60 years	14 (27.4%)	37 (72.6%)	
≥61 years	08 (26.7%)	22 (73.3%)	
Duration of disease			
≤3 years	21 (32.3%)	44 (67.7%)	0.580
>3 years	28 (31.5%)	61 (68.5%)	
RA Factor status			
Positive	34 (34.7%)	64 (65.3%)	0.431
Negative	15 (26.8%)	41 (73.2%)	
Anti-CCP Antibody status			
Positive	26 (33.0%)	53 (67.0%)	0.402
Negative	23 (30.7%)	52 (69.3%)	
Disease Severity			
LDA/Remission	22 (28.6%)	55 (71.4%)	0.107
Active Disease	27 (35.0%)	50 (65.0%)	

DISCUSSION

Carpal Tunnel Syndrome, a constellation of signs and symptoms, can result from various mechanisms which cause median nerve compression.[18] CTS in RA patients is usually due to inflammatory process whereas in idiopathic CTS inflammation is characteristically absent.[19,20] CTS can also be an initial presentation of RA. In the UK, Muller *et al*[21] conducted a retrospective case-control study to highlight that patients with CTS may go on to develop RA in the following two years after consultation, having odds ratio 2.96.[21]

In the present study 154 patients of RA were enrolled and CTS was seen in 49 (31.8%) patients. In Italy, Smerilli *et al*[12] reported CTS to be present in 26.3% patients of RA. In Turkey, Subasi *et al*.[13] reported CTS in 13.2% of RA patients. Karadag *et al*.[14] enrolled 100 of RA to document prevalence of Carpal tunnel syndrome as 17.0% using combination of history, examination and ultrasonography. In the present study there was no statistically significant association of CTS with age (p=0.709), gender (p=0.118), duration of disease (p=0.580), RA factor positivity (p=0.431) and Anti-CCP antibody positivity (p=0.402). Karadag *et al*[14] found that RA patients having CTS were older, had a longer disease duration, diabetes mellitus and poor functional status scores.[18] However there was no difference in prevalence of carpal tunnel syndrome depending on disease severity of RA.[14] In the present study, CTS was seen in 32 (41.5%) patients with active disease compared with 17 (22.1%) patients with LDA/remission. However there was no significant statistical association (p=0.107).

Splinting is usually recommended as first-line in patients with mild symptoms.[22] Corticosteroid injection into the carpal tunnel is indicated in moderate CTS to provide relief of symptoms, but the effect is usually temporary.[23] For patients not responding to conservative interventions, surgical release is recommended to decompress the median nerve.[24]

The present study has some limitations that it was a single centre study, had a relatively small sample size and enrolled out-patients only. Case-control or cohort studies are a better option.

CONCLUSION

Carpal Tunnel Syndrome is not an uncommon extra-articular manifestation of Rheumatoid Arthritis and was seen in almost one-third of the patients with Rheumatoid Arthritis It is relatively more common in patients with active disease. It is recommended that clinical assessment of CTS should be done routinely in patients with RA, so that lifestyle modifications and pharmacological treatment may be modified accordingly to control and reduce disease morbidity and disability. More work is recommended to find association of CTS and RA disease severity.

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ORIGINAL ARTICLE

RETROSPECTIVE STUDY OF MEDICOLEGAL AUTOPSIES CONDUCTED AT KHAWAJA MUHAMMAD SAFDAR MEDICAL COLLEGE SIALKOT

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Background: Autopsy is performed to establish the manner and cause of death, and can help the authorities to implement effective protective measures against crime. Objective of this study was to determine manner, cause, gender predominance and target age group of medico-legal autopsies in government hospitals of Sialkot. **Methods:** Data for this retrospective cross-sectional study was collected from autopsy registers of Allama Iqbal Memorial Teaching Hospital and Sardar Begum Hospital of Sialkot for the years 2018–2022. The data was entered in self-made proforma and analysed using SPSS-20. **Results:** The autopsies were done on 77.5% males and 22.5% females. The most sensitive group was 21–30 (25.6%) followed by 31–40 (20.5%). Out of 512 deaths, 290 were homicidal deaths, 105 (56.4%) were accidental, 66 (20.50%) were suicidal, 27 (12.89%) deaths with undetermined method, and 24 deaths were found to be natural. Firearm was the cause of deaths in 66.20% cases followed by blunt weapons in 11.37% cases, and penetrating injuries in 10.0% cases. Hanging was the most common cause of death among suicidal deaths (28.78%) and road traffic accident was the most common cause of accidental deaths (80.0%). **Conclusion:** Homicidal deaths are the most common deaths among unnatural deaths. Most commonly used weapon is firearm. There is male predominance. The most common target age group is 21–30 years.

Keywords: Autopsy, Unnatural deaths, Manner of death, Cause of death

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INTRODUCTION

Medico legal autopsies are conducted in cases of sudden, suspicious and unnatural deaths, the primary aim being establishment of cause and nature of death.[1] It caters the need of society to detect any foul play.[2] Autopsy is the scientific examination of bodies after death, where the whole surface of the body as well as all body cavities and organs are explored and findings recorded.[3]

A medico-legal autopsy is indicated for all unnatural fatalities (suicidal, homicidal and accidental), and natural deaths that occur in suspicious circumstances. The medical aspect of this investigation is performed by the forensic pathologist to determine exact cause and manner of death, establish identity of the deceased, determine time since death, collect trace evidence, reconstruction of the crime scene, correlate his findings with the circumstances surrounding the death and above all demystify the cause the death.[4]

Worldwide the number of medico legal cases is rising due to urbanization, poverty, unemployment, drug addiction, illiteracy, economic crisis and other factors contribute to its burden on society.[5] Homicides are caused by fire arm injuries, sharp edged weapons, blunt force trauma, asphyxia, and poisoning while hanging, drowning, poisoning and fire arm injury are common methods of committing suicide.[6] A detailed medico legal examination of the injuries is of paramount importance to find their nature, causative weapon and manner of infliction. This information can not only help the police to link the assailant with the crime but will also provide important statistical data for research purpose. This will in turn help to develop and implement effective preventive measures at national level to reduce the burden of injuries.[7]

In Pakistan, audit of medico legal autopsies has been done in various cities like Multan[6], Lahore[8], Faisalabad[9], Sukkur[10], Karachi[11] and many others and there have been substantial published reports on this subject. However, despite high frequency of medico-legal autopsies no such study has been conducted in Sialkot. This study is, therefore, aimed at determining cause, mode, manner, target age group, gender at risk and frequencies of medico legal deaths confirmed through autopsy studies in Sialkot in order to learn about the current trends of unnatural deaths in Sialkot. This study will draw concerned authorities' attention to the crucial issue of unnatural deaths and situation of law and order in society.

MATERIAL AND METHODS

This retrospective cross sectional study was conducted in mortuaries of Allama Iqbal Memorial Teaching Hospital and Sardar Begum Hospital. The data was collected from autopsy registers of Allama Iqbal

memorial teaching hospital and Sardar Begum Teaching Hospital via self-made study proforma for the year 2018–2022 after obtaining ethical approval from the Ethical Committee of Khwaja Muhammad Safdar Medical College.

Cases of unnatural death, i.e., homicide, suicides and accidents were included. All those cases having partial post mortem examination, cases of exhumation and cases including putrefied bodies were excluded. The data were recorded and analysed using SPSS-20. Descriptive statistics were used to analyse the frequency and percentage of variables such as age, sex, cause and manner of death. The statistical analysis of data from this study was carried out using relevant tables in order to present information in an understandable manner.

RESULTS

A total of 512 medico-legal autopsies were analysed out of which the highest number occurred in 2022 (25.4%) while the lowest number occurred in 2020 (16.4%). Out of total, 397 (77.5%) were males and 115 (22.5%) were females. The most sensitive age group was 21–30 years. The lowest percentage were found to be age below 10 years (6.4%) and above 60 years (9.4%) (Table-1).

Table-2 depicts that homicide was the most common manner of deaths (56.64%) followed by accidents (20.50%) and then suicides (12.89%). The manner remained undetermined in 27 cases and 24 cases turned out to be natural deaths.

Firearm, blunt trauma, penetrating trauma were found to be the commonest cause of homicidal death as 66.20%, 11.37%, 10.0% respectively as shown in Table-3. RTA caused 80.0% deaths while 28.78% of suicidal deaths were due to hanging. Other causes of death such as poisoning, burn, drug overdose were less common. Cause of death couldn't be determined in 21.1% cases.

Table-1: Age-wise distribution of medico legal deaths

Age group	Number	Percentage
1–10	33	6.44
21–30	131	25.5
31–40	105	20.50
41–50	71	13.86
51–60	53	10.35
61–70	32	6.25
71–80	14	2.73
81–90	1	0.19
91–100	1	0.19
Total	512	100.0

Table-2: Manner-wise distribution of deaths

Manner	Number	Percentage
Homicide	290	56.64
Accident	105	20.50
Suicide	66	12.89
Natural	24	4.68
Undetermined	27	5.27
Total	512	100.0

Table-3: Causes of unnatural deaths with gender distribution [n (%)]

Cause of Death	Total n (%)	Male n (%)	Female n (%)
Firearm	192 (37.5)	171 (49.56)	21 (17.76)
Strangulation	25 (4.88)	12 (3.47)	13 (11.02)
Smothering	3 (0.25)	0 (0.00)	3 (02.54)
Blunt trauma	33 (2.75	27 (7.82)	6 (05.08)
Penetrating trauma	29 (5.66)	23 (6.66)	6 (05.08)
Poisoning	15 (2.93)	7 (2.02)	8 (06.77)
Burn	20 (3.90)	14 (4.05)	16 (13.55)
Hanging	19 (3.70)	14 (4.05)	5 (04.23)
Drug overdose	13 (2.54)	12 (3.47)	1 (0.84)
RTA	84 (16.40)	71 (20.57)	13 (11.01)
Drowning	18 (3.50)	11 (3.18)	7 (05.93)
Medical negligence	3 (0.58)	2 (0.57)	1 (0.84)
Unknown causes	58 (11.32)	33 (6.56)	25 (21.1)

DISCUSSION

In the last five years, 512 autopsies were conducted in Khawaja Muhammad Safdar Medical College, Sialkot. Majority of autopsies were performed on men. The role of women in our society is dormant and they have less exposure to the outside world, but the majority of women die as a result of domestic violence or honour killings. Earlier studies in Faisalabad[9], Lahore[8,12] and other cities also documented male victims outnumbering females. A recent study in Ethiopia also reported a male to female ratio of 3:1.[13] While no age group is immune to unnatural deaths, the data showed that age group 21–30 year is the largest target group, followed by 31–40 year because mostly young people are involved in medico-legal cases and criminal activities which include murders and accidents. These age groups are active, mobile, aggressive and daring. These findings are consistent with previous studies. A study conducted in Faisalabad revealed that 80.4% autopsies were of males.[9] In our study 6.44% of fatalities occurred within the age range of 1–10 with a significant portion being newborn females!

The leading cause of death was homicide. The same is documented by many other workers.[6,8,9] However, this is in contrast with studies conducted at Dhaka[14] which revealed accidental deaths as dominant manner in all deaths. Homicide is a global phenomenon and its causes vary from society to society. In Pakistan, the main reasons are lawlessness, poverty, personal dispute, unemployment, femicide and ethnic clashes. This is in agreement with studies conducted at national[6,11,15] and international level[14,16.]

Guns have long been part of traditional Pakistani culture, used for defence and firing ceremonial rosettes. The use of firearm is common due to their easy availability and sure result even from a distance. A study in Faisalabad reported homicide as the most common mode of death followed by accidents. Firearms accounted for 57.36% of all homicide deaths and 82.19% of accidental deaths were due to traffic

accidents[9]; this is consistent with our study. Bad roads, careless driving, drunk driving, disregard of traffic rules and increasing number of cars on the roads can be the reason. A similar study[8] conducted in Sheikh Zaid Hospital showed results almost similar to our study.

Most of the suicides are committed by hanging. This aligns with the study conducted at Poland where majority of self-inflicted death occur through this method.[17] This is also in accordance with study conducted at the mortuaries of two large Forensic Departments in Punjab and Sindh.[18] But this is in contrast with the study conducted at Multan where poisoning was the leading cause of suicidal deaths.[6]

The cause of death could not be determined in 11.32% cases, which increases the burden of unknown causes of death. A study from Lahore12 is in agreement to our findings.

CONCLUSION

Homicidal deaths were the most prevalent, followed by accidental, suicidal, undetermined, and natural deaths. The primary methods in homicidal, accidental, and suicidal cases were firearms, road traffic accidents, and hanging, respectively. Male gender predominance was observed, and the maximum number of cases pertained to age range of 20–30 years.

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ORIGINAL ARTICLE

AETIOLOGICAL FACTORS OF GRADE-III PROTEIN-CALORIE MALNUTRITION AMONG ADMITTED CHILDREN IN A TERTIARY CARE HOSPITAL

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Background: Aetiological factors of Protein-Calorie-Malnutrition (PCM) in underdeveloped countries are an established fact. An increase in number of children with grade-III PCM secondary to myriad of reasons has been noted recently. This study aimed to recognize the aetiological factors of grade-III PCM among admitted patients of grade-III PCM in Ayub teaching hospital Abbottabad. **Methods:** Severe acutely malnourished (SAM) children 6–60 months of age were selected following non probability random sampling technique. The chosen patients were selected according to WHO criteria of PCM grade-III. Primary data was collected from patients admitted to inpatient facility, on a questionnaire from patients whose anthropometric measurements fell under the criteria of severe acute malnutrition (SAM) by WHO during their hospital stay. **Results:** Higher number of SAM children was due to reversible aetiological factors like inaccessible food, inadequate breast-feeding and weaning practices, and improper food choices for weaning, illiteracy, ignorance, poor sanitation and large family sizes that led to SAM. From 100 patients (52 males), primary malnutrition was the most common cause for grade -III PCM present in 45 patients (23 females). **Conclusion:** Primary malnutrition was the main aetiological factor for grade-III PCM, more common among females, perhaps due to cultural issues in our region. It was also the main contributing cause in the toddler age group.

Keywords: Grade-III PCM, Severe acute malnutrition, SAM, primary PCM

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INTRODUCTION

WHO reported 47 million children <5 years of age who are wasted. Of these, 13.6 million children suffer from severe wasting, this being the cause of 1 in 5 deaths in age group <5 years hence making it one of a top threat to child survival.[1] Data from Pakistan reports that within the age group <5 years, 4 out of 10 children are stunted and 17.7% suffer wasting. Approximately 1 of 3 children were reported underweight (28.9%). Malnourished children, especially those with severe acute malnutrition (SAM) face higher death risk from ordinary childhood illnesses such as diarrhoea, pneumonia and malaria. Severely wasted child is at 11 times more risk as compared to a healthy child to die of common childhood illnesses such as pneumonia. PCM related factors contribute to about 45% of deaths in children <5 years of age.[1–3] PCM also called protein-energy malnutrition or PEM occurs when a child doesn't eat enough protein and energy (measured by calories) to meet nutritional needs. PCM most often occurs when both a child's calorie and protein intake are inadequate and sometime becomes potentially life-threatening disorder. Malnutrition in developed countries is unfortunately still more common in situations of poverty, social isolation and substance misuse. Poverty, family instability, poor environmental sanitation, faulty weaning practices, illiteracy, ignorance, large family size and preventable infections are the main factors responsible for malnutrition.[4–6] This study aimed to recognize the aetiological factors of grade-III PCM among admitted patients of grade-III PCM in Ayub teaching hospital Abbottabad.

MATERIAL AND METHODS

This study was conducted in Paediatric B Ward of Ayub Teaching Hospital, Abbottabad from October 2021 to September 2022. After approval of the study from Institutional Review Board of Ayub Teaching Hospital, data was gathered on self-designed proforma after informed written consent from parent/attendant of each participant. One hundred of severe acutely malnourished children between 6 and 60 months of age were included following non-probability random sampling technique. The chosen patients were selected according to WHO criteria of PCM grade-III. Data was collected from patients admitted to inpatient facility on a questionnaire to collect information from patients who were under 60 months old and whose anthropometric measurements fell under the criteria of severe acute malnutrition by WHO[1] during their hospital stay.

Anthropometric measurements included weight (Kg), Height/Length (Cm). Children with Weight for Height (z score <-3SD), and mid upper arm circumference (MUAC) less than 11.5 Cm were included. History was taken from parent/guardian regarding age, gender, birth weight, birth order, age at

the time of weaning, number of meals offered, cause of malnutrition, previous hospitalizations and their underlying cause. History regarding primary caretaker and their socioeconomic status was also included.

Causes of malnutrition were further classified into 7 broad categories including primary malnutrition, low socioeconomic status, and chronic diseases like celiac disease, metabolic disorders, cerebral palsy, syndromes and others. Effect of malnutrition in the form of recurrent infections and compromise on quality of life was also recorded.

Data were analysed using SPSS-19. Percentages and frequencies were calculated. Cross-tabulation was used for correlation between variables, and $p<0.05$ was considered as statistically significant.

RESULTS

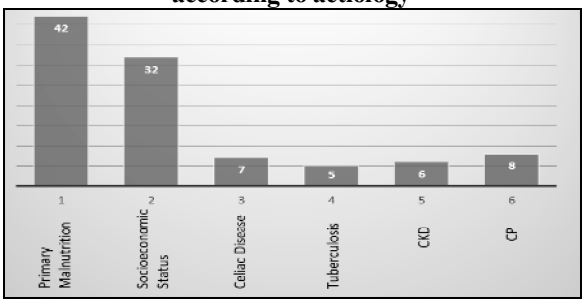
A total of 100 patients (52 males and 48 females) were enrolled in this study. The patients were grouped in age range 6–12, 13–36, and 37–60 months, and they numbered to be 27%, 57% and 16% respectively. Most (75%) of the patients enrolled in study had normal birth weight and 68% belonged to good socioeconomic status. In 96% of children, mother was the primary caretaker, however only 46% of the children were exclusively breast-fed. Those on formula feed and pre lacteal feed were 31% and 27% respectively. Weaning was not properly started after 6 month of age in 48% of the children, 78% patients in total had insufficient caloric intake to meet their daily energy requirements. Eighty-seven percent patients had past history of recurrent infections while 63% of them also had history of previous hospitalizations. The correlation between the demographics and causes of PCM are shown in Table-1.

The most prevalent causes were primary malnutrition (42%) followed in frequency by low socioeconomic status (32%). Less prevalent causes included systemic illnesses like celiac disease (7%), tuberculosis (5%), chronic kidney disease (6%) and cerebral palsy (8%). (Figure-1).

Table-1: Demographics and correlation of causes of PCM in the study group of childeren[n (%)]

Variables		Primary Malnutrition	Low Socio-economic Status	Celiac Disease	TB	CKD	CP	*p*
Gender	Male	19 (36.5)	16 (30.8)	4 (7.7)	3 (5.8)	4 (7.7)	6 (11.5)	0.664
	Female	23 (47.9)	16 (33.3)	3 (6.3)	2 (4.2)	2 (4.2)	2 (4.2)	
Age	6 months to 1 year	12 (44.4)	9 (33.3)	2 (7.4)	1 (3.7)	1 (3.7)	2 (7.4)	0.481
	1–3 years	23 (40.3)	19 (33.3)	4 (7.01)	2 (3.5)	5 (8.77)	4 (7.01)	
	3–5 years	7 (43.75)	4 (25)	1 (6.25)	2 (12.5)	0 (0)	2 (12.5)	
Birth Weight	Low	14 (56)	9 (36)	1 (4)	0 (0.0)	1 (4)	0 (0)	0.243
	Normal	28 (37.3)	23 (30.7)	6 (8)	5 (6.7)	5 (6.7)	8 (10.7)	
Meals offered	Sufficient	5 (22.7)	3 (13.6)	5 (22.7)	2 (9.1)	4 (18.2)	3 (13.6)	0.000
	Insufficient	37 (47.4)	29 (37.2)	2 (2.65)	3 (3.8)	2 (2.6)	5 (6.4)	
Weaning	Proper	19 (34.5)	21 (38.1)	4 (7.27)	4 (7.27)	4 (7.27)	3 (5.45)	0.162
	Improper	23 (51.1)	11 (24.4)	3 (6.7)	1 (2.2)	2 (4.4)	5 (11.1)	

Figure-1: Number of patients with Grade-III PCM according to aetiology



DISCUSSION

We investigated the aetiological factors contributing toward grade-III malnutrition in children admitted to our hospital in the age group of 6 to 60 months. The results of this study were in favour of the fact that the age, frequency of complementary/dietary intake per day, socioeconomic status, meals offered were significantly associated with SAM among children under five and it can further contribute toward community and hospital burden.

There was no statistically significant gender-based differences. Most of the cases of SAM were in age group from 12 to 36 months which made up to 57% of total enrolled patients. This is most probably due to smaller stomach size compared to the older children, and younger children are in transition from milk based-diet to complementary feeding. This is an agreement to the studies done in Nepal[7] and India[8]. For younger children, the frequency of milk feeds whether breastfeeding or complementary may be increased to reach optimal caloric intake. Though this is easier choice especially if mother-fed when compared to the older children for reaching optimal caloric intake, but it requires counselling for both birth spacing and encouraging breast feeding by lady health workers.[9] But the practice of optimal feeding are not adequate as only 48% of the patients were started on weaning and only 22% of the patient had adequate caloric intake.

Breast milk is rich source of carbohydrates, proteins (including immunologic components), fats,

vitamins and various immune protective ingredients required for a growing child, thus not only supplying nutrition but also providing resistance to infections in the first 6 months of life[10] but only 46% of our patients were exclusively breastfed up to 6 month of age and that can be a contributing factor towards SAM, recurrent infections, and hospitalizations.

Most of our patients had normal birth weight, however, they later developed malnutrition as most common cause of SAM was primary malnutrition which was directly linked to nutritional status and childcare practices observed. Second most prevalent factor contributing toward SAM was poor socioeconomic conditions. Most of the patients had birth order of 3 or more. Higher family sizes can lead to poor *per capita* income[12] and may compromise intra-house food allocation and optimal caring that each child is expected to get from parents, putting them at higher risk of being undernourished[9].

Our study is congruent to initial hypothesis made for the aetiological factors of grade-III malnutrition. However, there were some minor contributing factors toward SAM which due to secondary malnutrition like celiac disease, cerebral palsy, tuberculosis and chronic kidney disease made up to 26% of total cases. Severity and duration of disease seems to affect more on nutritional status in such patients, especially considering that special needs formulae are expensive and out of reach in Pakistan for low socioeconomic groups.[12]

CONCLUSION

Primary malnutrition was the main aetiological factor for grade-III PCM and can be attributed to poverty and ignorance. It was more common among females, perhaps due to cultural issues. It was also the main contributing cause in the toddler age group. These findings can't be generalized as they are limited to only one hospital. Larger studies are suggested to include other regions.

RECOMMENDATIONS

There is need to encourage the mothers the value of breastfeeding and adequate dietary consumption for their children. Mass education to raise awareness among community by utilizing community workers and social media to impart knowledge about preparation of homemade affordable meals with balanced macronutrients can be executed. This will help to decrease the burden on health system by preventing the complications with which grade-III PCM children are admitted and will give the children a chance to achieve their full potential in life.

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ORIGINAL ARTICLE

RELAPSE VULNERABILITY AND PSYCHOLOGICAL ADJUSTMENT AMONG DRUG ADDICTS: ROLE OF INTEGRATED SELF AS A PREDICTOR

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Background: Drug addiction can cause a physical and biological harm, causing problems in family structure, and can contribute to the delinquency and high rates of crimes in a society. The aim of this study was to test the association between integrated self, relapse vulnerability and psychological adjustment. **Method:** To measure the integrated self, a scale was constructed in first phase of the study. In second phase 400 psychometric properties of new scale were determined. Integrated Self Scale, AWARE Questionnaire and Psychological Adjustment Scales were used. Sample comprised of 200 male drug addicts using purposive convenient sampling. Drug addicts suffering from any psychotic illness were excluded from the sample. **Results:** Findings indicate a significant negative relationship of integrated self with relapse vulnerability and positive relationship with psychological adjustment. The integrated self acts as a predictor of relapse vulnerability and psychological adjustment. Graduate drug addicts have integrated self, low relapse vulnerability and show better psychological adjustment as compared to undergraduate drug addicts when compared on educational level. **Conclusion:** This study is beneficial in finding ways to enhance self-integration of drug addicts so that their drug relapse can be reduced and in turn they can experience better psychological adjustment.

Keywords: Integrated Self, Relapse Vulnerability, Psychological Adjustment, Drug addicts

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INTRODUCTION

Among various causes, the self plays an important role in many mental health problems like drug addiction. The self can be referred as an individual person, it is the object of its own introspective awareness.[1] A fully functioning person may be characterized by a unity in all aspects of his/her life. It means that he/she must have a balance in his/her thoughts, emotions, and action that aggregates to 'being someone' or having 'an integrated self'.[2]

It is found that persons having lower level of self-integration may exhibit more depressive symptoms, anxiousness and neurotic symptoms. Moreover, they also score less on self-esteem. Besides, they show several forms of psychopathologies, and drug addiction is amongst one of them.[3,4]

Sometimes drug addiction seems to be a chronic illness because relapse is very common in it. The relapse of drug addiction can even occur after a long period of abstinence. This is the reason that drug addiction is much difficult to treat.[5] When an individual is not focusing on all aspects of his self properly, he may suffer from relapse.[6] As he does not change his thought patterns, focus on improving his level of spirituality, gain insight about what is wrong in his physical self, he actually deviates from his nature that is why he experiences relapse again and again.[7]

Psychological adjustment refers to the process through which individuals adapt and cope with the various challenges and changes in their lives. It encompasses their ability to manage and regulate their thoughts, emotions, and behaviours in response to different situations and stressors. Drug addiction has negative relationship with psychological adjustment. The individuals who start using cannabis at early ages exhibited psychological maladjustment, and individuals not using cannabis, or abstain from drugs, show the best psychological health.[8]

According to Wildgoose *et al*[3], a fundamental factor found in the drug related problems is an unstable and discontinuous sense of self. Besides, it has been revealed from another study that patients with substance use disorders show significant lower level of self-integration when compared to non-clinical group. Along with this the lower levels of self-integration were positively related to psychological maladjustment as well.[9] To maintain good psychological health, it is essential to nurture and maintain physical, cognitive, emotional and spiritual aspects in harmony. Human personality is a reflection of their thoughts and ideas, with thoughts playing a central role in mental health. When all elements are in harmony and balance, the individual remains in a state of equilibrium. However, any disruption or imbalance in these areas can lead to a corresponding imbalance in the person's overall well-being and psychological sickness as well.[10]

Most researchers only focused on prevention of drug addiction.[11] How self is playing a role on drug relapse is still not studied much. A study to see how Integrated Self can contribute in such behaviours is warranted. The aim of this study was to provide foundation and to instil insight into the elements of

selves upon which the human identity is composed. This study focused more on integration of self to prevent drug relapse and its adverse effect on mental and psychological health of the society. Objectives of the current study were to measure the level of integrated self among drug addict, to determine the relationship between integrated self, relapse vulnerability and psychological adjustment among drug addicts, and to measure the effect of some demographic variables like education and family system on study variables.

METHODOLOGY

The current study comprised of two phases. In the first phase, following the customary steps and procedures, 70 items Integrated Self Scale was constructed. Responses were given on a 4-point rating scale. To establish the psychometric estimates a purposive convenient sample (n=400; men=200, women=200) was recruited. The participants were 15–65, (31.69±9.96) years old. In the second phase, validation of the Integrated Self Scale was done by administering it on a large sample of drug addicts. Along with this, two other scales, i.e., Urdu version of Advance Waning of Relapse Questionnaire (28 items)[12] and Psychological Adjustment Scale developed and translated by Fizza Sabir[13] were also administered to measure its relationship with those variables as well. A purposive convenience sample (n=200 male drug addicts) was recruited for Phase-II after taking informed written consent. The ages of the participants were 15–65, (36.77±11.79) years. Participants with at least 5 years of education were included. It was taken into account that no drug addict must be having any psychological disorder like depression, personality disorder, schizophrenia etc. Participants were given detailed instructions about scales and how to complete them.

A series of statistical analyses were done in order to meet the objects of the study and to test the framed hypotheses. Factor analysis was done by applying Principal Axis Factor analysis by using oblique rotation to explore the factor structure and validity of the ISS.

RESULTS

Integrated Self Scale is clearly clustered into four separate factors. Final form of the scale consisted of 20 items in factor I. Factor II contained 18 items, Factor III was also comprised of 18 items. The fourth factor comprised of 14 items. Eigen value of Factor I was 16.72 indicating 16.09% of variance. Eigen value of Factor II was 6.46 (5.84% variance). Eigen value of factor III was 4.19 (3.49% of variance). And factor IV had Eigen value 3.08 (2.34% of the variance). The cumulative variance explained by four factors was 27.78%.

Table-1: Mean±SD, alpha reliabilities and correlations between integrated self-scale, its subscales, relapse vulnerability and psychological adjustment (n=200)

Scales	n	Mean±SD	α	PASS	CAS	EAS	SAS	ISS	AWARE	PAS
PASS	14	14.49±4.78	0.88	-	0.43**	0.52**	0.63**	0.91**	-0.32**	0.18*
CAS	18	15.18±2.86	0.73			0.35**	0.89**	0.73**	-0.18*	0.14*
EAS	18	13.78±1.4	0.75				0.57**	0.66**	-0.25**	0.21*
SAS	20	18.38±4.76	0.87					0.88**	-0.32**	0.19**
ISS	70	23.46±7.4	0.84						-0.88**	0.19**
AWARE	28	2.8±0.42	0.82							-0.34**
PAS	27	4.43±1.48	0.79							-

PASS= Physical Aspect Subscale, CAS= Cognitive Aspect Subscale, EAS= Emotional Aspect Subscale, SAS= Spiritual Aspect Subscale. ISS= Integrated Self Scale, AWARE= Advance Warning of Relapse, PAS= Psychological Adjustment Scale

To determine the internal consistency of the scales, reliability coefficients were computed. High value of Alpha coefficient is indicating that the scale is internally consistent and is reliable measure to assess the underlying construct. It is clear from the results that all subscales show significant correlation with the total confirming construct validity. Correlation coefficient indicates that there is a negative significant relationship between relapse vulnerability and integrated self. While psychological adjustment is positively correlated with integrated self and its subscales. A Regression equation was found significant (R^2=0.38, F(198)=98.832, p<0.001). The results of the regression analysis reveal that the predictor integrated self-contributed 38% of variance in Psychological adjustment of drug addicts. Thus, findings reveal that integrated self significantly predicted psychological adjustment (β=0.087, p<0.001). (Table-2).

A Regression equation was found significant (R^2=0.32, F(198)=7.71, p<0.001). The results of the regression analysis reveal that the predictor integrated self-contributed 32% of variance in relapse vulnerability among drug addicts. Thus, findings reveal that integrated self significantly negatively predicted relapse vulnerability (β= -0.19, p<0.05). (Table-3).

Results of Table-4 show that there is a significant difference in integrated self, relapse vulnerability and psychological adjustment of graduate and undergraduate drug addicts. Mean±SD indicates that graduate drug addicts have higher level of self-integration and ultimately have better psychological adjustment than undergraduate drug addicts, while undergraduate have high relapse vulnerability than graduate drug addicts.

Table-2: Linear regression analysis showing integrated self as predictor of psychological adjustment

Variable	Psychological adjustment			
	β		95% CI	
			LL	UL
Constant	133.21*		113.92	141.28
Integrated Self	0.087*		0.07	0.14
R^2		0.38		
F		98.832*		

CI=Confidence Interval, LL=Lower Limit, UL=Upper Limit, *p<0.001

Table-3: Linear regression analysis showing integrated self as predictor of relapse vulnerability

Variable	Relapse vulnerability			
	β		95% CI	
			LL	UL
Constant	5.34*		4.66	6.01
Integrated Self	-0.19*		0.01	0.25
R^2		0.32		
F		7.71*		

*p<0.001

Table-4: Comparison between graduate (n=80) and undergraduate drug addicts (n=120) on integrated self, relapse vulnerability and psychological adjustment

	Graduate		Undergraduate		t	p	95% CI		Cohen's d
	N	Mean±SD	N	Mean±SD			LL	UL	
IS	80	28.93±7.69	120	23.75±6.63	0.58	0.01	1.48	2.68	0.08
RV	80	18.15±3.32	120	27.88±4.17	0.45	0.03	0.915	1.46	0.04
PA	80	38.02±4.23	120	27.43±2.23	0.70	0.001	1.06	2.24	0.09

IS=Integrated Self, RV=Relapse Vulnerability, PA=Psychological Adjustment, LL=Lower limit, UL=Upper Limit, CI=Confidence Interval

DISCUSSION

There are many factors which can contribute in drug abusive behaviour but when focusing on personality and aspects of self it has been seen that if an individual does not focus on each and every aspect of self properly he may get some psychological problems, and drug addiction is one of them. Drug addiction is a spiritual disease if we focus on the Islamic perspective. So it can clearly be related that individual having less focused on spiritual aspect of self can easily be trapped in drug abusive behaviour.[14]

Integrated Self Scale (α=0.84), AWARE Questionnaire (α=0.82), and Psychological Adjustment Scale (α=0.79) were used in current study to explore the study variables. Results indicated strong negative correlation between relapse vulnerability and psychological adjustment. Individuals having high relapse vulnerability don't have will power to control this behaviour and they have the recurrent thoughts of having drugs so they are unable to focus on any other task of their life. This leads to psychological maladjustment. Individuals who had already quitted the abusive behaviour, showed the best psychological health.[8]

Second hypothesis stated that there is a negative relationship between integrated self and relapse vulnerability and positive relationship between integrated self and psychological adjustment. Results of the study have confirmed this hypothesis. One of the core component of the drug related problems is a personality fragmentation.[9] Results of a comparison between patients with substance use disorders and a non-clinical group found that drug abusers showed significantly higher level of fragmentation as compared to the non-clinical group and also found high levels of fragmentation, positively related to psychological maladjustment. Their strong relationship can explain that relapse vulnerability is an outcome of lower level of integrated self.[9]

If concerning to participants' education, regrettably, very few researches showed the association of level of education to integrated self and relapse vulnerability of the drug addicts.[15] The available studies indicate inconsistent findings regarding educational differences in experiencing relapse vulnerability associated with integrated self. In one study no significant differences were found between educational levels relapse vulnerability among the drug abusers.[16] Less education or leaving school at an early ages are associated with more disordered and chaotic drug use.[17]

It can be speculated that if individual is highly educated he may take special care of his self. He will consider all aspects equally important so will try to maintain harmony among them. He will have integrated self, eventually will show less abusive behaviour, and may exhibit better psychological adjustment.

LIMITATIONS

Generalization and validity of this research is limited because of the issues of sampling and measurement. In the present study only structured questions were used and any other information about drug addicts was not gathered. It did not allow exploring other reasons except their functioning of self behind their drug use. Only males were examined due to inaccessibility to female sample. Results cannot be generalized to female population and it doesn't explore the role of integrated self in female drug users.

IMPLICATIONS

The present study can have the following possible implications:

1. Integrated Self Scale is mainly constructed for the current study. This can also be used efficiently in future researches related to the same area.

2. It will help future researchers to get valuable literature in the relevant area.
3. In the light of current results it can be suggested that proper intervention should be planned to work on the self of drug addicts. If they can get balance in different aspects of their selves they will live better lives.

CONCLUSION

Drug addiction is caused by disharmony in different aspects of self, and it also effects psychological adjustment of drug addicts. Disintegrated or fragmented self can act as a covariate of psychological maladjustment among drug addicts. Educated addicts have integrated self, low relapse vulnerability and have better psychological adjustment than less educated drug addicts because they are better aware of the issues related to addiction and can cope with the situation.

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ORIGINAL ARTICLE

RESILIENCE AS A PROTECTIVE FACTOR FOR DEPRESSION AMONG INFERTILE WOMEN OF FAISALABAD

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Background: Infertility is one the major cause of depression among married women of Pakistan. Resilience is a psychological skill that can help to manage depression in married women. This study was designed to assess depression and resilience among infertile women of Faisalabad. **Methods:** A correlational study was conducted from May to Aug 2022. Purposive sampling technique was used to gather information from different infertility centers and hospitals of Faisalabad, Pakistan. The Mean age of the subjects was 31.38±5.57 years. To assess the level of depression and resilience among infertile women, the Urdu version of the Siddiqui-Shah Depression Scale (SSDS) and the Resilience Scale (RS) were used. Statistical analysis was done on SPSS-26. **Results:** Out of the 110 participants, 89 (81%) were primary while 21 (20%) were secondary infertile. Resilience and depression negatively correlated significantly (p=0.000) in infertile women. The respondents from rural areas (p<0.05), those with increased number of treatments (p<0.05) and those having primary type of infertility (p<0.05) showed significantly high level of depression. **Conclusion:** Resilience and depression have negative association. Depression is predominant among rural as compared to urban residents, and in primary infertile women with increased number of treatments compared to secondary infertile women.

Keywords: Infertility, Depression, Resilience

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INTRODUCTION

Infertility is defined as the inability of men and women to reproduce. The World Health Organization's definition of infertility is based on 12 months (or longer) of unsafe sexual relation.[1] In Pakistan current infertility ratio is 21.9%, 3.5% primary (not yet conceived) and 18.5% secondary infertile cases (at least one conception but not repeated).[2] All over the world 10–15% couples in their reproductive age are affected by infertility.[3]

Unfortunately, women are considered sole responsible of infertility. This inequality has caused extensive psychological changes such as depression.[4] Level of depression is higher among women than men. Fertility-related distressed is more common among primary infertile than secondary.[5] This health issues are prevailing rapidly in Pakistan because of limited resources and unawareness about the aetiology or treatment process.[6] Family and cultural pressures exacerbate the stress which results into anxiety and depression. Infertility related social stigma, loneliness, separation, and uncertainty about treatment process also contribute a lot in the development of depression in females.[4]

Infertility is positively associated with distress or depression. Anxiety, tension, guilt, hopelessness, loss of self-control, worthlessness, humiliation, inadequacy and negative cognitive scripts impair acceptance and psychological flexibility in women.[7] Suicidal ideation and attempts also have been reported in infertile women.[8] Infertility is more stressful experience than COVID-19 pandemic.[9] Infertility-related depression level resembles to female cancer patients.[4]

Resilience improves psychological tolerance and reduces the negative effects of infertility. Resilient individuals are optimistic, confident, problem solvers and satisfied with their lives. Resilience is the individual's ability to stay calm in stressful and challenging situations.[10] Individual's infertility-related stress response is determined by this factor. It works as a non-specific protector against psychological distress among the infertiles.[11]

Keeping in view the above it was aimed to explore a relationship between depression and resilience among infertile women. In addition, it is aimed to investigate the differences in terms of demographic variables (residential area, type of infertility, number of treatments) in women with primary and secondary infertility in Faisalabad city and suburbs.

SUBJECTS AND METHODS

This correlational study was conducted from May to Aug 2022. Purposive sampling technique was used to gather information from different infertility centres, private clinics and hospitals of Faisalabad, Pakistan. Outdoor patients aged 21–45 years who came from different cities of Punjab diagnosed with infertility were taken as study sample after written informed consent. G*Power 3.9.1.2 was used to calculate sample size.[12]

The study included infertile women with any reason of infertility, and from a nuclear or joined familial system diagnosed with primary or secondary infertility while living with their husbands. Infertile women with any chronic condition, having special children, as well as whose husbands were addicted to any kind of drug were excluded from the study.

A brief interview form was designed in Urdu to collect socio-demographic information as well as the participants' marital history. To assess the level of depression Urdu version of Siddiqui-Shah Depression Scale (SSDS)[13] was used. On a 4-point rating scale, each item was given a score ranging from 0 to 3 (0=never to 3=most of the time) with alpha coefficient 0.94. Urdu translated Resilience Scale (RS)[14] was administered for measurement of resilience among infertile women. Resilience scale was a 25-item questionnaire with a 7-point likert scale (strongly agree to strongly disagree, from 7 to 1). The translated scale reliability was 0.91. Descriptive statistics, correlational analysis, and independent-sample *t*-test were applied using SPSS-26.

RESULTS

Of the 110 subjects, 89 (81%) were primary while 21 (19%) were secondary infertile. Mean age of the subjects was 31.38±5.57 years. Demographic characteristics of the subjects are presented in Table-1.

Depression and resilience scales proved highly reliable measures (Table-2). Resilience and depression significantly negatively correlated (r= -0.42, p=0.000) (Table-3). Level of depression and resilience were significantly different in urban and rural residents, with type of infertility, and number of treatments (Table-4).

Table-1: Demographic Characteristics

Participant's Characteristics	n	%
Birth order		
1st Born	30	27
Middle child	60	55
Youngest	20	18
Education		
Matric	36	33
Above Matric	74	67
Family system		
Nuclear	25	23
Joint	85	77
Residential area		
Rural	31	28
Urban	79	72
Type of infertility		
Primary	89	81
Secondary	21	19
Treatment number		
1–3 times	84	49
≥4 times	56	51

Table-2: Psychometric properties of study variables scales

Scale	Mean±SD	Range	*a*
Depression Scale	31.70±18.80	2–84	0.94
Resilience Scale	133.97±26.89	27–175	0.91

a=Cronbach's alpha

Table-3: Summary of correlational analysis

Variables	Depression	Resilience
Depression	-	
Resilience	-0.42*	-

*p<0.01

Table-4: Mean comparison of demographic variables on depression and resilience (Mean±SD)

Variables	Rural (n=31)	Urban (n=79)	*t* (108)	*p*	Cohen's d
Depression	40.58±20.59	28.22±16.95	-3.23	0.002*	0.65
Resilience	124.65±27.50	137.63±25.92	-2.32	0.022*	0.48
	Primary (*n*=89)	Secondary (*n*=21)			
Depression	33.81±19.38	22.76±13.07	2.47	0.015*	0.67
Resilience	133.57±26.40	135.65±29.50	-0.31	0.752	0.07
	1–3 times (*n*=54)	≥4 times (*n*=56)			
Depression	27.59±19.69	35.93±17.20	-2.35	0.020*	0.45
Resilience	140.11±23.04	128.16±29.40	-2.35	0.020*	0.45

*Significant

DISCUSSION

Siddiqui-Shah Depression Scale (SSDS) and Resilience Scale (RS) Urdu versions appeared to be highly reliable measures to assess depression and resilience among infertile women. Depression and resilience have a negative relationship. Literature showed that infertility stress had positive connection to depression, whereas resilience and depression are negatively associated.[15] Infertility stress brings depression and marital adjustment issues, but resilience can help people to effectively manage this problem as shown by our study results. Resilience may be utilized to help people to avoid clinical depression.[16]

The level of depression is reported significant among rural residential, primary type of infertility and increased number of treatments. Rural women suffered more from depression.[17] Cultural expectations, societal pressure and conservative views on life and parenting are commonly observed in rural communities.[18] Infertility may have a greater negative impact on people living in rural areas, resulting in more emotional anguish.[19] It brings more detrimental effects and mental agony for rural women.

Depression is prevalent among primary than secondary infertile women.[20] Primary infertile women experienced more fertility-related sufferings as compared to secondary infertile women.[21] Only 21 (19.09%) women had secondary while 89 (80.9%) had primary infertility in this study. Secondary infertility is prevalent in Pakistan. Some studies found that secondary infertility is more common in Asian countries, while Shamila *et al*[22], reported that 82.48% of women had primary infertility, which backed up our findings.

Prolonged infertility and infertility treatment failure boost psychological discomfort among women.[23] The prevalence of depression was high among primary type of infertile women because factors like the duration of infertility, treatment, and fear of husband remarrying contribute a lot in this perspective.[24] Depressed women have less possibility to initiate infertility treatment and have more chances to abandon it.[25]

CONCLUSION

Infertility is a distressing health condition for women. It affects their personal, societal and psychological aspects of life. Due to depressive symptoms their marital adjustment also suffers a lot. In this condition, resilience protects their mental health. Women who live in rural areas and have primary infertility with increased number of treatment (repeated referrals) face significantly high depression and less resilience than urban residents, decreased number of treatment failure and secondary type of infertility. There is a negative association between resilience and depression. Depression is predominant among rural residents and primary infertile women with increased number of treatments.

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ORIGINAL ARTICLE

TYPES OF ITEM WRITING FLAWS IN MULTIPLE CHOICE QUESTIONS IN MEDICAL EDUCATION AND THEIR EFFECT ON PASSING RATE OF STUDENTS

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Background: The most popular written exam in health professions education is the multiple-choice style question (MCQ). This study sought to understand the effects of multiple-choice writing errors on students' academic performance in medical education. **Methods:** This descriptive study was done from December 2017 to June 2019 in Azad Jammu Kashmir (AJK) Medical College, Muzaffarabad. Ten block examinations were included. The item review committee reviewed all MCQs for flaws. Two tests from each class of MBBS were taken. The original tests containing all items were labeled as flawed tests and the result of each flawed test was evaluated. The students were graded into high, moderate and low achievement groups with scores of more than 79.9, between 50–79.9 and less than 50 percent respectively. Flawed items were then removed from the tests by the review committee and the scores of each test (standard test) were determined and compared with flawed tests and its effects were assessed in three achieving groups of students. Optical mark reading (OMR) classic-4 software was used for post-exam analysis and data were analyzed by using SPSS-25. **Results:** The passing rate ranged from 68.18% to 90.82% in flawed and 75.54% to 93.69% in standard tests. Most standard tests (7) had higher passing rates than flawed tests. **Conclusion:** Tests containing in-house developed MCQs have frequent item writing flaws and their inclusion in assessment did affect the passing rates of students but were not statistically significant.

Keywords: MCQs, Flawed items, Academic achievements, Medical Education

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INTRODUCTION

Assessment significantly impacts on students' learning and contributes to the achievement of instructional objectives. In the study of the health professions, multiple-choice questions (MCQs) are frequently employed as a form of written assessment.[1]

Concerning reliability, validity, and cost effectiveness, MCQs offer extensive material coverage for evaluating many pupils. A well-designed MCQ can evaluate several cognitive knowledge levels, ranging from memory and comprehension to application, synthesis, and analysis.[2] Moreover, MCQ examinations separate high- and low-achieving students.[3] Unfortunately, even for a well-qualified medical educator, creating a high-quality MCQ is a time-consuming, exhausting effort.[4]

There aren't many institutions in Pakistan that have medical educators who have had official training in creating MCQs. Most internal MCQs are of low quality since they are created by teachers with little to no training. There are a number of rules for creating excellent MCQs.[5] A thorough taxonomy of 31 item-writing rules has been given based on Haladyna *et al*[6], item writing principles from the National Board of Medical Examiners (NBME). The evidence-based guidelines for creating the best MCQ are frequently disregarded by item authors, which results in the creation of substandard MCQs that harm students' educational outcomes.[6]

The validity of an assessment is undermined by multiple-choice questions of poor quality. The post-examination psychometric analysis offers precise, unbiased information on the quality of the items. This quantitative analysis aids in locating various item flaws and establishes a statistical distinction between 'good' and 'poor' products.

There is no formal system for Pakistan Medical & Dental Council (PMDC) or any other supervisory entity to monitor and assess the quality of examinations. Due to shortage of medical educators and institutionalized medical education departments, local faculty members in various medical institutions are free to create MCQs in their own ways. The professor's level of expertise and experience, which differs from institution to university, has a major impact on the quality of MCQs. This study will assist in addressing the requirement for regulatory authorities to provide some system to oversee the quality aspects of MCQ-based examinations in Pakistani medical institutions.

METHODOLOGY

This non-experimental descriptive study was conducted in the AJK Medical College, Muzaffarabad from December 2017 to June 2019. This study includes 10 summative and end-of-block exams from the AJK Medical College, Muzaffarabad. These exams included two tests from 1st, 2nd, 3rd, 4th, and 5th year classes. The modules included in the study were those in which college faculty had the most influence on the development of the MCQs. The internal assessment portion accounted for 30% of the overall professional summative assessment.

Operational definitions:

1. MCQ Items:
   a) Standard Item: MCQ with no item writing flaws
   b) Flawed Item: MCQ violating one or more standard item writing principles were flagged as flawed item

It is based on Haladyna *et al*[6], item writing principles from the National Board of Medical Examiners (NBME).

2. Tests:
   a) Standard test: Test after exclusion of flawed items
   b) Flawed test: Test inclusive of flawed items
3. Groups of students based on scores in tests:
   a) High achievers: Those who score 80% or above marks
   b) Moderate achievers: Those who score between 50–79.9% marks
   c) Low achievers: Those who score less than 50% marks

The Item Review Committee of Department of Examination, AJK Medical College examined every MCQ for errors in item authoring. Examinations from first-, second-, third-, fourth-, and fifth-year classes yielded two tests from each category. The study included tests from summative and end-of-block assessments, tests with post-examination statistical data including the reliability of the test, difficulty index, point biserial and discrimination indices of items. Number of students was 90 or more per test, number of MCQs was 50 or more per test, and MCQ items were written by local faculty. With all test items included, the first result of each test (flawed test) was produced, and students were classified appropriately into high, moderate, and low groups.

RESULTS

There were 145 (29%) flawed items in 500 MCQ items in 10 tests. In these flawed items, the five most common ones were K-type (26%), negative stem (20%), non-homogenous distracters (17%), all of the above (14%) and implausible distracters (9.6%). These flaws accounted for 86.6% of all flaws (Table-1, 2).

Table-1: Frequency of flaw items

Test No	Number of students	Total MCQ items	Number of flawed items
1	106	50	13
2	98	50	7
3	88	50	16
4	95	50	12
5	93	50	18
6	95	50	17
7	95	50	19
8	106	50	12
9	87	50	15
10	87	50	16
Total	**950**	**500**	**145**

Table-2: Types of flawed items

Type of flaws	No of Flaws
Negative stem	29
K-type	38
Implausible distracters	14
Unfocussed stem	9
Unequal length of distracters	3
None of above	0
Logical cues	0
More than one flaws	2
True-False	0
Trival Content	2
All of above	20
Repeat words/grammatical errors	0
Complex partial type	3
Non homogenous distracters	25
Total	145

There were observed differences in the passing rates of students in flawed and standard tests as shown in Table-3. The passing rate ranged from 68.18% to 90.82% in flawed and 75.54% to 93.69% in standard tests. In tests 1, 5 and 10 the student's pass percentage was higher in flawed tests. In remaining tests, standard tests had a higher pass percentage. One-hundred-sixty-three students failed in flawed tests while 119 students failed in standard tests. Hence 44 more students could get through examinations if the tests had no flawed items. Mann Whitney U test was used to determine the statistical significance in the passing rates of flawed and standard tests (Table-4, 5). In this study Null hypothesis could not be rejected as in Mann-Whitney U test the 2-tailed significance was 0.226.

Table-3: Passing rates (%) of students in flawed and standard tests

Test No.	Flawed	Standard
1	81.13	78.24
2	90.82	91.83
3	68.18	75.54
4	88.42	93.68
5	88.17	83.87
6	81.05	93.69
7	85.26	90.52
8	77.36	84.90
9	83.90	90.65
10	83.86	81.60

Table-4: Statistical analysis of passing rates in flawed and standard tests

Ranks				
	Groups	n	Mean Rank	Sum of Ranks
Passing rates	Flawed	10	8.90	89.00
	Standard	10	12.10	121.00
	Total	20		

Table-5: Test statistics Man-Whitney-U

Test Statistics[a]	
	Passing rates
Mann-Whitney U	34.000
Wilcoxon W	89.000
Z	-1.209
Asymp. Significance (2-tailed)	0.226
Exact Significance [2*(1-tailed Sig.)]	0.247[b]

DISCUSSION

These tests had high rate of flawed items ranging from 14% to 38% (mean 29%). The five most common flaws were K-type (26%), negative stem (20%), non-homogenous distracters (17%), all of the above (14%), and implausible distracters (9.6%). Out of all flawed items, these flaws accounted for 86.6%. These findings are very similar to the findings of Downing[8] where the most common five flaws accounting for 90% of all flaws were an unfocused stem, a negative stem, all of the above, none of the above options and partial K-type items in his study. Tarrant and James[9] had similar findings in their study, where the most common eight flaws encompassed 85% of all flaws were negative stem, unnecessary information in the stem, no correct or more than one correct answer, implausible distracters, greater detail in correct option, logical clues and word repeats. The item writing flaws found in this study were the ones which are well-reported in medical literature.

Training and experience of the faculty involved in item writing directly determine the quality of MCQs items. In AJK Medical College, though the faculty is highly trained in their related subjects, they have little training in assessment methodology. There are few such training opportunities in our country with a limited number of formally trained medical educationists. Furthermore, the regulatory authorities do not impose any requirement for such training. In order to write high-quality MCQs, one must not only be aware of item writing principles but also have supervised training. Only through training and experience the faculty develops the ability to write high-quality MCQs. These item writing flaws can be corrected by faculty development programs in medical institutions. In the presence of item writing flaws, the test results validity is threatened by construct irrelevance variance. According to Downing the training of the faculty for item writing and pre-examination item review for correction of these flaws improves validity of test results.[1]

This study revealed that in tests 2, 3, 4, 6, 7, 8, 9 the pass percentage of students was higher in standard tests than in flawed tests. However, in tests 1, 5, and 10, the pass percentage was less in standard tests than in flawed tests. In most of the tests more students passed when flawed items were excluded from the tests. Thus, the flawed items resulted in higher failure rates in flawed tests and acted as a disadvantage for these students. These results were similar to the results of two different studies by Downing.[7,8]

In three examinations (tests 1, 5 and 10), the pass percentage was higher in flawed tests than standard tests. These results were similar to the results found in the study of Tarrant where flawed items had a positive effect on borderline students and their inclusion resulted in the passing of greater number of students.[9] Tests 2 and 10 had small differences in the pass percentage of students in standard and flawed tests similar to the results found in the study of Wadi.[10]

Including flawed items in the test leads to construct-irrelevant errors in the tests.[7] Therefore, assessment does not determine the true competence level of the students and lack construct validity. These inaccuracies resulting from the inclusion of flawed items in tests lead to the failure of the students who deserve to pass and the passing of students who deserve to fail.

Przymuszała *et al*[11] found that guidelines on writing multiple choice questions were a well-received and effective faculty development intervention. Most of the medical teachers in undergraduate institutions excel in their respective specialized fields but have little insight into the complexities of the assessment in health professional education. At the same time assessment has become a specialized field even for medical educationists. The quality of assessment cannot be improved without educating 'specialty-trained' teachers in assessment methods.

Fayyaz Khan *et al*[12] examined multiple choice questions from 2009 to 2011, finding that technical flaws in the questions were common, particularly in test-wiseness and irrelevant difficulty, highlighting the need for better MCQ quality.[12]

CONCLUSION

Tests containing in-house developed MCQs have frequent item writing flaws. The use of flawed items in the assessment has various unexpected negative consequences on students' academic achievements. In spite of acceptable psychometrics of flawed items in the tests, their inclusion in assessment did affect the passing rates of students but it was not statistically significant.

RECOMMENDATIONS

- This was a short study, a step forward but undoubtedly insufficient to settle all disagreements. A bigger, ideally multicentre, randomized control research will be required to address this problem.

- Programs for faculty development may offer the foundation needed to improve the standard of evaluation in medical institutions. The faculty frequently cites a select number of writing errors as particularly prevalent. The institution particularly the medical education department is accountable for recognizing and fixing these persistent problems during faculty development.
- The regulatory bodies must support and enable medical education departments and educators to take on the role of guardians of quality evaluation in medical institutions.

LIMITATIONS

This sample does not accurately represent the best type of multiple-choice questions used during assessments at other medical colleges nationwide because the study was only conducted at one public medical institution.

The study was also impacted by the training of the item writers because they varied in their levels of expertise across subjects. Only a small number of faculty members who had attended item writing workshops had received training. These professors were not equally spread across subjects, with some having higher quality item writers than others.

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