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Editorial **Open Access**

Telemedicine in Pakistan – Future of Healthcare Services

Iqbal Hussain Udaipurwala

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"Telemedicine is the practice of medicine over a distance, in which interventions, diagnoses, therapeutic decisions, and subsequent treatment recommendations are based on patient data, documents and other information transmitted through telecommunication systems". This is the definition of telemedicine as described by the World Medical Association (WMA) in 1999 and also adopted in 2018.[1] This form of communication can be between a clinician and a patient or between two or more clinicians or healthcare worker. With enormous change in the field of information technology, there is a radical change of people's perception regarding time and distance. Previously, for any medical expert advice, they go to their physician but today increasing number of people are seeking medical advice online. Similarly, telemedicine is very useful for patients who cannot physically consult a physician because of any reason. According to a study, until 2016, only 15.4% of the physicians in USA are utilizing telemedicine facility to interact with their patients.[2] Similarly till 2019 only 1% of the rural population in Unites States of America had any experience with telemedicine where this facility is already available.[3] No reliable statistics are available on how many people in Pakistan are utilizing facility of telemedicine or are aware of this facility.

During the COVID-19 pandemic, telemedicine usage has increased much which helped in saving human lives allowing patients and doctors to come together without infecting each other.[4] As a result of COVID-19 pandemic the concept of online 'work from home' was developed around the globe, similarly in healthcare services usage of telemedicine was popularized giving opportunity for virtual patient-physician relationship to continue.[5] In Pakistan as well during the pandemic, practice of telemedicine up surged steeply because of strict lockdown specially in major cities.[6,7,8]

Few of the advantages and benefits of telemedicine are; any patient can consult any doctor/physician in any part of the world round the clock, rural patients where healthcare facilities are very inadequate can be benefitted, patient's time can be saved that will otherwise be lost in travelling and waiting queue in the clinic, cost-effective by saving travelling expenses, carrying of disabled or bed ridden patients to clinics/hospitals can be reduced, chances of cross infection can be reduced specially in pandemics, follow-up visits can be reduced in cases of chronic and long-standing diseases etc. Another important and significant role of telemedicine is during natural disasters like earthquakes, floods, ice-storms, cyclones, land-slides, hurricanes etc. where mass mobilization of the healthcare workers to the affected site is not possible. Telemedicine stations can be set at the site of the disaster which is connected with other specialized healthcare units of the country. Telemedicine can also be employed as a method for "forward triage" to sort out different patients, visiting in emergency room in any hospital, thus it can improve efficiency to focus on critical patients more.[9] Through telemedicine, local physicians can help to generate foreign revenues to improve Pakistan's economic condition by offering medical consultation to other countries.

In spite of these unquestionable advantages of telemedicine there are many shortcomings. Due to physical distance in consultation, physician as well as patient's satisfaction is compromised and it lacks humane warmth.[10] Many of the clues can be missed as the patient's body language is difficult to assess that can otherwise help a lot in management of the disease. In addition proper clinical examination cannot be done. Although multiple aids are available for performing clinical examination during telemedicine but these cannot replace proper physical clinical examination. Another major hindrance of telemedicine is availability of good quality internet connection for seamless communication between the physician and the patient.[11] In Pakistan this issue is very pertinent as fast internet connection may not be available in remote/rural areas and even in some bigger cities. Lack of computer/smart phone literacy is another important barrier in implementing successful telemedicine practice.[12] Physician-patient relationship is very pertinent in delivery proper healthcare management. This relationship is a bit difficult to develop during telemedicine. This relationship should be seen and understood in cultural and social background of the country. The expectations of the doctor as well as patients must be addressed for successful acceptance of this program. There are so many challenges for wide acceptance of

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telemedicine in future and it is related with physicians, patients, service provider and overall health care system. Majority of the physicians otherwise with years of clinical experience are not properly trained for telemedicine and to successfully perform an online consultation with "No Touch policy" to the patient.

Different modes may be utilized for telemedicine like phone calls, video conferencing, email, texting/messaging etc. In addition different online portal are also available that provides complete solution for online consultation with video conferencing, record keeping, prescription writing, uploading investigations/radiology films etc. In Pakistan also there are so many portals for online consultation that provides all these facilities like Oladoc, Marham, Dawaai, eshifa, ringadoctor, icliniq, shifa4u and so on. These portals can be easily accessed by smart phone through its apps. With the new concept of Metaverse (virtual world with virtual and augmented reality), virtual clinics can be set up where patient and physician can meet giving a real life simulation.

In conventional physical consultation, there is a mutual trust and respect between the patients and physician. Likewise in telemedicine consultation, similar trust and respect must be present and both should reliably know and identify each other for better results. Confidentiality, privacy and data integrity of the patient must be strictly maintained by the physicians during telemedicine consultations. Patient's data and personal information obtained during this electronic process must be secured enough from unauthorized access and illegal use. Privacy of the physician can be compromised due to constant availability round the clock. He must inform the patient about the timings of telemedicine consultation and alternative arrangement in case of any emergency situation in odd hours. There are many instances where it is not advisable to do telemedicine in patient like who requires proper clinical examination, having respiratory distress, cases of acute and severe trauma, with acute and severe abdominal pain, profusely bleeding from any site, sudden unconsciousness etc.

To summarize, telemedicine is of great help and support for healthcare services especially in developing countries like Pakistan if practiced ethically and except for few instances, it can be used in almost all scenarios. Following are the recommendations to promote culture and benefits of telemedicine in Pakistan are:

1. Government policies are lacking regarding the practice of telemedicine in Pakistan. Proper policy has to be formed and its implementation should be strictly ensured.
2. Accreditation, licensure and monitoring of the online portals offering online physician consultation is required.
3. Cyber security should be strictly maintained to safeguard confidentiality, privacy and personal information of the patient.
4. Proper training of the doctors and physicians is required to use online portals and other apps for telemedicine.
5. Subject of telemedicine should be introduced in the all under-graduate curriculums of medical and health sciences.
6. Promotions regarding benefits and use of telemedicine should be done through print media, radio, television and social media etc.

Authors Contribution:
Iqbal Hussain Udaipurwala: Substantial contributions to the conception criticaly evaluation of intellectual content, final approval of the version to be published

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Original Article **Open Access**

Association of Polycystic Ovarian Syndrome with Metabolic Disorders

Saba Khan, Sana Rehman, Geeta Chughani, Memoona Rehman, Erum Majid, Farheen Amir, Khadija Bano

ABSTRACT

Objective: To determine the association of Metabolic Disorders in women of reproductive age with polycystic ovarian syndrome (PCOS)

Study Design and setting: Cross Sectional Study conducted in the Department of Gynecology and Obstetrics, Ward 9, Jinnah Postgraduate Medical Center, Karachi.

Methodology: The study was conducted from November 2021 to February 2022. A total of 227 diagnosed patients of PCOS were included in this study. Five components of Metabolic syndrome were assessed: Body Mass Index (BMI), blood pressure, central obesity, fasting blood sugar and lipid profile. Informed consent was obtained from all participants. Patients' history, physical examination and laboratory investigations in terms of symptoms and findings relating to MS were recorded and assessed using SPSS version 21. Descriptive statistics were calculated and stratification was done. Chi-square test used post stratification and p-value =0.05 were considered significant.

Results: Mean age was 27.05±4.51 years. Mean symptom duration was 11.26±3.02 months. Central obesity, hypertension, hypertriglyceridemia, HDL-cholesterol <50 mg/dl and fasting glucose >100 mg/dl were found in 44.9%, 31.7%, 38.3%, 27.3%, and 38.8% patients, respectively. A total of 47 (20.7%) study subjects were identified with two or more above components of MS. Significant association of MS with age (>27 years; p<0.000) and duration of disease (>12 months; p<0.000) was observed.

Conclusion: A higher prevalence of MS was observed when participants aged more than 27 years and had symptoms for more than a year. Higher BMI was also found nearing statistical significance.

Keywords: Central obesity, Hypertension, lipid profile, Metabolic Syndrome, Polycystic Ovarian Syndrome

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INTRODUCTION:

Polycystic ovary syndrome (PCOS) is one of the most common reproductive health problems and endocrine disorders afflicting approximately 5-8% of premenopausal women.[1, 2] Recently, a local study has quoted the prevalence of PCOS among Pakistani women as 52%.[2] It is associated with a broad range of clinical presentation including hirsutism, menstrual irregularities and infertility. Most women with PCOS have hyperandrogenemia, elevated luteinizing hormone (LH) and normal or decreased follicle stimulating hormone.[2]

PCOS is characterized by insulin resistance and compensatory hyperinsulinemia and women are often over weight. Furthermore, it is associated with dyslipidemia, systolic hypertension and hyper fibrinogenaemia. Thus women are at an increased risk of type 2 diabetes mellitus, gestational diabetes, atherosclerosis and other risks.[3] Overall, it is believed that both PCOS and metabolic syndromes are common in reproductive-aged women in the general population and that there is a substantial overlap between them.[4, 5]

In the present study, PCOS is defined based on the Rotterdam classification (ESHRE/ASRM), 2003 [6] and MS is defined based on the International Diabetes Federation (IDF) definition (Fig. 1).[7]

Rotterdam Classification of PCOS include two of the following three criteria:

1. Oligo/or anovulation

2. Clinical and /or biochemical signs of hyperandrogenism

3. Polycystic ovaries on Ultrasound exam

Metabolic syndrome (MS) is another cluster of endocrine disturbances with similar adverse outcomes as PCOS. Metabolic syndrome (MS) is a constellation of cardiovascular risk factors, including impaired fasting glucose, central obesity, dyslipidaemia and raised blood pressure (Figure.1)[1,2,5] Its clinical significance, although still debatable, lies in the fact that MS may predict a higher risk for cardiovascular events than the sum of the risks imparted by its individual components. According to one careful estimate, around 25% of world population has symptoms clearly indicative of MS. [7] Not surprisingly; untreated MS increases the risk of coronary and cerebro-vascular complications including death. MS in the presence of Type 2 Diabetes Mellitus and uncontrolled obesity further compounds the risk of long term disability as well as increases risk of mortality at an early age among the untreated population. [2, 7] Therefore, it is extremely important that risk factors of MS be identified in target populations like women with PCOS to reduce their incidence of adverse life events due to these risk factors. Researchers have identified Insulin resistance (IR) as the common denominator present in these abnormalities. [1, 2] MS has exponentially increased in prevalence during the last few years and women have seen a particularly larger share of this increase, especially in the younger age group.[5, 8, 9] The rationale of this study is to determine the frequency of MS in patients with PCOS in order to establish the local perspective as there is paucity of local data. In a recent study, the prevalence of PCOS was found to be higher in Pakistani women (52%) than among Western Caucasian women (20%–25%) in the UK.[2, 9] Therefore, the current study is planned to ascertain the prevalence and to identify it through regular screening of suspected patients to prevent adverse outcome.

METHODOLOGY:

This cross sectional study was carried out from mid-November 2021 to February 2022. A total of 227 diagnosed patients of PCOS (Rotterdam Criteria) [1,6] were recruited for this study. All had the diagnosis established for more than 6 months, or had history of repeated miscarriages or infertility and were not on any medication.

Patients were excluded from our study when their presenting symptoms did not meet the criteria for diagnosis of PCOS, or they were on various medications for other endocrine or systemic illness.

Five components of MS were assessed: Body Mass Index (BMI), blood pressure, central obesity, fasting blood sugar levels and lipid profile. Before the actual data collection, study design and data collection protocols were approved by the Institutional Review Board (IRB) via letter NO.F.2-81/2021-GENL/3727/JPMC. Informed consent was obtained from all participants in a language they could fully understand. Patients were reassessed for their suitability for the study in terms of the diagnosis of PCOS and presence of symptoms. Patients' history, physical examination and laboratory investigation in terms of symptoms and findings relating to MS were recorded and assessed using SPSS version 21. Descriptive statistics were calculated and stratification was done. Chi-square test used post stratification and p-value =0.05 were considered significant.

The sample size was estimated by considering the prevalence of MS in PCOS as 18% [10], margin of error as 5% and Confidence Interval (C.I.) as 95%. Sample size was calculated to be 227. Non probability consecutive sampling was used for the study.

RESULTS:

A total of 227 patients were included in the study with mean age of 27.05±4.51 years. The mean duration of disease of study subjects was 11.26±3.02 months. Mean height, weight and BMI of study subjects was 147.06±7.85 cm , 52.26±6.75 kg and 24.34±3.81 kg/m^2, respectively. Patients with BMI=25 kg/m^2 were considered as overweight. The mean waist circumference of study subjects was 76.92±6.71cm. The mean systolic and diastolic blood pressure of study subjects was 115.88±14.24 mmHg and 75.60±8.49 mmHg, respectively. The mean triglycerides, HDL-cholesterol and fasting plasma glucose of study subjects was 147.64±22.10 mg/dl, 56.50±10.46 mg/dl and 99.03±20.06 mg/dl, respectively.

We determined the frequency of MS in 47 patient as represented by figure 2. Stratification with respect to age, duration of disease and BMI was done to observe effect of these modifiers on outcome i.e. metabolic syndrome. P-value =0.05 was considered as significant. Metabolic syndrome was associated significantly with higher age (p=0.000) and duration of disease (p=0.000). The detailed results of frequency and associations are presented in Table1.

In our study, central obesity was seen in 102(45%) patients followed by fasting glucose (>100mg/dL) in 88 (39%).Figure 3 represents distribution of various features associated with MS.

DISCUSSION:

The present study showed a high prevalence (47; 20.7%) of MS in PCOS. During the last decade, the prevalence of MS has increased in the general population – and this increase has been steeper in women, particularly in young ones.[2,5,9]

A cross sectional study done at the Gynecologic Endocrinology Unit in Bangkok enrolled 250 PCOS Thai women who were diagnosed using Revised Rotterdam 2003 criteria and found the prevalence of MS by the definitions

Figure-1: Definition of Metabolic Syndrome for women (IDF criteria)

Central Obesity **plus any two of the below four factors defined as Metabolic Syndrome (MS)**	
Raised Triglycerides	>150 mg/dl
Low HDL	<50 mg/dl in women
High Blood Pressure	Systolic BP>130 or Diastolic >85 mmHg
High Fasting Blood Glucose	>100 mg/dl

Figure 2: Frequency of metabolic syndrome (n=227)

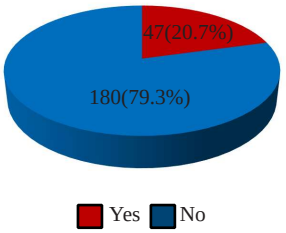
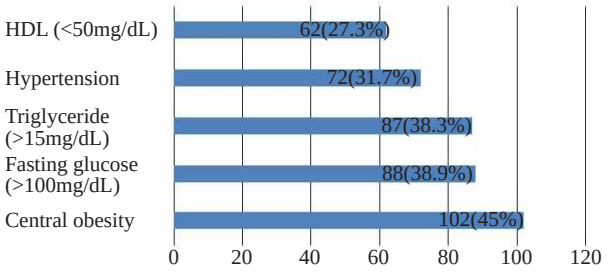


Table – 1: Frequency and Association of Metabolic Syndrome with Age, Duration of Disease and Body Mass Index (n=227)

Factor	**Metabolic syndrome**		**Total**	**P-value**
	Yes (n=47)	**No** (n=180)		
AGE				
=27 years	12 (8.9%)	123 (91.1%)	135	P<0.000*
>27 years	35 (38%)	57 (62%)	92	
Total	**47**	**180**	**227**	
Duration Of Symptoms				
=12 months	14 (9.2%)	138 (90.8%)	152	P<.000*
>12 months	33 (44%)	42 (56%)	75	
Total	**47**	**180**	**227**	
Body Mass Index				
<25	13 (14.6%)	76 (85.4%)	89	P<0.069*
=25	34 (24.6%)	104 (75.4%)	138	
Total	**47**	**180**	**227**	

Chi Square Test was applied.
P-value = 0.05 considered as significant.
* Significant at 0.05 levels.

Figure 3: Distribution of observed features of Metabolic Syndrome (MS) in The Study Population (227) Of PCOS Patients



of NCEP ATP III to be 18.0%.[10] Several international studies showed variable frequencies. Deswal et al. in a meta-analysis of well conducted studies from around the world found the prevalence of PCOS based on the Rotterdam Criteria to be between 2.2% and 22.5%.[11] Brazilian and Chinese studies found the prevalence to be 28.4% and 24.9%, respectively.[12,13] Mandrelle et al and a German study found a prevalence of 37.5% and 33.8%, respectively. [14, 15] A meta-analysis looking at the risk of MS in PCOS patients and controls concluded that there was a 2 fold risk of diagnosis of MS in women diagnosed with PCOS as compared with healthy controls. [1] Another study by Cheung et al. concluded that there is a five-fold increased risk of developing MS in women with PCOS. [13] Both PCOS and MS are closely related entities producing significant effect on fertility and having profound influence on cardiovascular morbidity and endocrine functioning. [1, 5]

This persistent increase in the prevalence is a major concern due to the potential of adversely affecting cardiovascular health profile in terms of its morbidity and mortality in women. The Metabolic derangements are more obvious in obese as compared to non-obese PCOS counterparts. [2, 13]

In the present study the relationship between a higher BMI (>25) does not reach statistical significance (table 2; p<0.069), but does show an obvious increased (1.5-fold) clinical association of a higher BMI with MS. This could be because of a smaller sample size of this study. Various studies [16, 17] have identified that Metabolic Syndrome and its individual features are quite common among patients with the BMI on the higher side. In contrast, Akram and Roohi [9] and Shanmugham et al. [17] have reported obesity in only a third of their study patients. This finding can be interpreted as a normal variance in the incidence of obesity in different geographical regions and the social norms associated with weight of a person. [2, 7]

The National Diabetes Survey of Pakistan (NDSP) reported the prevalence rate of obesity among PCOS patients as 62.1% during the years 2016-2017. [18]

This high prevalence of obesity may be responsible for the increased frequency of MS in our study population. So it is understood that MS is a common finding in obese women. However, obesity is only one of the putative denominators of MS, as the others are linked to the individual's metabolic susceptibility. [17]

The polycystic ovary syndrome (PCOS), the commonest endocrinopathy of women, has been associated with such a metabolic susceptibility, mainly attributable to the recognized association of the syndrome with insulin resistance (IR). Insulin resistance, as well as central adiposity, appears to affect not only obese but also lean PCOS women**.** Therefore, these women may be predisposed to develop MS, independently of obesity *per se*. [1 - 4, 17, 18]

An exhaustive meta-analysis by Hallajzadeh et al [1] reported

the prevalence of MS in PCOS as 37.9% and 47.5%, utilizing the NCEP III and IDF criteria, respectively. In the same NCEP III criteria a BMI in excess of 32 kg/m^2 was used as a surrogate for a waist circumference greater than 88 cm.

In our study obesity incidence was reported as 44.9% (Table 3; 102 patients) and mean waist circumference was 76.92±6.71cm (65-98 cm).

An increased waist circumference is typically highly correlated with hyper-insulinemia and is thought to reflect an increase in the proportion of total body fat that is deposited in the visceral compartment compared with the subcutaneous space. [2, 8, 19]

In our study raised fasting blood sugars of more than 100mg/dl was seen in 88 patients i.e. 30.8%. Women with PCOS are at an increased risk of developing dysglycemia due to Insulin resistance (IR). [2, 8] However, in contrast to our findings, Amato et al. noted impaired fasting glucose/T2DM in 12% of women with PCOS. [20] The observed diversity may be due to the variance in the prevalence of diabetes in different parts of the world due to various factors like dietary habits, culture of physical exercise and pre-diabetic surveillance.

Forty seven (20.7%) out of 227 patients of PCOS had at least one component of MS at presentation (Table 1). Of the individual metabolic components of MS, the most prevalent in women with PCOS was decreased serum high-density lipoprotein (HDL) cholesterol level (27.3%) followed by obesity (44.9%) and hypertension (31.7%). Out of the total study population (227 patients), 38.3 % had raised Triglycerides (Table 3). In our study, high triglycerides contributed more as compared to low HDL (27.3%) to MS. Similarly, Celik et al.[21] revealed significantly high triglyceride levels in PCOS women as compared to control.

In our study one third (72; 31.7%) of the participants with PCOS were hypertensive, and similar finding was observed in other studies.[1,2,7,9] In contrast to our finding, one study reported the frequency of hypertension in only 10.7% of study participants.[22] This disparity in data is reflective of varied lifestyles, dietary habits and medication use in different study populations representing different geographical areas.

In the present study we found a statistically significant association of MS with increasing age ($p<0.000$). MS was seen in 35 out of 92 patients (38%) of age above 27 years as compared to 8.9% in women less than 27 years (Table 2). Recent studies also reported a higher age group (above 25 years) having a higher incidence of MS in women attending infertility clinics due to PCOS. [2, 18]

In a recent study from Brazil (2020) a higher incidence of MS was reported among women with a median age 25 (21-29) and with a median BMI of 28.7. These results are in agreement with our results (Table 2). [22] It was also observed that longer the duration of symptoms of PCOS, the higher was the incidence of MS (Table 2). When the duration of PCOS was more than 12 months the prevalence of MS was 44% (33 patients) in comparison to 9.2 % when the duration of symptoms was less than 12 months.

There are some limitations to this study. The present study included a single-center experience and nonrandomized study design. It was conducted with small sample size and in an urban environment therefore, the results might not be generalizable to larger populations.

CONCLUSION:

A high frequency of MS (n=47; 20.7%) was observed in women of higher age group having a BMI above 25 and with longer duration of symptoms (>12 months) of PCOS. The findings support the inference that PCOS should be considered a general health disorder with serious public health implications and indicate that physicians should comprehensively screen all women with PCOS for the metabolic syndrome to avoid adverse health outcomes.

Authors Contribution:
Saba Khan: Concept, Design
Sana Rehman: Interpretation of data
Geeta Chughani: Design, interpretation of data
Memoona Rehman: Concept, analysis
Erum Majid: Design
Farheen Amir: Analysis
Khadija Bano: Final approval, concept

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Original Article **Open Access**

Evaluation of Antiamnesic and Cholinesterase inhibitory effects of *Illicium verum* hook.f (Star anise) against Scopolamine induced memory impairment in Mice

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ABSTRACT

Objectives: The current study is carried out on the methanol extract of *Illicium verum* hook.f (MEIV) to evaluate and examine anti-amnesic effects of *Illicium verum* hook.f by using the radial arm maze model.

Study design and setting: This experimental observational study was performed in the Department of Pharmacology, Hamdard university from 20th November 2017 to 20th May 2018. after ethical approval from Board of Advanced studies and Research under agenda item NO.5.1 held on October 20, 2016.

Methodology: Total N=30 healthy albino mice were treated with graded doses of methanol extract of *Illicium verum* hook.f (MEIV) (300 and 500mg/kg p.o.) to verify its effectiveness regarding scopolamine induce memory impairment. Afterward, in-vitro studies were performed on isolated parts of brain mice by using an F2000 fluorescent spectrophotometer (Hitachi) to analyze the acetylcholinesterase level.

Results: Investigation reveals that methanol extracts of *Illicium verum* hook.f (MEIV) by oral administration reduces the incidence of working and reference memory errors additionally this investigation was proved that active avoidance responses in scopolamine-treated group decreased. The acetylcholine esterase level was significantly reduced at the dose of 300 mg/kg (102.05±1.93µmol/min/mg) as compared to the positive control group (161.33±2.347 µmol/min/mg).

Conclusion: Based on behavioral and biochemical investigations, we concluded that MEIV produces anti-amnesic effects by the inhibition of acetylcholinesterase, which might be due to the presence of various essential phytochemicals such as alkaloids, flavonoids, triterpenoid, polyphenols. Our finding reveals that *Illicium verum is* among the screened plants to be assessed further as an herbal substitute for the treatment of Alzheimer's disease.

Keywords: Antiamnesic effect, Working memory, Reference memory, *Illicium verum* hook. f, Alzheimer's disease.

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INTRODUCTION:

Memory is the complex process of the neurocognitive system including the accomplishment of surrounding knowledge also strengthening of the obtained information and then saving it for further prospects.[1,2] Dementia is loss of memory and mental infirmity severe enough to disturb daily life activities which usually occurs in older age.[3] Neurogenerative disorders such as Alzheimer's disease (AD) and amnesia occurred as a result of discrepancies in the cholinergic nervous system.[4] Acetylcholinesterase (AChE) is an enzyme responsible to terminate cholinergic neurotransmission by hydrolysis of Acetylcholine (ACh) into acetate and choline in the synaptic cleft.[5] Neurological and psychological disorders are treated by several herbal medicines since a long time ago[6] Many preclinical studies had proposed several agents from the natural origin which increased cholinergic activity by inhibiting the cholinesterase enzyme to reduce oxidative stress and generate positive effects on learning, concentration, and memory Investigation reveals that *Illicium verum* hook. f having the property to inhibit the cholinesterase enzyme.[7]

Illicium verum hook.f (*Illiciaceae*) usually recognized as star anise, a spice consumed traditionally in Chinese medicine for thousands of years.[8] It is used as a flavoring agent in cuisine, additionally numerous therapeutic and pharmacological applications along with pharmaceutical and cosmetics employment.[9] This spice contains many major phytoconstituents including anethole (85%--90%), trans-anethole responsible for cholinesterase inhibiting activity.[10] Additional constituents including astragalin, cinnamaldehyde, citronellol, caffeic acid, kaempferol, quercetin and their derivatives p-coumaric acid, neurotropic sesquiterpenoids,

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veranisatins A, B and C, phenylpropanoids, Limone, safrol, lignans, and several others were reported as neuroprotective, cholinergic activating, and as an antioxidant agent.[11-13] Star anise has been numerous remedial and therapeutic uses such as colic, spasmodic pain, and flatulence in China and Japan. Additionally consumed as a flavoring agent for cuisine furthermore a chief part of cosmetics and pharmaceutical preparations. Keeping this view in mind that star anise has an action on the central nervous system the current investigation is designed to evaluate the anti-amnesic activity of this spice.

METHODOLOGY:

This experimental observational study was carried out in the department of pharmacology, Hamdard university from Aug 2019 to March 2020 after ethical approval by institutional review Board of Advanced Studies and Research (BASR) of Hamdard university with reference no:HU/DRA/2018/977.

The study was performed on thirty 30 healthy albino mice of either sex weighing between 25-30 grams of age (6-8 weeks). The apparent physical condition of these animals was monitored during this particular period. The laboratory environment was checked for a week, before administration of the drug. Specific changes were observed in animals like aggressive behavior, loss of hair, loss of activity, hematuria, and diarrhea, etc. Animals were housed in separate cages under standard conditions, humidity (55-60%), and temperature (23 ± 2°C) and circadian cycle of 12 hours light/dark was maintained. Mice were fed with a standard diet and water regularly. The entire experimental procedures, including the handling of animals, were operated according to the National Institute of Health guidelines and research protocol approved by the ICCBS Animal Care and Use Committee.

Fruits of Star Anise (*Illicium verum* Hook. f) were purchased from the general store in Karachi. Later on recognizing and authenticated by Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Pakistan. The voucher specimen number (IV-01-17) was issued and deposited in the Pharmacognosy Department, University of Karachi, Pakistan.

For the prepration of plant extract the dried fruits of Star anise (*Illicium verum* hook.f) in the form of raw material were washed, air-dried, crushed and the extract was prepared via the addition of 100 ml methanol in approximately 100 grams of star anise dried sample in the coarse powder form having a particle size <0.890mm. Soak it for 24 h at room temperature with occasional shaking. The saturated material was then clarified and filtrated by Whatman filter paper (150mm) and the filtrate was accumulated separately. Afterward, methanol extract was evaporated under reduced pressure in a rotary evaporator at 40 °C.[14] The final extract yield (17.5% w/w) in the dried powder form was kept at -20°C until practice.

All chemicals and drugs were utilized of analytical standard, including (Scopolamine hydrobromide, APP Pharmaceuticals, LLC, Piractim, Global Pharmaceutical, Pakistan), which was used as a standard. Ellman's reagent, Acetylcholine chloride, 5,5-dithio-bis2-nitrobenzoic acid, acetyl thiocholine iodide, trichloroacetic acid, thiobarbituric acid (TBA) purchase from Martin Dow marker specialties (Pvt) Ltd Pakistan.

According to the OECD 423 guidelines, an acute toxicity test was performed.[15] The methanol extract of *Illicium verum* (MEIV) at different doses of (100-2000mg/kg body weight) was administered orally to the normal healthy mice. After administration of the drug animals were observed for the first 4 hours. Primarily symptoms such as convulsion, tremors, salivation, diarrhea, weight loss, hematuria, loss of activity, lethargy were noticed. Similarly, as per guideline animals were observed for a further 14 days for any changes in behavior pattern and mortality. Investigation reveals that there was no toxicity up to the dose of 2000mg/kg of methanol extract of *Illicium verum* hook.f.

The several consecutive methanol extracts of *Illicium verum* hook. f. (Star anise) was directed to a preliminary phytochemical screening by employing various qualitative assays for confirming the presence of phytoconstituents. The presence of these phytoconstituents (alkaloids, carbohydrates, phenols, flavonoids, and glycosides) in *Illicium verum* was verified by thin-layer chromatography (TLC).

The animal was distributed into five groups, each group containing six animals. The resulting groups were the following.

Group 1: Vehicle control; only purified water is given to mice.

Group 2: Positive control; only vehicle was given to mice against scopolamine (1mg/kg, i.p.) induced amnesia.

Group 3: Standard drug (piracetam 200mg/kg i.p) was given to mice against scopolamine induced amnesia.

Group 4: Test drug 1 (MEIV 300 mg/kg, p.o) treated mice against scopolamine-induced amnesia.

Group 5: Test drug 2 (MEIV 500 mg/kg, p.o) treated mice against scopolamine-induced amnesia.

Active avoidance test is used to assess the associative learning about the animal. A significant increase in the active avoidance test is the principal determinant for improved cognitive activity.[16] A radial arm maze model was modified to assess the memory function of animals. The radial arm maze consists of eight (8) arms extended to an octagonal-shaped and 30 cm diameter of a central hub. The platform of the radial maze is 40 cm above the floor. At the end of each arm contains a small black metal cup which is 3cm in diameter and 2 cm deep that serves as a receptacle for reinforces food.

Memory was assessed on pre-selected animals in one day

exercising track. An experimental trial was started by placing a food pellet on one receptacle. All night fasted rats were retained in the central hub of arm maze and permitted them to select the arm freely to pick up the food. A trail was completed vigilantly when mice visited all eight arms. Each entry into the arm was noted as the correct response, in which mice were not entered previously; however, re-entries were recorded as an "Error". A "successful" trial (animals made no or only one error out of eight choices) was recorded. 60 minutes after administration of the last dose at eight days, animals of corresponding groups were exposed to drug scopolamine (1mg/kg i.p) for the induction of amnesia. Subsequently, after 30 minutes each animal one by one were placed in the central hub and tested for another successful trial. Afterward trained rats were chosen for analysis. Animals were dosed once a day for 8 days with their respective drugs. On the 8th-day scopolamine 1, mg/kg was given 45 minutes before the treatment and after one hour all animals were tested on the behavior model (radial arm maze). Each successful trial was recorded by a single investigator.[16,17]

After 24 hours of concluding behavioral test, animals were euthanized by cervical displacement with care and the whole brain were removed. Afterward, the brain were homogenized with ice-cold phosphate buffer having pH 8. The homogenates (10% w/v) were then centrifuged at 10,000 rpm in a centrifuge machine (Biofuge) for 15 min and the supernatant liquid was used for the biochemical estimations.

Acetylcholinesterase (AChE) (enzyme considers as a marker for loss of cholinergic neurons in the forebrain) activity was measured by Ellman method.[18] The assay mixture consists of supernatant (0.4 ml), phosphate buffer of pH 8 (2.4ml), 20 ul of acetylcholine iodide and 100ul of DTNB (5,5-dithionitrobenzoic acid) (Ellamn reagent). The biochemical reaction of the choline with dithiobinitobenzote ion was producing a yellow color end product. The optical density of the yellow color compound was measured by an F2000 fluorescent spectrophotometer (Hitachi) at 412nm for 10 min at 2 min intervals. AChE activity was specified in 1mol/min/mg of protein.

SPSS version 23.0. was used for data analysis. Statistical analysis was performed by applying one- way ANOVA follow by Bonferroni's test. All value was presented as mean ± Standard error mean (SEM) and P value <0.05 was considered as a significant statistically.

RESULTS:

The mice treated with MEIV dose from 100-2000mg/kg, p.o., showed normal behavior. All animals were alert with normal touch and pain response. There was no sign of apathy and inactiveness was noticed at all doses. However, slight convulsions were observed at higher doses. The other effects like loss of hair, aggressive behavior, and diarrhea, blood in urine, tremors, salivation and lethargy were not observed. The motor activity of all animals was normal and exhibits no sign and symptoms of depression. Attentiveness, muscle tone and grip strength of limbs along with the walking pattern of the animal were typical. The toxicity study reveals that the extract was safe up to the doses of 2000 mg/kg in mice.

Numbers of avoidance were found to be significant (P<0.05) reduce in the group treated with scoplamine as compared with control group (Table 1). Conversely piracetam, which is a standard drug showed significant results. Similarly, test drug MIEV at the dose of (300 and 500 mg/kg, p.o.) appeared to indicate the protective effects against memory impairment by scopolamine induction thru inhibiting the less number of avoidances. However, MEIV at the dose of 500mg) 10.16 ± 0.41s showed more noticeable results contrary the dose of 300 mg/kg by the cumulative increase in the avoidance reactions 8.69 ± 0.33s as compared to positive control group 6.13 ± 0.45s. Working memory errors were significantly (P<0.05) raised in animals treated with scoploamine as compared to control group. While animals group pre-treated with (300 and 500 mg/kg, p.o.) with MEIV and (200mg/kg, i.p.) treated by standard drug (piracetam) showing a significant reduction of working memory errors when contrasted with the positive control group 19.7 ± 0.11s as presented in (Table-2). Lower dose of MEIV i.e. is 300mg dose has revealed more clear and noticeable outcomes 12. 7 ± 0.15s to reduce the errors of working memory. The incidence of reference memory errors was less appearing in the group receiving the standard drug (piracetam) and the animal group treated with MEIV (300 and 500 mg/kg, p.o.). Each group is comparatively observed in the positive control group as displayed in (Table-3). *Illicium verum* improving memory by inhibiting reference memory errors. Low dose (300 mg/kg p.o.) of MEIV revealed more noticeable results 9.1 ± 1.19s in decreasing the incidence of reference memory errors as compared positive control group 19.6 ± 1.30s and standard drug group 9.4 ± 1.55s. Brain actylcholine-estrase level was decreased at the dose of 500mg of MEIV (P<0.05) as shown in (Table-4) highly significant result 102.05±1.93 and 300mg of MEIV show significant 122.98±2.15 result as compared to the positive control group. However positive control group that (scopolamine treated) raised the level acetylcholinestrase 161.33±2.347 in brain as compared to control group treated mice.

DISCUSSION:

Alzheimer's disease (AD) is an irreversible neurodegenerative disease with the manifestation of many neuropsychiatric and cognitive impairment that leads to progressive disability and incapacitation in old age.[4] The neurotransmitter of the cholinergic system plays a major role in the regulation of cognitive function. According to the researcher's loss of cholinergic neurons in the area of the brain, the cortex reduces the synthesis of acetylcholine neurotransmitters, which is the main featuring of AD.[19] This process can be inhibited by inactivating acetylcholinesterase (AChE), an

Figure 1: Radial arm maze Model for Sample recording

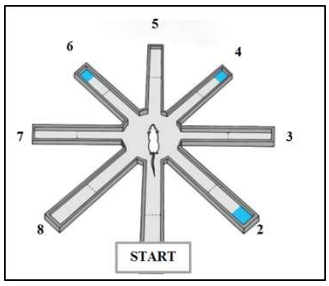

Table 1: Effects of *Illicium verum* hook. f. (Star anise) on active avoidance response against scopolamine induce amnesia

Groups (n = 6)	Treatment	Response of Active avoidance (s)
1	Control (Vehicle)	13.10 ± 0.22
2	Positive (Scoplamine 1mg/kg, i.p)	6.13 ± 0.45*
3	Standard (Piracetum 200mg/kg,i.p)	12.16 ± 0.13#
4	Test 1 (MEIV 300 mg/kg, p.o)	8.69 ± 0.33#
5	Test 2 (MEIV 500mg/kg, p.o)	10.16 ± 0.41#

N = 6, All values are presented as mean ± S.E.M.
P < 0.05 considered as statistically significant.*P < 0.05 compared with the normal control group.
#P < 0.05 compared with the scopolamine treated group. Statistical analysis was done by using one way ANOVA followed by Boneferroni test.

Table 2: Effects of *Illicium verum* hook. f on working memory against scopolamine induced impairment

Groups (n = 6)	Treatment	Working memory error (s)
1	Control (Vehicle)	7.9± 0.13
2	Positive (Scoplamine 1mg/kg, i.p)	19.7 ± 0.11*
3	Standard (Piracetum 200mg/kg,i.p)	13.0 ± 0.23#
4	Test 1 (MEIV 300 mg/kg, p.o)	14.3 ± 0.31#
5	Test 2 (MEIV 500mg/kg, p.o)	12.7 ± 0.15#

N = 6, All values were presented as the mean ± S.E.M.
P < 0.05 considered as statistically significant.*P < 0.05 compared with the normal control group.#P < 0.05 compared with scopolamine.Statistical analysis was done by one way ANOVA followed by Boneferroni test.

Table 3: Effects of Methanolic extract of *Illicium verum* hook. f on impairment of reference memory

Groups (n = 6)	Treatment	Reference memory error (s)
1	Control (Vehicle10 ml/kg))	7.3 ± 1.21
2	Positive (Scoplamine 1mg/kg.ip)	19.6 ± 1.30*
3	Standard (Piracetum 200mg/kg.i.p)	9.4 ± 1.55#
4	Test 1 (MEIV 300mg/kg.p.o)	9.1 ± 1.19#
5	Test 2 (MEIV 500mg/kg.p.o)	13.3 ± 1.40#

Abberivation: MEIV (methanol extract of *Illicium verum*), p.o per oral,i.p intraperitonial
N = 6, All values were presented as the mean ± S.E.M. P < 0.05 was considered a significant.*P <0.05 compared with the normal control group.# P< compared with the scopolamine treated group. Statistical analysis was performed by applying one- way ANOVA follow by Boneferroni test.

Table 4: Effects of Methanol Extract of *Illicium verum* on acetylcholinestrase level in scopolamine

Groups (n = 6)	Treatment	AchE(µmol/ min/mg protein
1	Control (Vehicle)	85.04±1.760
2	Positive control (Scopolamine1mg/ kg,i.p)	161.33±2.347*
3	Standard Drug (Piracetum 200mg /kg, p.o)+(Scopolamine 1mg/kg,i.p)	97.55±1.36#
4	Test drug 1 (MEIV 300mg/kg, p.o) + Scopolamine	122.98±2.15#
5	Test drug 2 (MEIV 500mg/kg, p.o) + Scopolamine	102.05±1.93#

enzyme responsible to cleave acetylcholine and terminates neuronal signaling. Centrally acting cholinergic drug Scopolamine causing cognitive impairment.[20] Therefore such drug treatment is required which reduces cognitive impairment by increasing cholinergic neurotransmission in AD patients. Cognitive deterioration associated with age progression as a result of oxygen-free radical develops Alzheimer's disease in older people.[21] It has been proved from previous studies that *Illicium verum* possesses antioxidant activities as well. Previous investigations revealed that antioxidant properties of *Illicium verum* produce neuroprotective effects by decreasing oxidative stress in brain cells as a result of which reduction in brain damage along with improvement of neuronal function.[22] Dementia symptoms develop due to impaired neurotransmission and deterioration of neuronal circuits in the brain areas. In the brain of AD patient progressive loss of cholinergic neurons occur leading to the reduction of acetylcholinesterase level and cognitive deterioration.[23]

Previous studies reported that anethole is the major constituent abundantly present in *Illicium verum* responsible for enhancing memory and cognition by inhibiting the cholinesterase enzyme. Previous studies reported that some other active constituents of this plant such as flavonoids, quercetin, and Kaempherol also generating CNS effects.[24,25]

Previous pharmacological studies with *Illicium verum* showed that this spice possessed antioxidant and anxiolytic properties. In the current study, we examined that pre-treatment with MEIV at the dose of (300 and 500mg/kg) decreases enzyme acetylcholinesterase level and improved cognitive memory in mice on the behavioral model on a radial arm maze model which is based on appetite motivated task.

CONCLUSION:

Based on a current investigation we concluded that *Illicium verum* possesses antiamnesic effects which might be may the existence of major phytoconstituents such as flavonoids, sesquiterpenes, and polyphenol having the ability to inhibits acetylcholinesterase.

Authors Contribution:
Hafiza Tuseef Sayyar: Perceived the idea, conducted research, write-up of manuscript data analysis.
Muhammad Liaquat Raza: Supervised the wholeproject, critically examined the manuscript.
Syeda Rida Baqir: Bibliography and help in data analysis

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Original Article **Open Access**

Acanthosis Nigricans in Patients with Type II Diabetes Mellitus at a Tertiary Care Hospital of Lahore

Nauman Ismat Butt, Khalid Mahmood, Nimra Kanwal, Fahmina Ashfaq

ABSTRACT

Objective: Acanthosis Nigricans is characterized by skin thickening with hyperpigmentation dermatosis predominantly seen on flexural aspects & nape of neck. The objective of present study was to determine frequency of Acanthosis Nigricans among patients of type II diabetes mellitus.

Study Design and Setting: This observational cross-sectional study was undertaken at Department of Medicine Azra Naheed Medical College, Superior University Lahore from August 2021 to April 2022.

Methodology: Type II diabetes mellitus was defined as patients with HbA1c 7.0%, or two blood glucose random readings of =200mg/dl, or previous history of diabetes diagnosis, or taking anti-hyperglycemic medicines. Acanthosis Nigricans was defined as >2 cm poorly defined hyperpigmented skin lesions of brownish black color and velvety appearance present over the nape of neck, axillae and/or groin. Patients with non-diabetic causes of Acanthosis Nigricans were excluded. After informed consent, 340 patients of type II diabetes mellitus aged 30-75 years of both gender were enrolled using non-probability consecutive sampling technique. Demographic information was noted and the patients were examined for Acanthosis Nigricans. Data was entered and analyzed by SPSS version 20.0.

Results: Mean age was 48.2+13.8 years with 187 (55.0%) females. The mean height, weight and BMI were 1.5+0.3 meters, 57.8+11.6 kilograms and 28.8+9.5 kg/m^2 respectively. The mean duration of disease was 44.2+9.3 months and Acanthosis Nigricans was seen in 86 (25.2%). Acanthosis Nigricans was not significantly associated with age, gender, BMI or duration of disease.

Conclusion: Acanthosis Nigricans was present in almost a quarter of type II diabetes mellitus patients.

Key words: Acanthosis Nigricans, Insulin Resistance,Type II Diabetes Mellitus.

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INTRODUCTION:

Type II Diabetes Mellitus is characterized by hyperglycemia due to pathological processes such as increased insulin resistance and/or reduced insulin secretion.[1] Rising worldwide and International Diabetes Federation estimates that up to 552 million people will be affected by diabetes by 2030.[2] Pakistan is one of the top 10 countries according to diabetes prevalence. Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acanthosis Nigricans is characterized by skin thickening with hyperpigmentation dermatosis predominantly seen on flexural aspects and nape of neck.[3] High insulin levels are thought to play a role in pathogenesis of Acanthosis Nigricans.[4] By virtue of this association, it may be linked to increased risk for type II Diabetes Mellitus.[5]

The complications of diabetes affect nearly every tissue of the body and diabetes is a leading cause of cardiovascular morbidity and mortality, blindness, renal failure and amputations. Further, the early diagnosis of type 2 diabetes in adolescents and young adults (up to age 40 years) has been linked to a more aggressive form of the disease, with premature development of serious complications. Together, these sobering statistics underscore the vital importance of uncovering the root causes of diabetes and its complications in order to best design strategies for therapeutic intervention in this disorder. Patients with Acanthosis Nigricans due to diabetes generally suffer few or no skin complications and have a good prognosis with potentially complete resolution with adequate treatment and glycemic control. High-risk populations for development of Acanthosis

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Nigricans are African-Americans, Hispanics, and Native Americans, although this condition presents in all races. There are various studies that indicate different frequencies of several skin manifestations including Acanthosis Nigricans in type II diabetes mellitus and this variability maybe related to ethnicity.[3] Litonjua et al. reported Acanthosis Nigricans in 52.6% African-Americans as compared to 35.9% in Latin-American[6]. Burke et al. demonstrated It to be in 41.1% in diabetics opposed to 31.6% in non-diabetics[7]. Grandhe et al. reported its frequency to be 62.6% in diabetes mellitus compared to 40% in controls[8]. One study from India demonstrated Acanthosis Nigricans in 5.9% of diabetes mellitus patients.[9] Another study showed 11.6% prevalence in diabetics.[10] Although studies have been unable to establish a distinct link of Acanthosis Nigricans with type II diabetes mellitus, its association with raised insulin levels is well studied in literature and this suggests the possibility of an association of these conditions indicating that patients with Acanthosis Nigricans may be at elevated risk to develop type II diabetes. Furthermore it may be recognized as a cutaneous marker in type II diabetes.

Given the variable but markedly high presence of Acanthosis Nigricans in diabetes mellitus, it may be used as a cutaneous marker for patients with type II diabetes mellitus. Whether ethic differences play a role in pathophysiology of Acanthosis Nigricans in diabetes is not known. The association of acanthosis nigrcans, diabetes mellitus, hyperinsulinemia and insulin resistance highlight importance of incorporating it as a clearly visible cutaneous marker of diabetes, identifying patients who are at risk to develop diabetes, and thereby helping patients to institute lifestyle modifications to avert this potentially life-altering disorder to reduce disease morbidity and disability. Furthermore, Acanthosis Nigricans may aid in identification of patients that already have developed diabetes but are undiagnosed as diabetes may remain asymptomatic initially. Diagnosing diabetes in the initial stages leads to early treatment and glycemic control thus reducing long-term diabetes complications. The rationale of our study was to document presence of Acanthosis Nigricans among type II diabetes mellitus patients presenting to Department of Medicine, Allama Iqbal Medical College, Jinnah Hospital Lahore Pakistan so as to provide evidence for Pakistani population and to reduce scarcity of local data.

METHODOLOGY:

Data collection was done after taking approval from Institutional Review Board of Azra Naheed Medical College, Superior University Lahore Pakistan. The present observational cross-sectional study was conducted to find out prevalence of Acanthosis Nigricans among patients of type II diabetes mellitus at Department of Medicine Jinnah Hospital, Allama Iqbal Medical College Lahore Pakistan from August 2021 to April 2022. Type II diabetes mellitus was defined as patients with HbA1c of greater than 7.0%, or two blood glucose random readings of =200mg/dl, or previous history of diabetes diagnosis, or taking anti-hyperglycemic medicines. Acanthosis Nigricans was defined as >2 cm poorly defined hyperpigmented skin lesions of brownish black color and velvety appearance present over the nape of neck, axillae and/or groin. A sample size of 340 was calculated with confidence level 95% and margin of error 5% taking expected frequency as 5.8% as reported by Khokharo et al.[11] Patients with non-diabetic causes of Acanthosis Nigricans (endocrine disorders such as acromegaly, hypothyroidism, polycystic ovarian syndrome, Cushing's disease; malignancies of liver, lung, gastrointestinal tract, uterus; and drugs such as corticosteroids, nicotinic acid, oral contraceptives), pregnant females and patients already on treatment for Acanthosis Nigricans as assessed by detailed history and examination were excluded from the study.

After obtaining written informed consent, 340 patients of type II diabetes mellitus (both new cases and previously diagnosed as per operational definition) aged 30-75 years of both genders were included in the study using non-probability consecutive sampling technique. Demographic information including age, gender, weight, height, BMI and duration of disease were noted and the patients were examined for Acanthosis Nigricans. Data was entered and analyzed by SPSS version 20.0. Mean and standard deviation were calculated for quantitative variables like age, BMI (the WHO and NIH guidelines for Asian individuals define overweight as a BMI between 23 and 24.9 kg/m^2 and obesity as a BMI >25 kg/m^2) and duration of disease[12]. Frequency and percentage were calculated for qualitative variables like gender. Data was stratified to address effect modifiers by using Chi-square test with p-value <0.05 as significant.

RESULTS:

A total of 340 patients were enrolled in this study having mean age of 48.2+13.8 years with 153 (45.0%) males and 187 (55.0%) females as shown in Table 1. Ninety-two (27.1%) patients were <52 years of age while 248 (72.9%) patients were aged >53 years. The mean height, weight and BMI of the patients were 1.5+0.3 meters, 57.8+11.6 kilograms and 28.8+9.5 kg/m^2 respectively. Normal BMI was seen in 132 (38.8%) patients while 208 (61.2%) patients were overweight and obese. The mean duration of disease was 44.2+9.3 months with 213 (62.6%) patients having >24 months disease duration. In our study, Acanthosis Nigricans was seen in 86 (25.2%) patients as shown in Table 1. Stratification of data according to Acanthosis Nigricans is shown in Table 2.

In our study, Acanthosis Nigricans did not have a statistically significant association with age (p-value: 0.091), gender (p-value: 0.753), BMI (p-value: 0.833) or duration of disease (p-value: 0.360) as shown in Table 2.

Table 1: Demographic and Clinical Variables of the Patients

Mean Age	48.2+13.8 years
Mean Height	1.5+0.3 meters
Mean Weight	57.8+11.6 kilograms
Mean BMI	28.8+9.5 kg/m^2
Mean Duration of Disease	44.2+9.3 months
Age Groups:	
30-52 years	92 (27.1%)
53-75 years	248 (72.9%)
Gender:	
Male	153 (45.0%)
Female	187 (55.0%)
BMI:	
17-24 kg/m^2	132 (38.8%)
>25 kg/m^2	208 (61.2%)
Duration of disease:	
<24 months	127 (37.4%)
>24 months	213 (62.6%)
Acanthosis Nigricans:	
Present	86 (25.2%)
Absent	254 (74.8%)

Table 2: Stratification of Demographic and Clinical Variables with regards to Acanthosis Nigricans

Demographic and Clinical Variables	Acanthosis Nigricans		p-value
	Present	Absent	
Age (years):			
30-52	37 (24.1%)	116 (75.9%)	0.091
53-75	49 (26.3%)	138 (73.7%)	
Gender:			
Male	16 (17.3%)	76 (82.7%)	0.753
Female	70 (28.2%)	178 (71.8%)	
BMI (kg/m^2):			
17-24	34 (25.7%)	98 (74.3%)	0.833
>25	52 (25.0%)	156 (75.0%)	
Duration of disease (months):			
<24	37 (29.2%)	90 (70.8%)	0.360
>24	49 (23.0%)	164 (77.0%)	

DISCUSSION:

In our study with 340 patients of type II diabetes mellitus, Acanthosis Nigricans was seen in 86 (25.2%). Khokharo et al. showed Acanthosis Nigricans in 5.8% diabetes patients from Sindh[11]. In Karachi, Niaz et al. found Acanthosis Nigricans in 20% patients of diabetes with higher incidence in females and patients with poor diabetes control[12]. In Battgram Khyber Pakhtunkhwa, Ahmed et al. reported Acanthosis Nigricans in 2.9% of diabetes patients[14]. In Ludhiana India, Deepika et al. reported prevalence of Acanthosis Nigricans as 10.9% in diabetics[15]. There is a great variability in its prevalence in type II diabetes mellitus and these differences may be related to ethnicity even in the residents of a same geographical area which was also the case with results of our study.

Although studies have been unable to establish a distinct link of Acanthosis Nigricans with type II diabetes mellitus, its association with raised insulin levels is well studied literature and this suggests the possibility of an association of these conditions indicating that patients with Acanthosis Nigricans may be at elevated risk to develop type II diabetes. Furthermore, it may be recognized as a cutaneous marker in type II diabetes. It has been found in many studies that Acanthosis Nigricans is associated with insulin resistance or hyperinsulinemia, which are considered to be the major factors in the pathophysiology of type 2 diabetes, in a large number of patients.[5,16] Kobaissi et al. studied a population of overweight Hispanic children to determine if there was a relationship between Acanthosis Nigricans and insulin sensitivity, independent of the fat content of the body, and found that it was indeed an independent risk factor for the development of insulin resistance[16]. Kong et al. found that patients with this skin condition were almost twice as likely to have type 2 diabetes compared with patients without it, after controlling for age, BMI, and several other risk factors for type 2 diabetes including race, hypertension and family history of type 2 diabetes[5]. A high prevalence of this skin condition was also found in a population of the native Americans of Texas and Nebraska by Stuart et al. who concluded that presence of Acanthosis Nigricans in this population suggested the presence of insulin resistance and therefore its clinical detection may help to identify individuals who are at a high risk for developing the disease[17]. In our study, Acanthosis Nigricans was seen in 52 (25.0%) of overweight and obese patients as compared to 34 (25.7%) patients with normal BMI. Furthermore Acanthosis Nigricans was not significantly associated with age (p-value: 0.091), gender (p-value: 0.753), BMI (p-value: 0.833) or duration of disease (p-value: 0.360).

While the goal of therapy is to treat the primary cause, cosmetic resolution of Acanthosis Nigricans lesions can be important for patients and their quality of life. Treatment options for Acanthosis Nigricans have not been extensively studied; however, smaller powered clinical trials and case reports exist in the literature.[18] Patients with Acanthosis Nigricans due to diabetes generally suffer few or no skin complications and have a good prognosis with potentially complete resolution with adequate treatment and glycemic control.[19] It can fade over time with treatment of insulin resistance and controlling blood glucose by diet and exercise as weight loss and correction of insulin resistance reduces the hyperkeratotic lesions.[20] Topical ointments using keratolytics like topical retinoids and podophyllin may aid in lightening skin in selected patients mainly for cosmetic reasons.[21] Topical vitamin D analogs reduce keratinocyte

proliferation and may improve lesions of Acanthosis Nigricans.[22] However success rates of topical treatments is variable. Other agents that have been tried include metformin, rosiglitazone, melatonin and etretinate.[23] Octreotide also has been shown to improve Acanthosis Nigricans in insulin resistance. While these studies have the potential to shed light on its therapy, clinical trials are needed to examine topical and oral treatment options specifically for the improvement of skin lesions. The current literature that exists is limited, and higher powered studies with larger patient populations are needed to further elucidate the Acanthosis Nigricans treatment paradigm.

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the β-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action.[2] The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues.[1] Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia.[3] The complications of diabetes affect nearly every tissue of the body and diabetes is a leading cause of cardiovascular morbidity and mortality, blindness, renal failure and amputations. Further, the early diagnosis of type 2 diabetes in adolescents and young adults (up to age 40 years) has been linked to a more aggressive form of the disease, with premature development of serious complications. Together, these sobering statistics underscore the vital importance of uncovering the root causes of diabetes and its complications in order to best design strategies for therapeutic intervention in this disorder. Type II Diabetes Mellitus, characterized by hyperglycemia due to pathological processes such as increased insulin resistance and/or reduced insulin secretion,[1] rising worldwide and International Diabetes Federation estimates that up to 552 million people will be affected by diabetes by 2030.[2] Pakistan is one of the top 10 countries according to diabetes prevalence.

Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision.[1] Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome.[2] Long-term complications of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints; and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction.[24]

There are a few limitations of our study as well. Our study is a descriptive non-randomized cross-sectional study and therefore limited due to patient selection bias. A single center-based study having a relatively small sample size, our results may not be generalized to general population. Our study should be used as a stepping stone based on which further studies should be conducted to collect further evidence. The association of Acanthosis Nigrcans, diabetes mellitus, hyperinsulinemia and insulin resistance highlight importance of incorporating it as a clearly visible cutaneous marker of diabetes, identifying patients who are at risk to develop diabetes, and thereby helping patients to institute lifestyle modifications to avert this potentially life-altering disorder to reduce disease morbidity and disability. Furthermore Acanthosis Nigricans may aid in identification of patients that already have developed diabetes but are undiagnosed as diabetes may remain asymptomatic initially. Diagnosing diabetes in the initial stages leads to early treatment and glycemic control thus reducing long-term diabetes complications. With more information on therapies that treat the underlying causes of Acanthosis Nigricans, as well as treatment options for the cosmetic appearance of lesions, providers will have the opportunity to treat patients underlying diseases and the psychological consequences of the Acanthosis Nigricans to improve patient quality of life.

CONCLUSION:

We found Acanthosis Nigricans to be present in a quarter of patients with type II diabetes mellitus amongst our sample population. Acanthosis Nigricans was not significantly associated with age, gender, BMI or duration of disease in the present study. However still the its presence in some patients with diabetes mellitus highlight importance of incorporating it as a clearly visible cutaneous marker of diabetes, identifying patients who are at risk to develop diabetes, and thereby helping patients to institute lifestyle modifications to avert this potentially life-altering disorder to reduce disease morbidity and disability.

Authors Contribution:
Nauman Ismat Butt: Conception and design, Analysis and interpretation of the data, Literature review and drafting of the article
Khalid Mahmood: Collection and assembly of data, Critical review and revision of the article
Nimra Kanwal: Conception and design, Literature review and drafting of the article
Fahmina Ashfaq: Collection and assembly of data, Critical review and revision of the article

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Original Article **Open Access**

Self-Medication Among the Elderly and Factors Associated with It

Zaheer Ali, Rabeeya Saeed, Fatima Kanwal, Faridah Amin, Noureen Durrani, Areeba Abdullah

ABSTRACT

Objective: Our study aims to assess the frequency of self-medication in elderly people of Karachi, identify its reasons and associated risk factors.

Study Design & Setting: This cross-sectional study was conducted in waiting areas of OPDs at Liaquat National hospital and its outreach centers.

Methodology: Study duration was June-December, 2021. We approached all patients and aged 60 years and above. After taking written informed consent, targeted population was interviewed to find out self-medication performed within last three months and its reason and causes. Participants' demographics, symptoms for which self-medication was performed, different type of medications used, reasons of opting self-medication and different approaches for dose adjustment were also investigated. Data was recorded by a pre-designed questionnaire. Data was analyzed using SPSS version 21.

Result: Out of 200 elderly included in the study, 87% of them reported self-medication in a 3-month recall period. Pain (63.8%), fever (56.9%), headache (50%), cough, and cold (37.4%) were the most common symptoms. Pain killers (81.6%), fever-reducing drugs (58%) and cough syrup (39.1%) were the top three medicines used for self-medication. One-fifth of the respondents reported self-medication of antibiotics. Top three frequent reasons for self-medication were convenience (99.4%), disease of mild nature (85.1%) and for quick relief of symptoms (78.7%). None of the patient's demographic factors were found to be associated with self-medication practice.

Conclusion: Self-medication is a highly prevalent practice in elderly people of Karachi including non-prescribed usage of antibiotics. Major reforms in primary health care are needed to address this growing problem.

Keywords: Elderly, Frequency, Geriatric, Prevalence, Self-medication

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INTRODUCTION:

The World Health Organization (WHO) defines self-medication (SM) as the selection and utilization of medicines to treat self-recognized symptoms or ailments without consulting a physician.[1] It also encompasses the use or re-use of previously prescribed or unused prescriptions, the purchase of prescription drugs without consulting a physician, and the irrational use of over-the-counter medications.[2] Self-medication is a major worldwide issue that affects both industrialized and developing countries.[3, 4] According to several researches, self-medication has a frequency of 32.5–81.5 percent globally.[5] The most commonly self-prescribed medications are analgesics, antipyretics, antitussives, antidiarrheal, calcium and vitamin supplements, anabolic steroids, sedatives, certain antibiotics, and many herbal and homeopathic remedies.[3]

The proportion of adults of age >60 years are growing globally. In 2019, there were 1 billion people over the age of 60. This number is predicted to increase to 1.4 billion by 2030 and 2.1 billion by 2050. Low- and middle-income nations will house 80 percent of all elderly people by 2050[6].

Pakistan, with a population of 207.7 million people, is one of Asia's five biggest countries. Our current population

growth rate of 2.4 outpaces all of its neighbors. By 2050, Pakistan is predicted to have 26 million people aged =65 years.[7] Elderly have many changes in physical functioning that impact drug metabolism. They have several co-morbids, making them more vulnerable to the risks of self-medication.[8]

The downsides of self-medication, among the elderly, should be noted. Among them are excessive costs, delayed diagnosis and suitable therapy, potential dangers of combinations with prescription medications, bacterial resistance, adverse reactions, and intoxication.[9]

Majority of pharmacies in Pakistan sells medications without a prescription. As a result, antibiotics and potentially habit-forming drugs, notably benzodiazepines, are freely available. Because of this, as well as a lack of knowledge, the general population is uninformed of the possibly fatal repercussions of several of these drugs. The general public is forced to seek help from sources other than doctors due to a lack of a solid primary health care system and cost concerns. In Pakistan, there have been very few studies on self-medication, which has also revealed high rates of prevalence of around 51%[10]. This percentage is significantly higher in rural areas due to a lack of healthcare facilities. 70% of Pakistan's population does not have easy access to medicines or doctors[11]. It is especially concerning because, despite efforts to contain the problem, prevalence rates are rising.

Keeping in mind the increasing number of the elderly in society, the side effects of using non-prescribed medicine, is cultural patterns. The current study was conducted to investigate self-medication practice and its reasons and related factors among the elderly population presenting to Primary care clinics of a tertiary care hospital.

METHODOLOGY:

This cross-sectional study was conducted after taking ERC approval (App# 0654-2020 LNH-ERC) from Liaquat National Hospital. Based on 84.68% estimated prevalence of self-medication in Pakistan, sample size was calculated via Open-Epi tool with 95% CI and 5% margin of error, which came out to be 200[11]. We approached all patients and their attendants aged 60 years and above in the waiting areas of Outpatient clinics and Outreach centers of Liaquat National Hospital. People not willing to participate were excluded. After taking written informed consent, the elderly were interviewed to find out self-medication performed within last three months. The assigned data collector (medical student) was given training to conduct the interview and gather the data on a predesigned questionnaire. Participants' demographics, symptoms for which self-medication was performed, different type of medications used, reasons of opting self-medication and different approaches for dose adjustment were also investigated.

Data was entered and analyzed using SPSS version 22. Categorical variables were expressed as frequency and percentage. Numerical variable 'age' was expressed as median with interquartile range (IQR) after testing normality with Shapiro-Wilk test. Binary logistic regression was run to ascertain factors' association with self-medication in terms of odd ratio and their 95% confidence interval. Variable significant with $p<0.25$ in univariate analysis were used for building multivariable regression model. On final regression model, statistical significance was defined as two tailed p-value less than or equal to 0.05.

RESULTS:

A total of 200 participants were interviewed, with median age of 65 (IQR=62-70) years. Majorities were males (52.5%) and married (70%). Participants of different mother tongue such as Urdu (43.5%), Sindhi (13.5%), Punjabi (10.5%), Pashto (9.5%) and of other regional languages (23%) participated into the study. 41% were graduates, 15.5% primary pass, 18% secondary pass and 17.5% post-graduates. Few were uneducated (8%). Majority of the participants were unemployed (43.5%). 15.5%, 19.5%, 21.5% were self-employed, retried, working in private sector and part-timers respectively. Most participants had monthly income <25K (60%). Some reported their monthly income was 26-50K (14.5%), 51K-75K (9%), 76-100K (6%) and >100K (10.5%). Participants had diabetes (29%), hypertension 35.5%), osteoarthritis (19.5%) and ischemic heart diseases (10%).

87% reported that they self-medicated without prescription in the last 3 months. Figure 1 depicts different conditions for which self-medication was done. Table 1 represents reasons for using self-medications. All participants reported that medications are available at their home. Figure 2 shows the usage of different medications among study participants.

Participants reported that pain killers (99%), fever reducing drugs (94%), anti-allergy (48%), cough syrup (73.5%), anti-depressant (10.5%), anti-diarrheal (45%), antibiotics (88%), multivitamins (57%), sleeping pills (22%), weight reducing pills (2%), sexual activity enhancement pills (6.5%), homeopathic medicines (14%), herbal medicines (11%) were available at their home. Table 2 represents ways of deciding dosage. 90.5% participants always check the expiry date of medicine before using it whereas 5.5% check it sometimes and 4% never check it. 57% participants considered self-medication as an acceptable practice.

Table 3 shows the comparison of participants' characteristics among those practiced and did not practice self-medication. None of the factors was found to be associated with practice of self-medication. Based on the criteria of $p<0.25$ in univariate analysis, only two variables age and gender were candidates to be enter in multivariable model. Multivariable regression analysis showed that age (aOR=1.04, 95% CI: 0.98-1.11, p=0.210) was significantly associated with practice of self-medication during past 3 years. The likelihood of performing self-medication was higher in males than females but statistically it was not significant (aOR=2.14, 95% CI: 0.88-5.21, p=0.094).

Figure 1: Frequency of symptoms for which self-medication was performed

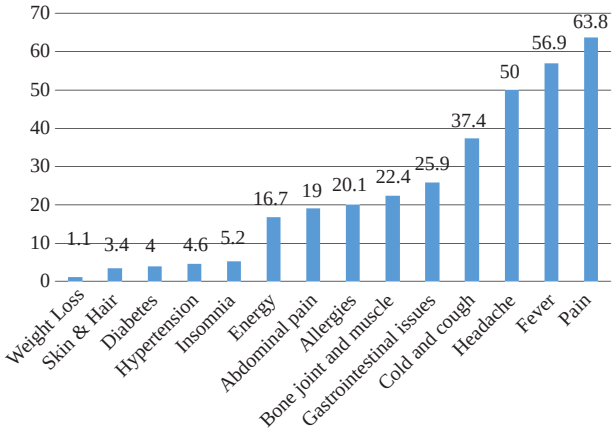

Figure 2: Usage of different types of medication among study participants

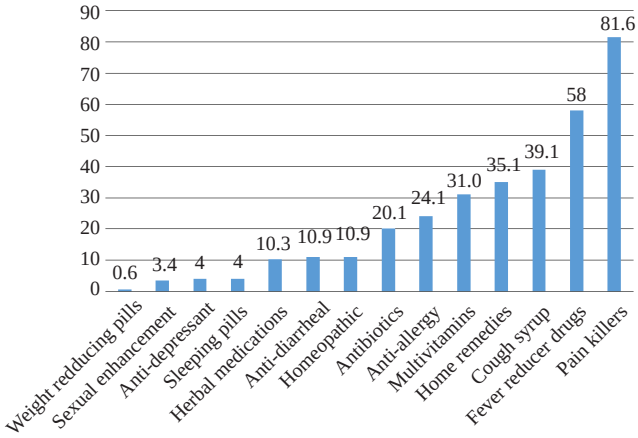

Table 1: Frequency of reasons for using self-medications

Reasons	Frequency	%
It was convenient	173	99.4
I had minor illness	148	85.1
For saving time and money	110	63.2
For quick relief of symptoms	137	78.7
I purchased directly from medical store	43	24.7
It was recommended by local pharmacist	38	21.8
Advised by friends/family	44	25.3
I had a social contact working in healthcare sector	71	40.8
I had experience about the drug	68	39.1
Unconsumed medication brought for family	8	4.6
I had no medical insurance	18	10.3
I was unable to afford doctor's fee	37	21.3
Unavailability of physician	26	14.9
Lack of trust in doctors	18	10.3
Attended a physician last year	78	44.8
Drug was advertised in TV	15	8.6

Table 2: Frequency of different approaches for dosage adjustments

Different approaches for dose adjustments	Frequency	%
Ask Family physician	77	38.5
Ask a doctor in family	98	49
Ask a friend	30	15
Ask local pharmacist	38	19
Read it on internet	14	7
Read the instruction on medicine	45	22.5
Patient Decided for themselves	119	59.5
Previous experience	119	59.5

DISCUSSION

In the '90s, the trend of self-treatment for different ailments was first recognized in various parts of the world.[12] Self-medication is now a global phenomenon and plays a huge part in potential drug resistance along with many other adverse effects.[13] The elderly group is the most vulnerable cohort for practicing self-medication due to suffering from several acute and chronic diseases because of the aging process.

In the present study, a high frequency of 87% self-medication without prescription during the past three months was observed. Similarly higher prevalence of self-medication was also noticed in other studies from the south Asian region including Iran (76.2%), India (88.5%). Outside region studies show a similar prevalence of 80%.[14-16] In contrast to this observation, very few studies in the region reported a low prevalence (38%), of self-medication. In another recent study from Karachi, a comparatively lower prevalence of 65.7% was observed in self-medication.[17,18] We assume that the variability can be explained due to the difference in study time as the study by Saif Ali et al, was conducted in pre-covid era and our study was conducted during covid times when patients preferred home treatment to avoid hospitals and clinics exposure.[18]

However, some surveys conducted in Pakistan among the middle age in the pre-pandemic era also reported use of medication without prescription of the doctors which requires investigating the health-seeking behavior and the factors encouraging them to use medication without prescription of the doctors.[19]

Minor illnesses are a common occurrence and self-medication for minor ailments offers low-cost, quick, and feasible solutions. The high frequency of self-medication reflects that there is significant potential in enhancing patient awareness regarding self-health care.[12] In the present study, the common symptoms for which self-medication was performed were pain, fever, headache, cough, and cold. Another study conducted in Karachi also reported headache (73.5%) and fever (69.8%) as the top symptoms for which self-medication was taken followed by other complaints including diarrhea (39.1%), sore throat (18.1%), runny nose (16.7%) and other pains (9.1%).[18] The findings of the Iranian

Table 3: comparison of participants characteristics among patients practiced and did not self-medicate in the last three months

Variables	Groups	Medication without prescription in last 3 months		OR (95% CI)	p-value
		Yes n (%)	No n (%)		
Age (in years)#	-	65(62-70)	69(65-70.3)	1.1(0.98-1.11)	0.052
Gender	Male	87(82.9)	18(21.7)	2.3(0.93-5.44)	0.067
	Female	87(91.6)	8(8.7)	Ref	
Marital Status	Single	18(78.3)	5(6.4)	2.3(0.55-9.62)	0.308
	Married	123(87.9)	17(19.3)	1.1(0.36-3.62)	
	separated/divorced/widowed	33(89.2)	4(10.8)	Ref	
Mother tongue	Urdu	72(82.8)	15(18.1)	2.19(0.68-7.03)	0.506
	Sindhi	24(88.9)	3(3.4)	1.31(0.27-6.36)	
	Punjabi	20(95.2)	1(1.1)	0.53(0.06-5.01)	
	Pashto	16(84.2)	3(3.6)	1.97(0.40-9.79)	
	Others	42(91.3)	4(4.4)	Ref	
Educational level	Uneducated	15(93.8)	1(1.1)	0.40(0.04–3.73)	0.904
	Primary	27(87.1)	4(4.6)	0.89 (0.22 – 3.66)	
	Secondary	28(82.4)	6(7.3)	1.20(0.33–4.36)	
	Graduate	72(87.8)	10(11.4)	0.83(0.26–2.65)	
	Postgraduate	30(85.7)	5(5.8)	Ref	
Occupation	Unemployed	78(89.7)	9(10)	0.88(0.28-2.79)	0.372
	self employed	24(77.4)	7(9)	2.2(0.63-7.78)	
	Retired	34(87.2)	5(5.7)	1.12(0.30-4.19)	
	Private sector	38(88.4)	5(5.7)	Ref	
Monthly income	<25000	105(87.5)	15(17.1)	0.61(0.18-2.05)	0.654
	26,000-50,000	27(93.1)	2(2.1)	0.32(0.05-1.90)	
	51,000-75,000	15(83.3)	3(3.6)	0.85(0.16-4.43)	
	76,000-100,000	10(83.3)	2(2.4)	0.85(0.13-5.51)	
	>100,000	17(81)	4(4.9)	Ref	
Diabetes	Yes	48(82.8)	10(12.1)	1.64(0.70-3.87)	0.254
	No	126(88.7)	16(18)	Ref	
Hypertension	Yes	60(84.5)	11(13)	1.39(0.60-3.22)	0.437
	No	114(88.4)	15(17)	Ref	
Osteoarthritis	Yes	32(82.1)	7(8.5)	1.64(0.63-4.22)	0.306
	No	142(88.2)	19(21.5)	Ref	
Ischemic heart diseases	Yes	16(80)	4(5)	1.79(0.55-5.86)	0.304
	No	158(87.8)	22(25.1)	Ref	

CI: Confidence interval, Ref: Reference category, OR: Odds ratio

study demonstrated cold and cough (48%) and headache (38.9%) as the most common reasons for self-medication in the elderly population whereas one-third of elders performed self-medication for hypertension and cardiovascular diseases (33.4%).[14] In our study, self-medication to manage hypertension and diabetes was comparatively low. Hence it could be perceived that our patients were cautious about using the medication without a prescription for illnesses that may have a serious impact on their overall health in long term. A community-based study conducted in India also documented fever (66.3%), headache (54.7%) and cough and cold (38.4%) were the most frequent illnesses for opting for self-medication.[20] Even the studies investigating self-medication in students and the general population in different countries also reported headache, fever, and cough to be the most common symptoms.[3,5,19]

In Pakistan dispensing medications without prescriptions and over-the-counter availability of medications such as analgesics, anti-diarrheal agents, antihistamines, cough

suppressants, and even antibiotics, is an alarmingly common practice.[21,22] Even if new medicines develop, misuse of medications will continue to pose a challenge and will increase morbidity due to medication interactions, side effects, and antibiotic resistance. Disturbingly, one-fifth of our study participants reported the use of antibiotics without proper prescription. Another survey conducted in Karachi reported a closed prevalence of antibiotics usage (13%) to our study.[18] A lower prevalence of antibiotics usage was reported in the geriatrics population in a Karachi-based study which was conducted during the pre-pandemic period.[11] However, an estimated 5% of over-the-counter antibiotics are used without a prescription in most parts of the world.[23]

In Pakistan, the provision of primary health care is majorly a financial burden borne by the common man. That is a potential cause of the increased prevalence of self-medication practices.[24] In the present study, the majority of participants were found to be unemployed with monthly income for the most being <25K (60%). Almost all of the participants reported that they opted for self-medication because it was convenient for them. Other top reasons were time and money-saving, minor ailment, quick relief of symptoms, physician visits within a year, and having prior experience of the drug. Direct purchasing of medicines from pharmacies and recommendations by family/friends and local pharmacists were uncommon reasons in the present study. Similar reasons including mild illness (74.9%), time-saving (85.1%), and prior experience of treatment (70.2%) were reported in another study.[18] Familiarity with treatment was also reported as the most frequent reason for self-medication from a survey of the general population in UAE and along with high cost from an Iranian study (63.7%)[25]. A study from Iran reported prior experience with medication and high cost as the main reason for self-medication, Other reasons include minor illnesses and availability of medicines at home (38.2%).[14]

Further analysis was done to assess any significant difference in self-medication practices with respect to demographic features. In our study, we did not find an association of self-medication with any of the patients' factors including age, gender, marital status, monthly income, or existence of non-communicable diseases. Other studies from Karachi and outside do report some significant associations with gender, age, education, income, marital status.[14,15,18,19] We assume that a high frequency of self-medication and limited sample size were the potential reasons for this non-significant association of patients' socio-demographic factor with self-medication practice in the current study.

Our study had a few limitations, Firstly study was conducted in waiting area of a hospital setting with a limited sample size so being a patient or caretaker of the patient, chances of having knowledge and experience of medications are higher as compared to elderly people in the community, hence results cannot be generalized for an overall geriatric population of Karachi. Further, it was conducted during the first wave of the COVID-19 pandemic when the fear of acquiring COVID was high in every age group especially in elderly and people were avoiding hospital/clinical exposures which may have overestimated the true frequency of self-medication in the current study. Hence a future community-based study with a larger sample size may overcome the gaps of the current study and achieve generalizable research.

It seems justified to opt for self-medication when the disease is of mild nature and patients had prior experience with the treatment. However, self-medication practices such as frequent use of pain killers, and unjustified use of antibiotics based on suggestions of family, friends, and medicine dispensers should be highly discouraged. Inappropriate self-diagnosis and self-medication could worsen the disease course and increase morbidity.

CONCLUSION

A higher frequency of self-medication practice was determined in this study. Fever, headache, cough, and cold were the main symptoms of practicing self-medication. Reasons for self-medication were patients' convenience, disease of mild nature, and prior experience of the drug. None of the patients' factors was associated with self-medication practice. Increasing patient awareness, regular checkups, medication review by the primary physicians' and strict regulation of prescription-based medicine supply are suggested ways forward for better health outcomes, especially in the elderly population.

Authors Contribution:
Zaheer Ali: Study concept, design of the work, initial drafting of the manuscript
Rabeeya Saeed: Critical review of the initial draft and final approval
Fatima Kanwal: Initial drafting of manuscript
Faridah Amin: Study concept, design of the work
Noureen Durrani: Perform Data analysis, interpreted results, complied the manuscript
Areeba Abdullah: Data collection, data entry and assisted in result presentation and writing

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Original Article **Open Access**

Modifiable Cardiovascular Risk Factors in Adults Less than 40 Years of Age

Zulfiqar Ali Laghari, Naseem Attar, Noman Sadiq, Farzana Gul Baloch

ABSTRACT

Objectives: To determine the prevalence of modifiable cardiovascular risk factors in adults less than 40 years of age.

Study Design and Setting: A Cross-sectional study was carried out from 2018 to 2019 at University of Sindh, Jamshoro.

Methodology: After getting approval from ethical review board, 263 participants were included in the study using convenient sampling technique. Subjects over 40 years of age, with history of CVD, who was on medication, pregnant women, smokers, and drug addicts were excluded. A structured questionnaire was administered, and associated data was collected. Anthropometric and blood pressure measurements were made. Blood was drawn and analysed for total cholesterol, LDL, triglycerides, HDL, and blood sugar. The existence of modifiable risk variables is shown as percentages, and the difference between genders was evaluated using the chi-square test.

Results: Out of total subject, 76% had at least one risk factor present. The risk of Obesity was 29% and 30% for men and women respectively. Central obesity was higher in females (61%) as compared to males (35). Risk factors including hypertension, total triglycerides, and less-than-desired high-density lipoprotein were more prevalent in males as compared to females (p-value .0001). Whereas risk factors including total cholesterol and inactive lifestyle were more in females as compared to males (p-value 0.012 & .0007respectively).

Conclusion: Three risk factors (Obesity, Central obesity, and Total Cholesterol) were found to be higher in females, while 4 risk factors (Hypertension, Increased TG, raised LDL, and hyperglycemia) were higher in males.

Keywords: Cardiovascular risk factors, Cholesterol, Hypertension, Obesity

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INTRODUCTION:

Each year, 38 million people die from non-communicable diseases (NCDs). More than 17.9 million people die each year as a result of cardiovascular disease, which is the leading cause of non-communicable mortality. Cardiovascular disease was responsible for 14.4 million deaths in 1990; by 2005, that figure had risen to 17.5 million.[1] A projected 23.3 million individuals would die each year from cardiovascular disease (CVD) by 2030, according to the Centers for Disease Control and Prevention. The South Asian area is predicted to witness the greatest rise in mortality from cardiovascular disease.[2]

Being a part of the Indian subcontinent, Pakistan suffers from a larger proportion of cardiovascular disease than other countries in the region. About one-third of Pakistan's population dies from heart disease, which is the leading cause of mortality. In addition, Pakistan was just named the world's ninth-most obese nation. Urban and rural Pakistani populations have significantly varying prevalence rates of main risk factors, as do Pakistanis from various socioeconomic strata. The prevalence of cardiovascular disease risk factors and CVDs is greater among those from higher socioeconomic levels than among those from lower socioeconomic classes.[3] cardiovascular disease is expensive to treat. In addition to the costs of doctor's visits, hospital stays, and pharmaceuticals, workers may find that their performance at work suffers or perhaps disappears altogether.[4] As a result, taking the correct steps at the right time to avoid cardiovascular disease is advantageous to both people and the country's economy.[5]

From an early age, preventative measures should be taken to reduce the risk of cardiovascular disease and other risk factors. Cardiovascular disease-causing atherosclerosis does not appear out of nowhere. According to the studies,

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atherosclerosis may develop in healthy blood arteries at different stages of development, showing that it can occur even in the early years of life.[6-7]

Adults under the age of 60 account for 29% of all CVD-related fatalities worldwide, while people over the age of 70 accounts for over 50%. As a result, heart disease is not only a disease of the elderly or middle-aged, but also a major threat to the health of children and adolescents.[6]

Middle-aged and elderly persons are the primary source of current information regarding modifiable cardiovascular risk factors that might contribute to heart disease in the future or in the present. Adolescents and young adults are prime candidates for risk factor intervention, but the quantity of research conducted and the depth of information offered isn't sufficient.[8]

Identifying risk factors is a well-known concept in both the public and clinical health care sectors. These risk variables are used as a basis for avoiding morbidity and death from cardiovascular disease and other NCDs. A person's risk of acquiring a certain disease is determined by a person's risk factors. Cardiovascular risk factors can be prevented and the overall quality of life improved by gaining a thorough understanding of, assessing, and taking preventative measures.[9] Atheroma can develop in the arteries when certain risk factors are present. Cardiovascular risk factors fall into two categories: those that can be modified and those that cannot. Risk factors that may be adjusted or prevented account for around 80% of cardiovascular disease cases. Obesity, high blood pressure, dyslipidemia, and hyperglycemia are all changeable risk factors that contribute to death from cardiovascular disease, which in turn affects other modifiable risk factors such as smoking and alcohol intake. Another collection of ACVD risk factors that cannot be prevented, managed, or adjusted is naturally fixed. Gender, Age, Ethnicity, and Genetics are all non-modifiable risk factors. [10]

Preventing future cardiovascular disease by gaining a better knowledge of cardiovascular risk factors and their causes in young adults is only one benefit of a more comprehensive understanding of these variables. The current study was conducted to find the frequency of modifiable risk factors in the adult population under the age of 40 in both genders.

METHODOLOGY:

This cross-sectional study was conducted at the Department of Physiology, the University of Sindh from 2016 to 2018 after getting approval from the institutional ethical review board via letter no Physiol/IRB/199. 297 healthy individuals of both genders were initially contacted via convenient purposive sampling. A total of 263 people gave consent and were included in the current study. Thirty-four people opted not to donate blood or provide any information. All included participants were 20-40-year-old, residents of Hyderabad with no history of smoking, drug addiction or any CVD.

A self-designed structured questionnaire was administered to all participants and associated data was collected. Anthropometric measurements and blood pressure of subjects were taken in a standardized way. The height of the individuals was measured by using a stadiometer while the waist circumference of the individuals was measured by using a non-stretchable measuring tape. Blood was collected and serum was obtained by centrifuging the samples at 2000 rpm for 5 minutes. Serum was then kept at -20 centigrade until analyzed. Samples were analyzed using autoanalyzer Microlab 300 by Merck for high-density lipoproteins, low-density lipoproteins, triglycerides, and total cholesterol. A glucometer was used to measure blood sugar (glucose) levels automatically using the capillary method (Easy max by Biotechnology corp.). Physical activity at work and in their spare time was documented using a questionnaire. Being physically active meant that the subject was walking for at least 30 minutes, four or five days a week for the express purpose of maintaining their physical fitness (exercise). Being physically active meant that the subject was walking for at least 30 minutes, four or five days a week for the express purpose of maintaining their physical fitness (exercise). Sitting for most time of the day (desk job) with little to no physical movement intended to burn calories was considered a little activity. Walking for at least 30 minutes 4-5 times a week was considered a physical activity of low to moderate intensity. Vigorous activity of 30-60 minutes duration, including jogging and sports, was considered as physical activity of Moderate to High intensity. Data were analyzed via SPSS version 21 and the presence of modifiable factors is presented as percentages while the difference in the occurrence of modifiable risk factors amid both genders was calculated by applying the chi-square test and a p-value of less than 0.05 was considered as significant.

RESULTS:

Out of a total of 263 subjects, 168 subjects were males and 95 subjects were females with a mean age of 28.03 years. A higher percentage of total subjects (76%) had at least one CVD risk factor. Only 24% of subjects were without any CVD risk factor. 2 risk factors were present in 24% of subjects, 3 risk factors were present in 11% of subjects, and as high as 18% of subjects had more than 3 risk factors. Overall Inactive lifestyle was the common risk factor, affecting as much as 74% of subjects, followed by increased waist circumference i.e., central obesity (>80cms in women and >90cm in men), which was prevalent in 44% of total subjects. Out of all risk factors increased LDL concentrations (normal level <130 mg/dl) were least prevalent, with 6% sufferers, followed by increased TC concentration (normal level <200mg/dl) and hyperglycemia (7%). The overall frequency of risk factors in all the study participants is shown in table I.

Female subjects had higher frequency of obesity both general (>25 BMI) and central as compared to male subjects.

However statistical significance failed to reach. Total cholesterol was also higher in female subjects (p=.01). Results for hypertension were similar to most studies done, with more men (40%) suffering from hypertension (systolic blood pressure > 140 mmHg) as compared to 22% of females with hypertension (p=0.0001). In case of LDL concentrations significant difference were not reached, however still LDLwas higher in male subjects. Triglyceride levels (normal level < 150 mg/dl) were much higher in male and results were significant (0.0001). Hyperglycemia (normal blood glucose 100-140mg/dl) was twice as high in males (8%) as females (4%) and the difference was statistically significant (p=0.01). The difference in frequencies of modifiable risk factors among male and female study participants is shown in table II.

DISCUSSION:

Few studies have examined the prevalence of cardiovascular disease and its risk factors in young Pakistani adults. Most Pakistani studies have focused on people over 40; literature on those under 40 is scarce. Young and elderly people lack research on cardiovascular risk factors. Comparing this study to others was challenging. This study focused on young adults (under 40) to determine risk factor prevalence. Male and female gender differences were also studied.

Table1: Overall cardiovascular risk factors in study participants.

Individual risk factors	Number of individuals with risk factor (N = 263)	Frequency (%)
Obesity	78	30%
Central obesity	116	44%
Hypertension	89	34%
Increased TC	19	07%
Increased LDL	15	06%
Increased TG	92	35%
Hyperglycemia	18	07%
Less than required HDL	70	26%
Inactive lifestyle	195	74%

*Central obesity: increased waist circumference. * TC: Total cholesterol. * LDL: Low density lipoproteins * TG: Triglycerides. *HDL: High density lipoproteins

Table 2: Comparison of individual risk factors among gender

Gender	Male Total (N = 168)	Female Total (N = 95)	P-value
Individual risk factors			
Obesity	49 (29%)	29 (30%)	0.71
Central obesity	58 (35%)	58 (61%)	0.07
Hypertension	68 (40%)	21 (22%)	0.0001
Increased TC	07 (4%)	12 (13%)	0.012
Increased LDL	11 (6%)	04 (4%)	0.76
Increased TG	78 (46%)	14 (14%)	0.0001
Hyperglycemia	14 (8%)	04 (4%)	0.016
Less than required HDL	45 (27%)	25 (26%)	0.0001
Inactive Lifestyle	113 (67%)	82 (86%)	0.0007

This study's results mostly agree with other research. Males had more risk factors, indicating they are more prone to CVDs. Saleheen D et al. studied total records of diagnosed myocardial infarction patients and found that 16.1% were under 40 years old. Patients were mostly male (93.1%). Males are more prone to CVDs, and the risk rises with age.[11]

Obesity causes CVD. Pakistan ranked 9th in world obesity. Obesity was a major CVD risk factor in this study. BMI found 30% of subjects overweight or obese. Males (29%) had a lower obesity rate than females (30%). The results of this study are similar to other Pakistani studies that found obesity in young adults to be between 25 and 35% and more prevalent in females than males with a small margin of difference.[12] Females had a larger waist circumference than males, and it increased with age. These results match Noor M et al research, who also found that female waist circumferences increase with age.[13]

Hypertension is a well-studied risk factor for CVDs. In their seventh report, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure emphasized that systolic rather than diastolic Blood Pressure is linked to CVDs. Our study emphasized systolic blood pressure. Prehypertension and hypertension prevalence was 34%. Prevalence of HTN was higher in male than in female subjects, 22%; these results agreed with the study by Javed A et al. in Lahore.[14]

Dyslipidemia (high levels of at least one type of cholesterol/lipid) was present in 35% of subjects, with high triglycerides being the most common. Basit A et al found impaired triglyceride levels in 48.9% of subjects with dyslipidemia. Diabetes affects vascular and cardiovascular risk factors.[15] Khan Hu et al show that diabetics have higher Dyslipidemia levels than non-diabetics.[16] Hyperglycemia was 7% in total subjects, more common in men. The small sample size may explain why no diabetics were found.

Sedentary or inactive lifestyles cause obesity and risk factors.[17-18] 74% of subjects had this risk factor. Hayes L et al compared the activity levels of Indians, Pakistanis, and Bangladeshis to those of Europeans. 52% of European men don't get enough exercise, compared to 71% of Indians, 88% of Pakistanis, and 87% of Bangladeshis. Women had similar findings. European men and women participated in more moderate to intense sports and exercise than Pakistanis and Indians. Lack of exercise and improper diet (high fat, high carb, high calorie) are causing Pakistan's obesity epidemic (and subsequent risk factors).[19-20] Less active than men, women may consider household chores as exercise and believe that working at home keeps them physically active, which is not true on biological grounds. 1 hour of

housework uses less energy than 30 minutes of intense walking or 15 minutes of jogging. This may be why women are generally and physically more obese. Cultural inhibitions and ignorance prevent women from using jogging tracks and gyms. Men are allowed to go out, so more men are jogging, swimming, playing sports, and working out.

There are certain limitations of this study. The sample size used in this study should have been bigger. But due to limited resources available sample size couldn't be increased above thecurrent size. Furthermore, despite the increased prevalence of diabetes in Pakistan, not even a single diabetic was detected in this study. The possible reason for this again could be the sample size. With a smaller-scale study such as this, the magnitude of difference between the two young adult categories needed to be much larger in order to identify more factors that may have been subtly different.

More studies should be done on individual risk factors as well as on a combined group of risk factors. As cardiovascular events are nowadays occurring in adults as well it is important to stratify risk factors in adults and preventive measures should be taken into account.It is important for educational institutions to raise awareness and educate students about the risk factors for the cardiovascular disease since these risk factors not only contribute to the development of heart disease but also have an effect on a person's quality of life.

CONCLUSION

76% of research participants had at least one risk factor. High cardiovascular risk factors in young individuals are alarming. These risk factors will eventually lead to cardiovascular diseases and a poor quality of life. Three risk factors (Obesity, Central obesity, and Total Cholesterol) were more prevalent in females, while 4 risk factors (Hypertension, Increased TG, raised LDL, and hyperglycemia) were higher in males, making the male population slightly more at risk for developing CVDs at a young age.

Authors Contribution:
Zulfiqar Ali Laghari: Concept design, Overall Supervision
Naseem Attar: Data Collection
Noman Sadiq: Writeup, final drafting
Farzana Gul Baloch: Data Collection

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Original Article **Open Access**

Association of Text Neck Pain with prolonged Studying and Excessive Smart Phone Usage Among Medical Students

Shamaila Hassnain, M. Nouman Latif, M. Hassan Arshad, M Aneeque Adil, Noor Shahid

ABSTRACT:

Objective: Globally, neck pain is the most frequent pain, rating fourth among the disabilities. Text neck pain is an emergent epidemiological problem, especially among young adults. This study aims to check the frequency of text neck syndrome in both prolonged studying and excessive smartphone usage amongst the young undergraduates of medical college.

Study Design and Setting: A cross-sectional study was conducted among at Central Medical College, Lahore.

Methodology: The data was collected using a self-designed questionnaire.118 medical students were included in the study. The designed questionnaire gathered information on age, gender, academic year, any health issue, the experience of pain or discomfort, hours for use of any electronic device, and book reading. The reliability was 62% using Cronbach's alpha. Data were analyzed using SPSS 26.

Results: The mean age of the study participants was 22.35 +1.85 years. About 93.2% of the medical students reported discomfort or pain in the neck, shoulder, or back. About 74.6% of the female medical students and 54.5% of male students suffered from headaches with neck pain. The most used device was mobile among 94.1% of students. Experience of pain and discomfort was significantly associated with the number of hours consumed in using the device.

Conclusion: The frequency of text neck pain is found to be 93.2%, which is very high among the young population and smartphones are found to be the highest risk factor; use of laptop being the second most common. Female students comparatively suffer more from frequent pain and discomfort.

Keywords: Medical students, Musculoskeletal pains, posture, smart devices, text neck, .

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INTRODUCTION:

Text neck syndrome refers to repetitive stress to the neck triggered by having the head in a forward position for an extended period. Globally, neck pain is the most frequent pain, rating fourth among the disabilities.[1] It is the commonest musculoskeletal condition that limits the daily activity performance. Musculoskeletal pain is common children and adults.[2] Text neck pain is an emergent epidemiological problem, especially among young adults. This pain is caused by persistent usage of cell phones, tablets, or other devices mostly in frequent and longtime users.[3] Bending the shoulder, neck, and head while using cell phones or other portable devices, distorting the neck position while watching television, studying or sitting progressively increases stress on cervical spine.[2] Furthermore, a forward head posture may increase the mechanical load on joints and ligaments of the cervical spine and may boost the demand on the posterior neck musculature by the increased gravitational moment.[4] The increased use of mobile phones especially among the young age group has posed harmful effects with the growing prevalence of neck pain.[5] Mobiles are mostly used devices among adults, and text messaging is the most popular form of communication.[6] According to Pakistan Telecommunication Authority, cell phone users have reached 150 million in Pakistan.[7] Bad postures, over-use of modern technological tools, spine in neutral position, and excessive neck flexion for several hours were the habits that are difficult to avoid and hence becoming the major contributing factor for neck pain.[2]

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The term "Text Neck" is derived from the onset of spinal degeneration resulting from the repeated action of forward head flexion while looking down at the screen of mobile devices and "texting" for a long period.[8] The weight put on the spine dramatically increases when flexing the head forward at varying degrees. The weight of head increases intensely when it is forward flexed and the weight and effect progressively increased by changing the degrees.[2] A full-grown head weighs 4.54 to 5.44 kg in the neutral position. As the head tilts forward, the forces seen by the neck surges to 12.25 kg at 15°, 18.14 kg at 30°, 22.23 kg at 45°, and 27.22 kg at 60°.[9] The effects of forwarding flexion of the neck transcend pain, contribute to more associated complications. Most people display a forward head posture when viewing a mobile phone screen.[9] But still, the association between neck posture and neck pain is unclear. Forward flexion of neck can change the cervical spine, bony segments, curvature, posture change, supporting ligaments, and neck and associated areas pain. Frequency of head bending along with the degree of neck flexion induces additive effects on the human neck physiology.[2]

Increased usage of cell phones in the modern era for notes and communication adds to this problem.[3] It is suggested that when someone drops their head and rounds their shoulders while looking at a smartphone or a tablet, it is harder for them to take a full breath because of the restriction to their muscles.[10] Musculoskeletal pain follows the pattern of recurring exacerbations and remissions on the long-term and so the previous episodes can be a better predictor of new episodes. It may be important to observe the musculoskeletal conditions earlier in life to understand its main aspect and risk factors of the onset of illness and its symptoms.[2] This study aims to check the frequency of text neck syndrome among medical students due to prolonged studying and excessive smartphone usage among MBBS students of medical college. The frequency of other associated medical illness was also investigated.

METHODOLOGY:

This cross-sectional study was carried out in Central Park Medical College Lahore, Pakistan. The data were collected from 118 medical students using systematic random sampling in December 2021. The minimum sample size was calculated as 96 using 46.7% as the prevalence of neck pain, 5% as the level of significance and 90% as the power of the test.[11] The calculated sample size was quite small, however, it was good representative of the population. A list of all five-year MBBS students was generated. After a random start, every 5th student was included in the sample. Those students who were not interested to participate were excluded and next in the list was included.

This study was reviewed and approved by the Institutional Review Board (IRB) of Central Park Medical College. (CPMC/IRB-No/1307) Written consent was obtained before data collection to ensure the voluntary participation of each participant. Study participants were informed about the purpose of the study. Researchers were assured about the confidentiality of the data.

The data was collected using a self-designed questionnaire. The designed questionnaire gathered information on age, gender, academic year, any health issue, the experience of pain or discomfort, hours for use of any electronic device, and book reading. The reliability was 62% using Cronbach's alpha.

The prevalence of discomfort or neck pain, headache, and general pain in the shoulder were observed. The most common symptom regarding text neck pain were seen. The prevalence of various other health issues such as diabetes, hypertension, psychiatric issues, muscular or joint pain, anemia, iron and calcium deficiency, migraine, vitamin D deficiency and asthma were also observed. Test of association was performed to obtain the association of pain with the number of hours of device use and hours for book reading. Association was also tested between gender and pain experience. Binary logistic regression was applied to observe the intensity of pain for each increasing hour of book reading and device use. Data was analyzed using SPSS 26.

RESULTS:

In total, 118 medical students participated in this study. The mean age of the participants was 22.35 ± 1.85 years. The ratio of male to female students was 0.87. The total percentage of female participants was 53.5%. Approximately 93.2% of the medical students reported discomfort or pain in the neck, shoulder, or back. Among those, 55% were female participants. About 74.6% of the female medical students suffered from headaches with neck pain whereas the percentage was 54.5% for male students. The prevalence of general pain in the shoulder and back was seen as highest among other symptoms (Figure 1).

Female students comparatively suffer more from frequent pain and discomfort. Approximately 94.1% of the students use mobile phones relatively more as compared to other devices. Students who used desktop systems suffer more frequently from neck pain. About 01 (0.1%) of the patients used desktop system and suffered from pain.

Besides neck pain and discomfort, most of the students mentioned other health issues. Anemia is the most common followed by psychiatric issues, muscular or joint pain, and calcium deficiency (Fig. 1). Psychiatric issues include bipolar or depressive disorders, anxiety, schizophrenia spectrum, obsessive-compulsive behavior, trauma or stress, sleep-wake disorder, eating disorder and breathing related sleep disorders.

Chi-square test of association was used to observe the significant relation of neck pain with various factors such as gender, used device, hours spend each day using the device, and book reading. A p-value of 5% was used as significant. Experience of pain and discomfort was significantly associated with the number of hours consumed

in using the device and reading the book (Table 1).

Binary logistic regression was applied by taking the factors as independent variables and experience of pain being the dependent variable. Hosmer and Lemeshow showed a significant p-value for regression analysis. The overall percentage of correctly classified was 93.2%. The reference category was 1-2 hours for device use and for book reading. The odds were high for neck pain with more time spent using the device. Time spends in using the device was observed as significantly related to neck pain or discomfort (Table 2).

Most of the students who were engaged in book reading, read books in sitting position. Whereas the mid-chest level is the most popular position of using any device followed by leaning forward and laying down. The least common position for book reading was reading at eye level (Fig. 2)

Figure 1: Prevalence of Various Symptoms and other Health Issues

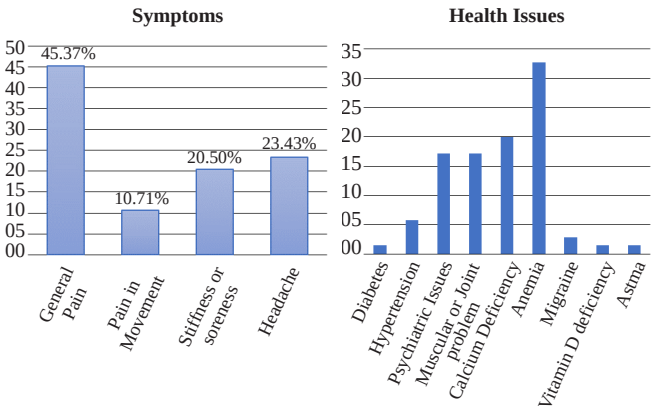


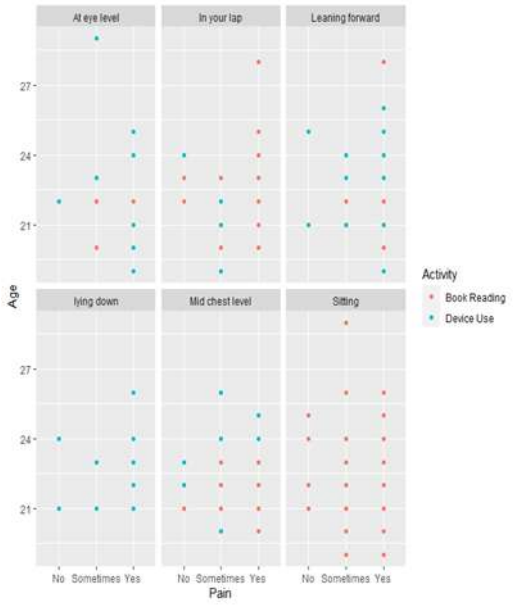
Table 1: Crosstab of Experience of neck pain with risk various factors

Factor	Categories	Experience Pain		Total	Chi-square (p-value)
		No	Yes		
Gender	Male	05	50	55	0.871 (0.470)
	Female	03	60	63	
Device	Mobile Phone	08	103	111	0.541 (0.910)
	Laptop	0	04	04	
	Tablet	0	02	02	
	PC	0	01	01	
Hours for device use	1-2 hours	04	11	15	14.981 (0.005)
	3-4 hours	01	28	29	
	5-6 hours	01	40	41	
	7-8 hours	0	22	22	
	9-10 hours	02	09	11	
Hours for book reading	No reading	0	10	10	26.238 (0.000)
	1-2 hours	02	26	28	
	2-3 hours	01	42	43	
	3-4 hours	01	28	29	
	5 or more hours	04	04	08	
Total		08	110	118	

Table 2: Binary Logistic Regression for Experience of Pain

Factors	B	p-value	OR	95% C.I
Device Time	1.761	0.030	5.818	1.191-28.426
Book Reading Time	-0.564	0.517	0.569	0.103-3.140

Figure 2: Prevalence of pain across various postures while book reading & device use



DISCUSSION:

In our study, 93.2% of participants experienced pain in the neck, shoulder, or back. Among them 45.3% had general pain, 23.4% reported headache, 20.5% with stiffness or soreness and 10.7% had pain on movement. This percentage was quite high in our population. This might be due to the fact that students mostly ignore initial symptoms of pain in neck and keep on going with the same routine. Another reason may be the lengthy curriculum in medical sciences. Similar findings regarding pain in the neck were found in a study conducted in India of (46.9%), whereas a contrast among findings of stiffness or soreness (42.5%) and pain on movement (29.2%) was seen in the same study.[12] The prevalence of neck and shoulder pain ranged from 15% to 28% among European adolescents.[13] In another study, the prevalence of neck pain in Chinese teenagers was 42.1%.[14] Female students suffered more frequently with neck pain. Another study based on observing musculoskeletal pain among adolescents reported the similar findings that musculoskeletal pain and headache was more prevalent among girls as compared to boys.[3] However, the pain symptoms were different among different age-group and gender and other demographic factors.[3]

Mobile phones (94.1%) were the most frequently used device used by the CPMC medical students with neck pain followed by 3.4% tablets, 1.7% laptops, and 0.8% desktops. These results are in contrast to research conducted in another medical college in Lahore stated that 48.5% preferred

smartphones.[15] Whereas another research identified 95% of the medical students with neck pain who preferred to use tablets as their main device.[16] Another study with the similar findings reported that all 100% participants had flawed flexion of their back and neck while studying and/or using smartphones and tablets.[11] A study also reported that there is strong association between text messaging and neck pain.[17]

The study results showed that 34.7% of students who had neck pain use devices for 5-6 hours daily. Whereas 26.3% had 3-4 hour use of device who developed neck pain.[18] Similar results are seen in an international study where longer than 2 hours duration increases the risk of neck and shoulder pain along with headache, blurred vision, dryness, and eyestrain.[15] Headache with neck pain was the main complaint in 65.3% of students in our study, among which 4.2% had a headache all the time and 61.1% had slight to severe headache along with neck pain. A study conducted in India showed that 89.83% of mobile phone users reported headaches with neck and shoulder pain.[19]

About 42.3% do stretching exercises for neck pain while 39.9% tried to improve their posture during the use of devices, 12.7% reduced their screen time, and 5.1% reduced study time in our study. These results are similar to a study conducted in India in which the majority of the participants do the postural correction by following stretching exercises daily to prevent the severity of text neck syndrome.[20] A study reported that there is no association between neck pain and neck posture. Also there was insignificant association between neck posture and frequency f neck pain.[21] Besides neck pain and discomfort, most of the students mentioned other health issues as well. Anemia is the most common (30%) followed by calcium deficiency (20%), muscular or joint pain (16%), and psychiatric issues (16%).

Our research has some limitations, one of them being a low student response rate. The paucity of sample size also prevents us to project observed trends upon students of all institutions. Since medical students of only one institute were included in this study, we cannot eliminate institutional bias. This sets the ground for further research work to be done to overcome these limitations.

CONCLUSION:

The frequency of text neck pain is found to be 93.2% which is very high among the young population and smartphones were found to be the highest risk factor for this text neck pain. Female students comparatively suffer more from frequent pain and discomfort. Experience of pain and discomfort was significantly associated with the number of hours consumed in using the device and reading a book.

Authors Contribution:
Shamaila Hassnain: Conceived the main concept, design, drafting revision
M. Nouman Latif: Discussion writing
M. Hassan Arshad: Contributed in initial drafting
M Aneeque Adil: Collected the data and assisted in analysis
Noor Shahid: Statistical analysis, interpretation of results

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Original Article **Open Access**

Association of Consanguinity with Abnormalities in the Descendants

Ammara Rafique, Hajra Naz

ABSTRACT

Objective: Consanguinity is often related to several abnormalities in descendants. This survey assessed the frequency of abnormalities in the descendants of consanguinity couples.

Study Design & Setting: The cross-sectional survey was conducted from 01-Feb-2021 to 01-Oct-2021 with consanguinity couples residing in Pakistan or abroad.

Methodology: Institutional Bioethics Committee (IBC) of Karachi University approved the study. Extensive research on PubMed, Scopus, Medline, Web of sciences, Direct Science, Springer, and Google scholar was carried out to design a structured survey after exploring major factors for special children.The form was divided into three sections encompassed fundamental and marriage-associated demographics, pre-and post-natal characteristics of normal and special children, extended family details, and perceptions regarding cousin marriage. Using snowball sampling, particularly the chain-referral method, data was collected. SPSS v.28 was used to predict the association of each variable with the existence and non-existence of special child/children.

Results: Among 503 consanguinity couples, 92.6% had none or normal descendants whereas 7.3% had special descendants of their own or from other cousin marriages in their extended families. Abnormalities including ADHD (n=9, 24.3%), Autism (n=4, 10.8%), cardiac issues (n=1, 2.7%), CP (n=5, 13.5%), deafness (n=3, 8.1%), Down's syndrome (n=1, 2.7%), dumbness (n=5, 13.5%), impaired vision (n=6, 16.2%), and mental retardation (n=3, 8.1%) were reported. However, no case of multiple sclerosis, thalassemia, Tay Sach's disease, or Schizophrenia was reported.

Conclusion: Consanguinity precipitated several abnormalities in 0.073% of the population.

Keywords: Abnormalities, Causes, Consanguinity, Cross-sectional survey, Pakistan

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INTRODUCTION:

Consanguinity is the marriage, sexual relationship, or close union between people having the same biological ancestors usually up to about second cousins. Consanguinity is a debatable topic as consanguineous marriages are exceptionally common in North Africa, the Middle East, and West Asia as well as among the emigrants from these countries now residing in Australia, Europe, and North America. Since the mid of 19th century, the subject of consanguineous marriage is of major scientific and public interest. There are several cultural, clinical, and social implications for consanguinity couples, which represent about 20-30% of total marriages.[1] Globally, cousin marriage is a tradition and respected social trend for a marital union and most women prefer cousin marriages for their progeny for the same reasons.[2] The frequency of first-cousin marriages differs within and between different communities and populations, based on their respective culture, geography, race, and religion.[3] Parents prefer cousin marriages due to the ease to find a spouse, family pressure, less expenditure of money, financial security reasons, same caste, and strengthening of family bonds.[2]

Pakistan has a substantial portion of consanguineous marriages in the world.[4] During the last 3 decades, 63% of the rise in the prevalence of consanguineous marriages has been reported in Pakistan and was more prevalent amongst uneducated and young women, in rural areas, less privileged, or unaware people.[4] A significant association between consanguinity and congenital defects is likely Charcot Marie tooth syndrome, congenital heart defects, Down's syndrome, mental retardation, and thalassemia in Pakistan.[5]

Consanguinity has been reported to develop several single-gene and multifactorial disorders such as Bloom syndrome, Becker muscular dystrophy, cancers, cardiovascular diseases, Cerebral Palsy, children's hypertension, cleft lip, cystic

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fibrosis, phenylketonuria, diabetes, muscular dystrophy, impaired vision, hearing issues, mental retardation, obesity, severe combined immunodeficiency, hemoglobinopathies, Tay-Sachs disease, and many others.[6-9]

Consanguinity also has several favorable attributes at the scientific level besides threats. It may preserve advantageous genetic traits by causing homozygosity of alleles in descendants. Consanguinity improves gross fertility, but the number of surviving descendants in both nonconsanguineous and consanguineous mating are similar due to increased morbidity and mortality.[7] The awareness and perception regarding the health risks associated with cousin marriages remains low and therefore about 60% of women prefer marrying their sons or daughters in relatives.[10]

There are often major health concerns if first-cousin marriages continue over several generations in a family. Therefore, this survey was designed to evaluate whether consanguinity can precipitate the descendants' mental and physical abnormalities.

METHODOLOGY:

Ethical approval was obtained from the Institutional Bioethics Committee (IBC) of Karachi University. For unlimited population size, the calculated sample size was 385 responses with a confidence level of 95%. The idea was to collect a maximum number of responses from consanguinity couples through the snowball sampling method. The initial consanguinity couples referred us to more alike couples which served as a chain-referral method for data collection. Using snowball sampling, this cross-sectional survey was conducted from 01-Feb-2021 to 01-Oct-2021 with consanguinity couples residing in Pakistan or abroad. The inclusion criteria were consanguinity couples i.e. cousins with first cousin marriage were included, and the exclusion criteria were those married to second or third cousins.

An extensive search on PubMed, Scopus, Medline, Direct Science, Springer, and Google scholar to explore established risk factors for special children. Twenty-seven variables were chosen to design a structured survey form which was divided into three sections.

It was mentioned on the top of the form that the survey was only for those consanguinity couples who were first cousins. The first section encompassed fundamental and marriage-associated demographics such as consanguinity relation among spouses, residence, age of spouses by the time of marriage, maternal age, health during pregnancy, and blood groups of parents. The second section encompassed details of pre-and post-natal characteristics of normal and special children such as type of delivery, birth weight, birth state, type of specialty, I.Q, miscarriage, and abortion particulars. The third section encompassed extended family details and perceptions regarding cousin marriage including details of the number of first cousin marriages in the extended family, number of special children, type of specialty, the major reason for cousin marriages, perception about cousin marriage, and their consideration of marrying their children with their cousins. Since they were all categorical variables so, multiple choices were given to the respondents.

The form was designed in English but later translated into Urdu too. Primarily hard-copy responses were prioritized but later the responses were also collected through Google forms in both languages. The form link was publicized on many social media platforms including Facebook, Instagram, Twitter, WhatsApp, Snapchat, Linkedin, ResearchGate, and many others to acquire a better response rate. The survey forms were floated in hardcopies in five big universities in Karachi including the Bahria University Medical and Dental College, NED University of Engineering and Technology, Institute of Business Management, University of Karachi, and Ziauddin University with due permission.

For statistical analysis, Pearson chi cross-tabulation values were obtained via SPSS version 28 to predict the association of each variable with the existence and non-existence of special child/children.

RESULTS:

About five hundred and twenty hardcopy forms were floated in the universities. Four hundred and thirty-three were returned finished, nine were unfinished, and seventy-eight were reverted blank. We got a minimal response online as only seventy respondents responded online form in eight months. Therefore, the response rate for hardcopies was 83.2% and for web-based was 13.4%. All special children were reported from Pakistanis residing in Pakistan whereas 3.86% of Pakistanis residing abroad reported no special children (Figure 1). Out of five hundred and three respondents, (92.6%) had none or normal descendants whereas (7.3%) had special descendants of their own or from other first-cousin marriages in extended families (Figure 2).

Multiple cross-tabulations were performed but only significant associations are presented in Table 1-3. The frequency of consanguineous marriages was higher in the age bracket of 23-24 years for women (33.9%) and 27-28 years of men (30.2%). Among parents of special children, most mothers were within the age bracket of 23-24 years at the time of marriage (35.1%) and husbands in the age bracket of 25-26 (18.9%), 27-28 (18.9%) or above 30 years (18.9%).

The statistical analysis for fundamental or marriage-associated demographics indicated that the existence of special children was only statistically associated with the blood group of mothers (p <0.01) (Table 1).

The analysis further showed that the presence of special children was statistically associated with the delivery type of normal (p <0.05) and special child/children (p <0.001), gestational age of special child/children (p <0.001), birth weight of normal (p <0.01) and special child/children (p <0.001), type of specialty in special child/children (p <0.001),

and I.Q of both normal and special children (p <0.01) (Table 2). Mental and physical abnormalities reported as ADHD (24.3%), Autism (10.8%), cardiac issues (2.7%), CP (13.5%), deafness (8.1%), Down's syndrome (2.7%), dumbness (13.5%), impaired vision (16.2%), and mental retardation (8.1%). However, no case of multiple sclerosis, thalassemia, Tay Sach's disease, or Schizophrenia was reported.

Table 3 presents that the presence of special child/children was statistically associated with first cousin marriages in the extended families of both spouses (p <0.01), special child/children in those marriages (p <0.001), type of abnormality (p <0.001), reasons for cousin marriage (p <0.05), views about cousin marriage (p <0.001), and non-willingness to marry their child/children in cousins (p <0.001).

Figure 1: Pakistanis residing in Pakistan or abroad

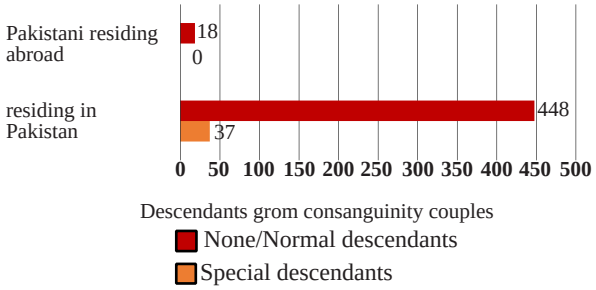

Figure 2: Descendants from consanguinity couples

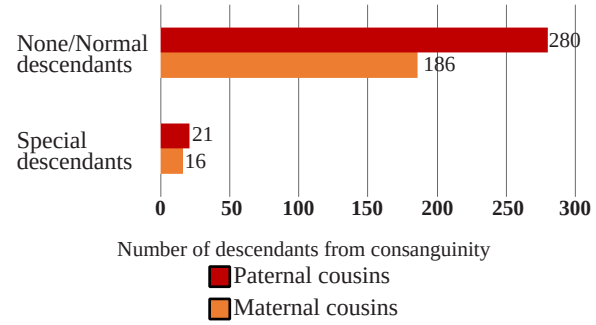

Table 1: Fundamental and marriage-associated demographics

Variables	Special child		p-value
	Present	Absent	
	N (%)	N (%)	
Wife's blood group			
B+	5 (13.5)	160 (34.3)	0.002
A+	9 (24.3)	83 (17.8)	
O+	3 (8.10)	99 (21.2)	
AB+	18 (48.6)	91 (19.5)	
B-	1 (2.70)	10 (2.14)	
A-	1 (2.70)	12 (2.57)	
O-	0	7 (1.50)	
AB-	0	4 (0.85)	

Values are cross-tabulations significant at p <0.01

Table 2- Pre- and post-natal characteristics

Variables	Special child		p-value
	Present	Absent	
	N (%)	N (%)	
Delivery type of normal child/children			
Normal	24 (64.8)	188 (40.3)	0.018
Other	11 (29.7)	175 (37.5)	
Both	1 (2.70)	53 (11.3)	
Not applicable/no child	1 (2.70)	50 (10.7)	
Delivery type of special child/children			
Normal	16 (43.2)	0	0.000
Other	21 (56.7)	0	
Not applicable/no child	0	466 (100)	
Special child's gestational age			
Full-term	27 (72.9)	0	0.000
Pre-term	10 (27.0)	0	
Normal child/children's birth weight			
Normal	18 (48.6)	276 (59.2)	0.002
Low	14 (37.8)	68 (14.5)	
Both	4 (10.8)	72 (15.4)	
Not applicable/no child	1 (2.70)	50 (10.7)	
Special child/children's birth weight			
Normal	20 (54.0)	0	0.000
Low	17 (45.9)	0	
Not applicable/no child	0	466 (100)	
Special child's disability			
ADHD	9 (24.3)	0	0.000
Impaired vision	6 (16.2)	0	
Cerebral Palsy	5 (13.5)	0	
Dumbness	5 (13.5)	0	
Autism	4 (10.8)	0	
Mental retardation	3 (8.10)	0	
Deafness	3 (8.10)	0	
Cardiac issues	1 (2.70)	0	
Down Syndrome	1 (2.70)	0	
IQ of both normal and special children			
Not applicable/no child	0	51 (10.9)	0.008
Low IQ	1 (2.70)	2 (0.42)	
Both low and high IQ	11 (29.7)	66 (14.1)	
Average	12 (32.4)	143 (30.6)	
High IQ	0	40 (8.58)	
Intelligent	13 (35.1)	164 (35.1)	

Values are cross-tabulations significant at p <0.05, and p <0.001

DISCUSSION:

The study revealed that the probability of a special child in consanguineous marriage is 0.073%. Most of the consanguinity couples (83.3%) reported first cousin marriages in their extended family as well (which helped in data collection via a snowball method) with the predominance of the absence of special children as disclosed by 43.2% of

Table 3: Extended family details and perception

Variables	Special child		*p*-value
	Present	Absent	
	N (%)	N (%)	
Presence of special child/children in other cousin marriages			
One	15 (40.5)	44 (9.44)	0.000
Two	0	1 (0.21)	
None	16 (43.2)	296 (63.5)	
Not applicable	6 (16.2)	125 (26.8)	
Abnormality in children from other cousin marriages			
ADHD	4 (10.8)	5 (1.07)	0.000
Impaired vision	0	6 (1.28)	
Cerebral Palsy	0	3 (0.64)	
Dumbness	0	1 (0.21)	
Autism	2 (5.40)	3 (0.64)	
Mental retardation	2 (5.40)	5 (1.07)	
Deafness	3 (8.10)	5 (1.07)	
Down Syndrome	2 (5.40)	5 (1.07)	
Genetic abnormalities	2 (5.40)	4 (0.85)	
Respiratory distress	0	5 (1.07)	
Sickle cell anemia	0	1 (0.21)	
None of the above	0	2 (0.42)	
Not applicable/no child	22 (59.4)	421 (90.3)	
Views about cousin marriage			
Discourage	14 (37.8)	63 (13.5)	0.000
Genetic defects	9 (24.3)	69 (14.8)	
Uncertain views	6 (16.2)	89 (19.0)	
No comments	3 (8.10)	96 (20.6)	
Good, reliable	5 (13.5)	149 (31.9)	
Reasons for cousin marriage			
Easy to find a spouse	7 (18.9)	113 (24.2)	0.024
Family pressure	2 (5.40)	106 (22.7)	
Same caste	11 (29.7)	86 (18.4)	
Property	0	4 (0.85)	
Less expenditure of money	0	3 (0.64)	
None of the above	4 (10.8)	74 (15.8)	
All above	13 (35.1)	80 (17.1)	
Like marrying your children in cousins			
Not applicable/no child	0	50 (10.7)	0.000
No	29 (78.3)	137 (29.3)	
May be	6 (16.2)	180 (38.6)	
Yes	2 (5.40)	99 (21.2)	

Values are cross-tabulations significant at $p < 0.05$ and $p < 0.001$

parents of special children and 63.5% parents of the normal children. In our survey, the parental demographics data showed maternal cousins reported more special children (56.7%) as compared to paternal cousins (43.3%) which are not concordant with Ben-Omran et al reporting paternal cousins have a higher risk of autosomal recessive disorder in the descendants.[12] When a large amount of DNA is shared, there is an increased probability of sharing a certain pathological allele identical by descent and a probability of having affected descendants with an autosomal recessive disorder.[11] Yet it is impossible to characterize low or high-risk couples among maternal or paternal consanguineous marriages.

In our survey, the majority of mothers with special children were within the age bracket of 23-24 years at the time of marriage but the literature supports that woman and their descendent experience significant problems if maternal age progresses above forty.[13] Several risk factors like consanguinity, parental age, and history of previous congenital anomalies have been identified in the central nervous system, renal, gastrointestinal, and other anomalies of descendants.[14] Numerous studies have claimed that the risks of illness and premature mortality are 3-4% greater in cousin marriages as compared to the general population. Consanguinity may be alarming for the descendants as it can rise the three-fold risk of CP, and the nine-fold risk of other disorders.[15]

Our data reported a significant association between a mother's positive Rh blood and special offspring. A study has reported that the blood incompatibility between mother and fetus (maternal blood with negative Rh and fetal blood with positive Rh) increased the probability to be born with disorders.[16] But this certainly cannot be asserted we only surveyed the blood group of parents. Rh incompatibility can trigger hyperbilirubinemia which may lead to chronic stress if not treated well. We anticipate that Rh incompatibility may have developed specialties reported in our survey (Table 2). Our data reported miscarriages (7.75%) and it has been reported that there is a higher incidence of abortions, miscarriages, and stillbirths in consanguineous marriages.[17] There is a higher rate of miscarriages in cousin marriages as compared to non-consanguineous marriages which might be the reason for such a high ratio of miscarriages reported in our data.[7,18]

Most of the special children in our data were born full-term (72.9%) with normal delivery (43.2%) however normal delivery is safest for both fetus and mother if a baby is delivered at full-term.[19] Among special cases, (35.1%) were intelligent as claimed by the respective parents and it has been reported that more than half of children from consanguineous marriages have intellectual disabilities.[20] The intellectual abilities can only be assessed through IQ tests so, there is a chance that the parents may have marked IQ levels without assessment.

Most consanguinity couples agreed to the fact that the main reason for cousin marriage is that it is easier to find a partner (24.2%). Most respondents with special children expressed that cousin marriages should be discouraged (37.8%) and (78.3%) of them denied marrying their children to cousins suggesting their concerns for future generations. A study has reported that most women in Pakistan still prefer cousin

marriages due to traditions and family security regardless of their education or social status.[21]

Unfortunately, there is inconsiderable awareness in mothers about the risk associated with consanguinity.[10] It is necessary to aware people of reproductive health to combat the deleterious effects of consanguineous marriage.[3] It is suggested that nonconsanguineous marriages are safer and may delay the manifestation of abnormalities until scientists attain a practical solution.[22]

Our study has a few limitations. Possibly some consanguinity couples may not have been fully truthful about every inquired detail. Our survey data collection was limited to the chain-referral sampling method thereby, more data is required to further validate our reported findings. The I.Q reported by the parents of special may be marked without assessment.

We believe that our findings will be beneficial in creating massive research about the abnormalities associated with consanguinity. It is questionable area how many descendants of consanguinity couples manifest abnormalities on a daily, monthly, or yearly basis in Pakistan. Government shall assign researchers from all provinces of Pakistan to establish an integrated manual or electronic database of abnormalities in the descendants of consanguinity couples.

CONCLUSION:

Descendants from consanguinity couples depicted several abnormalities including ADHD, Autism, cardiac issues, CP, deafness, Down's syndrome, dumbness, impaired vision, and mental retardation in 0.073% of the population. Extensive research is essential to identify the exact mechanism of the reported abnormalities. We anticipate that genetic counseling is prudent to reduce the genetic, social, and economic burden of abnormalities often associated with consanguinity.

Authors Contribution:
Ammara Rafique: Conception, developed the study design, interpretation, manuscript drafting, literature review, and bibliography
Hajra Naz: Research Supervisor, conception, and interpretation

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Original Article **Open Access**

Association of Oral Hygiene Practices with Dental Caries in Young Adults

Mariam Fatima, Nazli Gul Shujaat, Syeda Lalarukh Saba Shah, Shujaat Hasan Idris

ABSTRACT:

Objectives: To assess the association of dental hygiene practices and dental caries, check its relation and establish factors that can help in reducing the caries.

Study design and setting: A cross sectional study was conducted on 180 young adults who held a degree of bachelor's and 20- 35 years of age from Lahore, Okara and Gujranwala.

Methodology: Ethical approval was sought from the Research and Ethical Review Board of the Dental College. Confidentiality was ensured. Study was conducted over a period of six months. A confidence interval of 95% was established and p value <0.05 was considered significant. The questionnaire consisted of 26 questions related to oral hygiene and status of caries.

The participants were interviewed using a questionnaire about the frequency of brushing, technique used, type of toothbrush, fluoridated toothpastes, use of other aids, consumption of sugary snacks, dental visits, and established caries. The relation was established with the diagnosed caries through frequency charts, correlation and Chi- square test using SPSS version 26.

Results: Of the 180 participants 126 were females (70%) and all the participants were educated and held a bachelor's degree. Dental caries was known to 158 participants (87.87%) and 85(71%) of the people said they brush twice a day. A significant association of the diagnosed caries with the skipping of brushing, status of oral hygiene and visit to the dentist was found as suggested by the p-values 0.042,0.023 and <0.001 respectively.

Conclusion: Healthy oral hygiene practices can reduce the caries.

Key words: dental caries, fluoridated toothpaste, oral hygiene.

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INTRODUCTION:

Oral hygiene practices refer to "the maintenance of a healthy oral cavity with the aid of different methods like brushing, flossing etc".[1] Along with general well- being, keeping track of oral health is really important. Most commonly brushing is used to maintain a healthy oral cavity. It may be accompanied by other aids such as flossing, mouthwashes or home- based means of cleaning teeth. Meticulous oral hygiene maintenance not only helps in prevention of oral diseases like caries and gingivitis but also adds to the quality of life.[2]

Caries, more commonly known as "cavity" to the general population, is the most prevalent oral health problem. It is the breakdown of tooth structure as a result of demineralization caused by acidic release from fermentation of sugars in diet by the microorganisms present in biofilm present in oral cavity.[3] According to a survey "approximately 2.3 billion people have caries", so it is important to establish the factors that help in reduction of caries.[4]

There are a lot of factors that cause caries like plaque or calculus, increased carbohydrates in diet, underlying metabolic diseases (e.g., diabetes), chemotherapy etc. Dental plaque or oral biofilm is the major cause of dental caries. Oral hygiene practices help in removal of the biofilm. Different methods are available worldwide for removal of plaque.[5] Most common is tooth brushing followed by flossing, mouth washes, interdental cleaners, oral irrigators, rubber tip stimulators and tongue cleaners. Along with this there

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are many locally available options or home-based products used for cleaning purposes like miswak, baking soda, charcoal powder etc.

Though not recommended professionally but even these methods have been proven to have some beneficial effects in control of dental plaque and hence caries.[6,7] With brushing the questions like frequency of brushing, techniques of brushing, timings of brushing, use of other mechanical aids, the types of brushes etc. need to be asked to check if there is complete understanding of brushing. People may use different methods to clean the oral cavity depending on the awareness, ease, access, affordability and other factors. Along with all these measures it is also advised to get professional help in the form of scaling and fluoride application so as to achieve best oral hygiene status and the oral health problems, if present; and thus, may be detected and treated earlier.

Self-maintenance of oral hygiene is a more convenient way of reducing the burden of caries. It puts the responsibility on the shoulders of the individuals and reduces the burden on the health care system for provision of services. However, it may only be possible if proper awareness about healthy practices exists. This is the duty of the dental health professionals to ensure communication of evidence-based facts to the general population.[8]

Correlation of dental caries and of oral hygiene habits has long been established. Global studies do prove the benefit acknowledge about maintenance of hygiene possibly led to high DMFT which again ensures higher prevalence of the caries.[9] It is concluded by different surveys that there is still a lack of adequate knowledge about oral hygiene practices among the general masses especially in developing countries like Pakistan. People cannot afford to visit the dentist regularly and also self- maintenance of the hygiene is an issue. There is a need to assess the contributory factors by conducting more dedicated research in developing countries to project real time ground causes. Our study intended to check the awareness among masses, about the oral hygiene practices, help our community in adapting healthy practices and reduce disease burden.

METHODOLOGY:

Study was conducted after Ethical approval was first sought from the Research and Ethical Review Board of the Dental College, LMDC (NO. FD-1017-22). A cross-sectional study was conducted over a period of six months from June 2021 to December 2021, with an online comprehensive questionnaire owing to the COVID-19 epidemic in the young adults aged 20-35 years, included from Lahore, Okara and Gujranwala (convenience sampling). The inclusion criterion was defined as 20- 35 years old young adults with educational level of bachelors and who were willing to participate. The people who did not hold bachelor's degrees or were not willing to participate were excluded. The sample size was calculated to be 200 using the formula $n=SDpq/SE^2$ Convenience sampling (non- probability sampling) was done as it was not possible to reach every person in the COVID time. Online questionnaire was created with the help of google forms. Link was generated and then circulated among the contacts. Out of the 200 selected samples some of the subjects did not respond to the online questionnaire. One eighty subjects finally participated in the study. Confidentiality was ensured. Study was conducted over a period of six months. A confidence interval of 95% was established and p value <0.05 was considered significant. The questionnaire consisted of 26 questions related to oral hygiene and status of caries.

The participants were asked about the frequency of brushing, style of brushing technique used, type of toothbrush, fluoridated toothpastes, use of other aids, consumption of sugary snacks, dental visits, and established caries. SPSS 26 was used to evaluate the data, frequency chart, correlation and chi- square test was used to establish the relation between different variables as per requirement.

RESULTS:

Of the 180 participants 126 were females (70%) and all the participants were educated and held a bachelor's degree. Dental caries were known to 158 participants (87.87%). 85(71%) of the people said they brush twice a day and 78(43%) were brushing once a day. 71(39%) only brushed for at least 2 minutes and 122(67%) used the soft bristle brushes. 18(10%) only replaced their brush when the bristles were completely worn out. Fluoridated toothpastes were used by 102 (56.7%) of the total participants and the remaining were either unaware of the content of the toothpaste or used some other mechanical aids. 16(89%) used mouthwash regularly along with brushing. Only 18(10%) used dental floss or miswak and 144(80%) had a habit of using toothpicks. Majority of the sample never experienced bleeding gums. Limited fizzy drinks intake and moderate consumption of the sugary snacks was exhibited by 53.1% (96) of the sample. It is evident from the results that as the frequency of brushing increases the caries are less (Table 1). The participants were also asked about the knowledge of the brushing technique. We asked the participants if they were aware of different brushing techniques and 123 (68.2%) participants responded positively. Figure 1 shows the frequency of type of brush used by participants for brushing whereas Figure 2 shows the grading of oral hygiene by participants against the caries. Pearson Chi- square test was used to assess the reasons of skipping brushing, grading of oral hygiene status and last visit to dentist and against the carious teeth. Significant relationship was found between perception of the oral hygiene and also of reasons of skipping brushing when related with the carious teeth as shown in figure 2 and table 2 respectively; and a highly significant association between the dental visit and the diagnosed dental caries (Table 3).

Table 1: Frequency of Brushing (descriptive statistics)

Diagnosed Dental Caries	Once a day	Twice a day	Thrice a day	Irregularly	Total
Yes	38.4%	43.7%	66.6%	71.4%	77
No	61.5%	58.8%	33.3%	28.6%	103
Total	78	85	3	14	180

Figure 1: Types of toothbrushes used for brushing

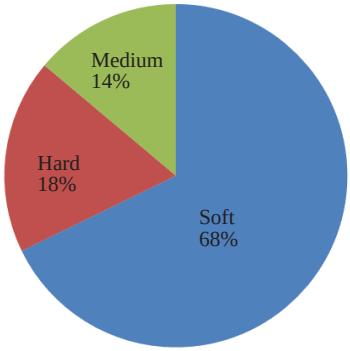
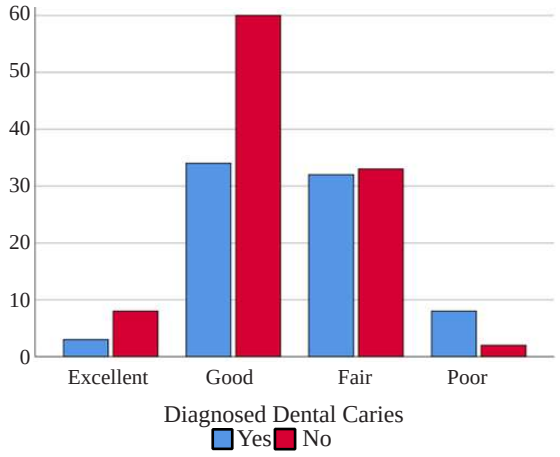


Table 2: Reasons for not brushing the teeth regularly

Diagnosed Dental Caries	Too lazy	Forget	Brushing is useless	Never skip brushing	Total	Pearson Chi-Square
Yes	25	20	4	28	77	
No	42	12	2	47	103	**0.042***
Total	67	32	6	75	180	

(*p<0.05)

Figure 2: Oral hygiene status



(p-value= 0.023) (*p<0.05)

Table no.3: last dental check- up

Diagnosed Dental Caries	2 month ago	6 month ago	1 Year ago	when I have a dental problem	Never been to a dentist	Pearson Chi-Square
Yes	6	5	12	48	6	
No	5	7	5	51	35	**<0.001***
Total	11	12	7	99	41	

(*p<0.05)

DISCUSSION:

Oral health can be kept at optimum if healthy oral practices are ensured. Healthy habits should be developed early in life and reinforced throughout life. Brushing is the key to oral health maintenance along with use of other aids. General oral hygiene home-care instructions were given to patients consistently after visit to dentist/dental hygienist. 77.7% of the participants in a study conducted on dental hygienists giving oral hygiene instructions were positive that emphasis on brushing helped reduce caries and gingival diseases in them.[10] Other factors like diet, general health and some local factors like malocclusion etc. all affect the oral health and its maintenance.

When we talk of brushing, we have to look into different aspects of the brushing which involve the brushing technique, types of brushing, frequency of brushing, timing of brushing and use of fluoridated toothpaste etc. Our study had the objective of assessing the association of dental hygiene practices and dental caries, establish factors that can help in reducing the caries. It was intended to assess the awareness about oral hygiene practices and help people in reducing caries.

As soon as the first tooth appears in the oral cavity the process of its cleaning starts. Parents are advised to clean the delicate deciduous teeth with a damp clean cloth after every meal. Later they may switch to soft bristles and once the child is able to spit, the toothpaste for children should be introduced with caution regarding the fluoride content. The toothpastes formulated for the children has low fluoride content which does not cause danger in case of swallowing yet provides the anti caries effect.[11] It was seen in a previous study that the introduction of the fluoridated toothpaste reduced caries to about 95%.[12] It is advised to continue with the supervised brushing till seven years of age and they are properly conditioned into brushing.[13] The parents also have a major role in modeling of the children.[14]

Our sample had a majority (70%) of female educated participants. There are several factors that play a role in dental caries. These include poor oral hygiene, high intake of sugars, less frequent use of brushing, use of improper brushing technique, less use of fluoride, xerostomia and malocclusion etc.

Brushing twice a day is advised, once before going to sleep at night and after breakfast in morning and then only it is effective in controlling the caries. A study conducted by Ashley shows that the mean DMFT decreases by 27% as you increase the frequency of brushing.[15] In our study we can appreciate that the caries is less in people who brush frequently while a higher percentage of caries is seen in people who brush irregularly (71.4%). Rinsing of the mouth after every snack can help further in improving the situation as the food does not adhere to the surfaces of teeth. It was established by the results that the diagnosed dental caries

was much more in the participants who less frequently brushed their teeth. One of the reasons could be a higher level of education and knowledge related to their hygiene status and oral health. This was further strengthened by the participants as they tell us how often they skip brushing. The brush used should have soft bristles whereas in our study only 67% used soft bristles. Rest used either medium or hard which can cause abrasion in the long run. There are different brushing techniques that are used to effectively remove plaque and calculus. These techniques are known to decrease plaque by 2.9 times as compared to normal practices.[16] We asked the subjects about the three popular brushing styles i.e., horizontal, round and up and down. Most prevalent was horizontal brushing technique and it is inadequate when it comes to proper cleaning. The modified bass technique among these is considered to be the ideal brushing technique and should be emphasized.[17,18] In our study 68.2% of the participants claim to have an idea of the brushing but previous studies reveal that horizontal scrub technique is most prevalent technique which is unable to clean the oral cavity thoroughly.[19] 31.8% are still unaware of proper brushing techniques so it is advised to include more demonstrations of these techniques either with the help of media or through active community programmes. Next important thing is the role of fluoridated toothpaste in control of caries.[20] The participants were asked if their toothpaste had fluoride and only 56.7% were aware of the content of the toothpaste and used the fluoridated toothpaste. If we increase the awareness about role of fluoride in prevention of caries, we can definitely reduce the prevalence of caries in general as shown by previous studies.[12]

Participants reported the use of toothpicks which might cause injury to gingiva. We need to educate people about the use of dental floss and interdental brushes for better interdental cleaning. We need to establish periodontal health and also be mindful of the physical ability of the people while using interdental cleansing devices. The awareness about the consumption of sugary snacks and fizzy drinks is also an important aspect of caries control programmes run worldwide. Excessive consumption of sugary snacks with little or no effort to maintain oral hygiene may result in higher prevalence. We need to make people aware about the modification required to prevent and reduce incidence of caries. Moreover, we need to educate people about reducing the consumption of these snacks and drinks and encourage use of healthy diet.

People who do not skip brushing have less caries as compared to the people who are lazy and do not brush regularly. These results confirm the previous research that the frequency of brushing and maintaining the habit of brushing daily helps us achieve good oral hygiene and decrease caries (p=;0.05)[21]

Rating of the oral hygiene status by the participants and establishing its relation with caries helped the subjects get a better perception for their future reference. The results exhibit that people who are meticulous about oral hygiene have less caries and hence proving previous conclusions of various studies done globally to establish the relation between caries and oral hygiene.[22,23] Every professional should play their part in reducing the burden of the dental caries and there should be awareness campaigns on different levels and different areas to address the problem.

Self- maintenance of oral hygiene is easy, accessible and affordable and this puts a lesser burden on the existing health care system. However, the role of a dental health professional cannot be overlooked in assurance of the disease- free oral cavity. It is advised to regularly pay visits to the dentist twice a year. Our results also showed a highly significant association between the two variables too and it is for this very reason that regular Dental visits/ check-ups are advised and the role of the dentist in diagnosis of caries and its management is crucial.[24] As we are a developing country, approximately 40% of our population is earning below the poverty line. The people do not have the money to pay for regular visits to the dentist.[25] Government sector should come forward and help establish dental camps for free.

Our study targeted the population with a bachelor's degree which is considered a fair level of education in a developing country like Pakistan. The results however are still far from what is expected in developed countries. Considering the number of uneducated people in our country, it is an alarming situation that the basic oral health awareness is not accessible to the majority of the population. Dentistry is added in the second level in the hierarchy of the healthcare system. Not even the basic oral health education is a part of the basic health care system. The oral health education regarding the oral hygiene practices and caries is really important in reducing the prevalence of caries. Thorough knowledge of these basic instructions needs to be spread among the general population.

CONCLUSION:

Objective of our study was to study the association between oral hygiene practices and dental caries and our results conclude that healthy hygiene practices can reduce dental caries. This study was conducted on a population with at least bachelor's level of education and still we can see a large caries count. Further studies should be carried out to assess the status of the general population from different backgrounds and more educational programmes should be ensured.

Authors Contribution:
Mariam Fatima: Searched the literature, wrote the first draft, analyzed the data, compiled the data and wrote the second draft
Nazli Gul Shujaat: Chose the topic, supervised the study, added the discussion and refined the draft.
Syeda Lalarukh Saba Shah: Collected the data and helped in compilation of data
Shujaat Hasan Idris: Critically reviewed the article

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Original Article **Open Access**

Antibiotic Sensitivity Pattern of *Serratia Species* from Clinical Samples at a Tertiary Care Hospital in Rawalpindi

Rafia Irfan, Iqra Sadiq, Amna Amer, Irfan Ali Mirza, Faisal Hanif, Wajid Hussain

ABSTRACT

Objective. To determine the antibiotic resistance profile of *Serratia spp* isolated from various clinical specimens.

Study Design and Settings: A descriptive cross-sectional study on antibiotic resistance profile of *Serratia spp* isolated from various clinical specimens was carried out in the Department of Microbiology, Armed Forces Institute of Pathology, Rawalpindi, from 1st July 2017 to 30th June 2021.

Methodology: 464 clinical specimens yielding growth of *Serratia spp* were included in the study. *Serratia spp* were identified by using Standard Microbiological procedures. Modified Kirby Bauer disc diffusion method was used for Antibiotic Susceptibility testing. The clinical data was analyzed prospectively from July 2017 to June 2021 for a period of 4 years. The spectrum of diseases caused by *Serratia spp* along with resistance profiles were analyzed. . Data obtained was analysed using SPSS 24.

Results: High yield of this bug was obtained from pus and tissue specimens 150 (32%).130(28%) isolates were retrieved from blood cultures, whereas respiratory specimens contributed to 89(19 %) isolates of *Serratia spp.* According to the antimicrobial susceptibility pattern, 154 (33.3%) isolates were sensitive to Meropenem, 150(32.2%) were susceptible to Doxycycline and 118 (25.5%) to Amikacin, making them the preferred antibiotics to be used in our setup.

Conclusion: *Serratia marcescens* isolates are increasingly resistant to antibiotics. Clinical isolates of *Serratia* exhibited highest resistance to Ciprofloxacin, Ceftriaxone, Gentamicin and Piperacillin/tazobactam.

Keywords: Antimicrobial, Neonatal Intensive care Units, Outbreaks, *Serratia*

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INTRODUCTION:

The genus *Serratia* belongs to family Enterobacteriaceae is Gram negative, motile, nonspore forming rod and is a facultative anaerobe. This bacterium was firstly discovered in 1819 by Bizio, he identified it as a cause of the bloody discoloration on cornmeal mush. He gave name to the organism in honour of the Italian physicist, Serratia who invented the steam boat. *Serratia marcescens* was originally thought to be an innocuous, non-pathogenic, saprophytic water organism, moreover it was often used as a biological marker because of its easily disguisable red colored colonies. *Serratia marcescens* produces a red pigment called prodigiosin. Prodigiosin was used as a dye for different textiles as well as for materials used for medical purposes. Serratia being ubiquitous in nature, it is widely distributed in environment including soil, water, insects, animals and plants.[1]To date, 14 species of *Serratia* have been identified, out of which eight are associated with human infection. Among these *Serratia marcescens, Serratia liquefaciens and Serratia odorifera* are the most important ones. *Serratia rubidaea* is also encountered though infrequently. *S. marcescens* is the most commonly isolated specie in the laboratory amongst all other species of this genus .[2]The presence of *Serratia* species in hospital environment such as medical equipment, lotions, antiseptics, medications, blood products and sinks, water supplies and instruments potentiate its ability to cause hospital acquired infections. The contaminated hands of Health care workers are an

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important mode of spread of this bacterium. The organism does not lead to primary invasive diseases, but it causes an infection when it gets access to an appropriate immunocompromised host. *Serratia* species harbor few virulence mechanisms thus it is considered to be an opportunistic pathogen. However, *Serratia spp* can also cause community acquired infections. The spectrum of infections varies from respiratory tract infections, intraabdominal infections urinary tract infections, skin and soft tissue infections, osteomyelitis, meningitis to bacteremia and sepsis. Thus, it is a notorious bug in microbiological world. Various risk factors which are associated with these infections are: Infants with low birth weight, prolonged immunosuppressive therapy, prolonged intake of antimicrobials, prolonged hospital stay, indwelling catheters like possession of central venous catheters, urinary catheters, mechanical ventilatory apparatus, respiratory tract instrumentation and various underlying diseases such as solid organ and hematologic malignancy, chronic pulmonary disease, and diabetes mellitus.[3]

In hospital settings, it has the propensity to cause outbreaks due to its presence in hospital environment, mostly in neonatal Intensive Care Units.[4,5.] Neonates are more prone to the infections by organisms owing to their immature immune system.[6] The most common site of infection in these cases is blood stream, followed by the respiratory and gastrointestinal tract. The high incidence of S. marcescens bacteremia in neonates is mostly associated with gut colonization during the first 3 days of life. In immunocompromised patients, there are reported cases of skin and soft tissue infections such as granulomatous ulceration, abscess, bullous cellulitis, and necrotizing fasciitis, which further explains this isolate being opportunistic in nature.[7] The mortality rates are higher in cases of septicemia, meningitis and endocarditis caused by *Serratia species*.[8] The effective diagnosis and treatment of these infections is crucial as this bacterium can exhibit dual antimicrobial resistance ability that is by both intrinsic mechanisms and acquired antimicrobial genes. The acquired resistance is for beta-lactam antibiotics, aminoglycosides and quinolone group of antibiotics whereas natural resistance is also there to many antimicrobials including narrow spectrum penicillins, aminopenicillins, amoxicillin-clavulanate, numerous cephalosporins, colistin and nitrofurantoin.[9] This ability of being multidrug resistant, makes this isolate difficult to be treated and eliminated from the colonized sites. So, clinicians have to tailor the empirical choices for this bacterium according the antibiogram of the hospital or the area whichever is available.

Serratia sp particularly *Serratia marcescens* causes a variety of local and systemic infections in both healthy and immunocompromised host. This facultative anaerobe poses an impending threat to patients admitted in intensive care units by causing outbreaks. Poor infection control practices and irrational use of broad-spectrum antibiotics are major contributing factors behind such outbreaks.[10] The frequency of *Serratia species* as well as the susceptibility pattern of this bacterium has not been studied in our setup. To fill these gaps in knowledge about this important microorganism, we studied the trends of isolation and antimicrobial susceptibility patterns of *Serratia* species in our setup. The rationale of this study was to determine frequency, distribution and antibiotic susceptibility profile of *Serratia spp.* which will help the clinicians to make choices for empirical treatment of nosocomial infections suspected to be caused by *Serratia species*. This knowledge can help in reducing morbidity and mortality in intensive care units especially neonatal ICUs. It can be helpful in establishing antimicrobial stewardship to minimize unnecessary use of antibiotics, which may prevent emerging antimicrobial resistance.

METHODOLOGY:

The department of Microbiology Armed Forces Institute of Pathology, Rawalpindi receives clinical specimens submitted from Combined Military Hospital (CMH) Rawalpindi, Military Hospital (MH Rawalpindi), Armed Forces Bone Marrow Transplant Center (AFBMTC), Armed Forces Institute of Urology (AFIU) and Army Liver Transplant Unit (ALTU). The clinical data was analyzed prospectively from July 2017 to June 2021 for a period of 4 years after taking permission from Ethical Committee of our institute (Ethical Review Board number 479). All *Serratia spp* isolated during the study period were included, however repeat specimen from the same patient yielding *Serratia* specie with similar antibiogram was excluded. *Serratia specie* were identified by its phenotypic and biochemical characteristics using Standard Microbiological procedures. All the specimens were inoculated on Blood agar and MacConkey agar. The culture plates were incubated at 37*c for 24 to 48 hours. Colony morphology particularly pigment production was noted. Modified Kirby Buer disc diffusion method was used for Antibiotic Susceptibility testing for the recommended Antibiotics by Clinical Laboratory Standard Institute.[11] *Eschrechia coli* ATCC 25922 was used as control organism. The spectrum of diseases caused by *Serratia spp* along with resistance profiles and other demographic data were analyzed over the described period. Data obtained was analysed using SPSS 24. Demographic data was assessed using descriptive statistics. Mean and standard deviation (SD) were calculated for numerical variables, like age. Categorical variables were expressed using frequencies and percentages. $P<0.05$ was considered statistically significant.

RESULTS:

Serratia species were identified in 464 of clinical specimens from July 2017 to June 2021. The frequency of isolation of *Serratia species* is shown in Figure 1. Out of total 464 isolates, 329 were isolated from male patients and 135 from female patients, Male to female ratio of 2.43:1. The age

wise distribution of patients in which *Serratia* species were isolated is shown in Figure2. The distribution of *Serratia* species according to specimen type which includes respiratory, pus and tissue, blood, urine, fluids is depicted in Figure 3. According to the antibiotic susceptibility tests, 325 (70%) isolates were resistant to ciprofloxacin while only 117 (25.2%) were resistant to Amikacin. The percentage of isolates resistant to other antibiotics is shown in figure 4.

DISCUSSION:

The frequency of *Serratia* species in various clinical specimens was studied. A total of 464 isolates were isolated over four-year time period from July 2017 to June 2021.There was surge in number of *Serratia spp* in years 2017 and 2019 due to outbreaks in Neonatal Intensive Care Units. In first six months of year 2019, highest number of 98 cases of Serratia were isolated. In remaining years, it was sporadic.

Figure 1: Six monthly distributions of cases of infection caused by *Serratia spp*

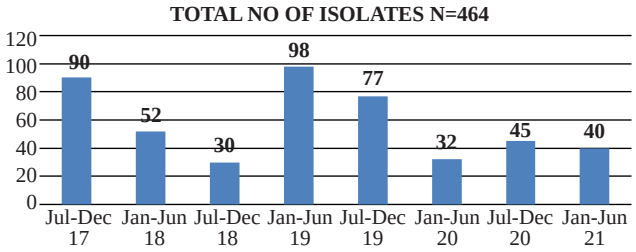


Figure 2: Total number of *Serratia* species isolated in patients of various age groups.

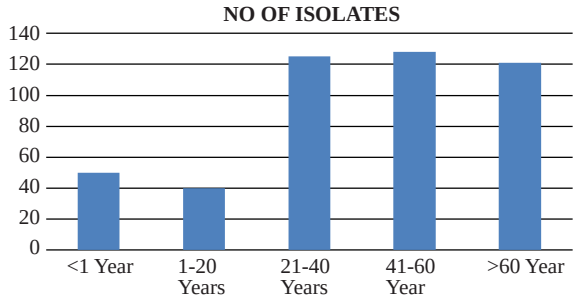


Figure 3: Frequency of isolation of Serratia spp from various clinical specimens

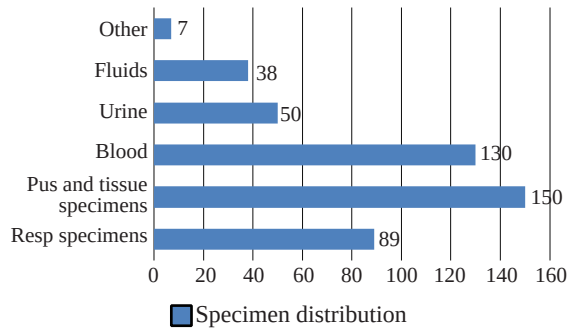
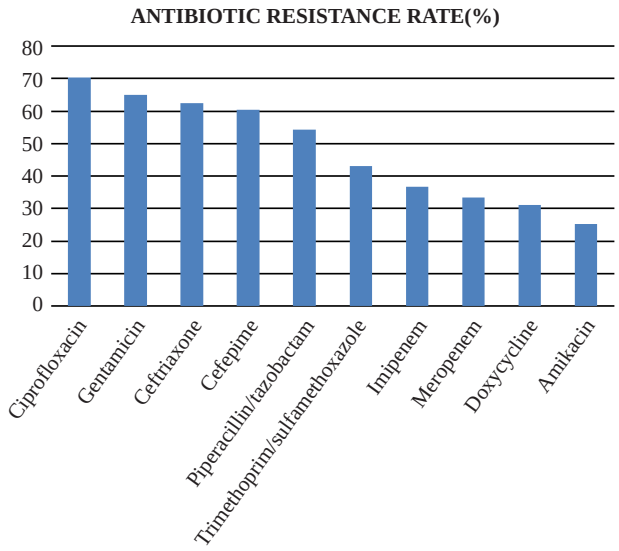


Figure4: Antibiotic resistance rates of *Serratia* species isolated from various clinical specimens



The baseline rate of infection or colonization due to *Serratia spp* in our setup was noted to be 7 to 8 cases/month which was in contrast to study done in Argentina in which the sporadic cases of *Serratia spp* infections were 1-4 cases /month in 2005 and 2006. In a similar study during the outbreak in 2007 to 2008, the rate reached 10 cases /month.[12.] It is comparable with our study being 11 and 10 cases /month in outbreak years.

In our institute outbreaks of this isolate occurred in Neonatal Intensive Care Units only. This finding is supported by various studies mentioned in literature as the bug is notorious to cause outbreaks in Neonatal and Pedriatic intensive care units. Lot of reported outbreaks occurred due to non-adherence to standard infection control and prevention practices. A study conducted by Cristina et al in February 2019 in Italy gave emphasis on outbreaks by *Serratia spp* in Neonatal Intensive Care Unit. The report urged that prompt enforcement of handwashing and application of contact-based precautions are essential factors in halting the spread of this pathogen.[10] Moreover a study published in Frontiers of microbiology by Claudia Saraleguei et al also highlighted the same issue that precautions taken in neonatal Intensive Care Units can prevent the infection by this isolate.[13]

We found out that male patients were much more commonly infected/ colonized with *Serratia spp* while clinical samples of female patients yielding *Serratia spp* were quite few in number. Although there is no plausible reason as to why this isolate is significantly affecting more males but our observation equates with Morillo *et al* who reported 13 male (72.2%) and 5 female children (27.8%) were having infection caused by *Serratia spp.*[14]

The present study revealed that Isolation of *Serratia species* was highest among persons aged between 40-60yrs (27.58%) and lowest incidence was in age group 1-20years (8.62%).

If we compare with other studies, Ferreira et al in Brazil in 2020 determined the prevalence of *Serratia* by age which unfolded to be 0–1 day (12.96%), 18-59 years (38.89%), 60 years or more (48.15%), the highest being more than 60 years age and lowest 1-20 years of age.[15] This is like some other studies that showed advanced age male patients as presenting a higher risk of contracting *Serratia* infections.[16-18]

In our study, Pus and Tissue specimens yielded maximum number of *Serratia Specie* which was then followed by blood culture samples, respiratory samples and urine. Sterile fluids including cerebrospinal fluid also accounted for the growth of this dreadful pathogen. Umblical venous catheter tips, Central venous catheter tips and biliary stent tips were the specimens included in "other" category and also yielded growth of *Serratia spp*. These findings suggest maximum cases having *Serratia specie* infection were of skin and soft tissue. Outbreaks of Wound infections particularly post operative surgical site infections have also been mentioned in literature.[19] *Serratia marscenes* is also an etiology of Bacteremia, Sepsis and Urinary Tract infections. In our present write up during outbreak years *Serratia* specie were most commonly obtained from Blood cultures. This finding is analogous with a study published in Journal of Environmental research and Public health by Christina et al in 2019.[20]A retrospective study done in General hospital in Nigeria in year2019, revealed *Serratia Spp* from Respiratory specimens including sputum (38%),[21] which is much higher observation from our narration. We also analyzed the Antibiotic susceptibility testing Data obtained from the electronic system of our Laboratory on *Serratia species* isolated in the defined time period. The antibiotic with the highest resistance rate was found to be Ciprofloxacin (70.2%). Antibiotic with the lowest resistance rate was determined as Amikacin (25.2%). In one study of India[8], however the resistance rate of these two drugs were quite different, Ciprofloxacin having 14.3% resistance while Amikacin having 71.4% resistance rate. This can be due to difference in use of these drugs in empirical treatment in both set ups which can lead to development of resistance in these areas.

If we analyze Cephalosporins sensitivity rate (particularly ceftriaxone) we see them to be having a very high resistance profile in our study (62.3%). The high proportion of isolates resistant to this beta lactam antibiotic was also observed from a study conducted in Turkey in 2018 by Simsek et al, which showed ceftriaxone to be the antibiotic with the highest resistance rate (22.7%).[21]

In our study, Carbapenems more specifically imipenem had low resistance rates (36.7%) as compared to most of other drugs, which is comparable to the study done by Hayashi et al in June 2021 in which all the isolates included in study were sensitive to Carbapenems.[22] The work done by Xu Q et al in Tertiary hospital in China in year 2020 also supported our study findings by demonstrating Amikacin to be the most sensitive drug.[23]Aminoglycosides were also found to be most sensitive for this bacterium in study done by Ferreira et al. [15]An extensive 8-year study done in Taiwan, revealed Ceftazidime and Imipenem with consistently high susceptibility rates to *Serratia species* while ciprofloxacin had highest resistance rate.[24]

Our study showed that isolates of *Serratia* Spp had high resistance to ciprofloxacin, gentamicin, ceftriaxone, cefepime and pipercillin/tazobactum. However, meropenem, imipenem, trimethoprim sulfamethoxazole, doxycycline and amikacin were found to be the most suitable antibiotics for treatment. We suggest Carbapenems particularly imepenem as agents for empirical treatment till the availability of susceptibility results. Amikacin though being most sensitive of all antibiotics should not be used as monotherapy and hence for empirical treatment.

The limitation of our study was there is no follow up data available which can explain the morbidity and mortality of the patients having infection by these strains of *Serratia spp*. Thus, the effectiveness of culture directed antimicrobial therapy to eradicate this pathogen was also not ascertained. Moreover, no clinical history correlation was done to ascertain the status of these strains being actual pathogen or colonizers.

CONCLUSION:

Our present account concluded that *Serratia* species in clinical isolates are increasingly resistant to antibiotics. The clinical isolates of *Serratia* specie exhibited highest resistance to ciprofloxacin, ceftriaxone, gentamicin and piperacillin / tazobactam. Carbapenem particularly imipenem and aminoglycoside particularly amikacin were least resistant antimicrobials, which fulfilled our objective to determine the antibiotic resistance profile of this notorious bacteria.

Authors Contribution:
Rafia Irfan: Idea and Concept
Iqra Sadiq: Sample Collection
Amna Amer: Sample collection and process
Irfan Ali Mirza: Process and analysis
Faisal Hanif: Writing, reviewing and conclusion
Wajid Hussain: Statistics and discussion

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Medical Education-Original Article **Open Access**

Health Sciences Students' Satisfaction with Quality of Online Distance Education

Syeda Zarreen Raza, Sanaa Ahmed, Ziyad Sanaullah, Zunairah Rais, Zahid Memon, Saad Saleem

ABSTRACT:

Objective: To assess the students' satisfaction with the online distance education at constituent institutes of a Medical University of Karachi.

Study design and setting: A cross-sectional study was conducted in 2021 March at JSMU to find out the experience across all the institutes of the university during the covid pandemic.

Methodology: A sample size of 338 was calculated through Open Epi. Ver. 3.0, keeping a confidence interval of 95% with a 5% chance of error from 357 students. Performa was specifically designed for this study, consisting of 3 parts that are content, teacher, and technical review, which contains 16 questions.

Results: Python ver. 3+ was used for descriptive analysis of the responses. A total of 338 responses were received. The lowest responses received in the teacher`s review were that most of the teachers inspired me to explore the subject further (Neutral = 33.73%), the lectures were boring and uninteresting to attend (Neutral = 28.4%), in the content review the lowest response. In the content review, the lowest response was for "your expectations regarding learning objectives were met" (Neutral 31.07%) and in the overall review, the subscale lowest response was for technical issues like problems in audio visual (Agree=33.4%), the learning environment was collaborative (Neutral=32.54%)and failure to meet the learning objectives by the teachers.

Conclusion: The responses of the students show that they were overall satisfied with distance education during the pandemic. A few problems were highlighted, including technical and content-related ones that could be resolved by providing training to the teachers and students.

Keywords: Online Education, Students` satisfaction, Medical education

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INTRODUCTION:

Covid-19 brought substantial transformation to daily life and routines. From education to domestic chores, it left nothing unmarked. Life in Pakistan has suffered, too. During these trivial times, nearly all educational programs switched to online sessions.[1] Classes were regularly held employing online platforms like Zoom, Skype, Google Meet and the Virtual Learning Management System (VLMS).[1-3] To address the challenges posed by online learning, American Dental Education Association requested the dental schools to follow the rules and policies set by the state. Work in coordination with the health department to make decisions that favour the safety of all the stakeholders.[4] Similarly, the Higher Education Commission in Pakistan also issued a policy for online distance education during this period to support the learning of students.[5]

The transition phase of the pedagogical shift was exigent, as the learning and assessment of students were largely affected and emanated in deficiency in clinical skills. To cover for this loss, one strategy adopted by the British Association of Oral and Maxillofacial Surgeons was by

conducting webinars on a variety of topics as part of the Fellowship program utilizing strategies such as case-based discussions and flipped classrooms.[6] Trainees' input from these sessions was availed to provide information on developing a regional Moodle-based Virtual Learning Environment (VLE).[6] While in India, the All-India Institute of Medical Sciences shared its learning experience amid the pandemic.[7] After preparing to adapt to Google Meet's modern learning climate, the faculty conducted seminars and Case Based Learning (CBL) sessions. Furthermore, lab videos were also made and shared online.

Online education varies from conventional classes, including teacher and student responsibilities, collaboration, engagement, and versatility. It undeniably puts heightened accountability on learners for their own learning.[3] Though there are sparse interpersonal ties between teachers and students in online education, a shift to a more collaborative instructional format and frequent contact will partially overcome the problem.[7] Roseman University of Health Sciences, America, looked at the impact of the pandemic on the overall lives of dental students.[6] The findings revealed that students felt their education suffered as dental education relies majorly upon the skills that they master during four years of education but had positive reviews regarding the academic sessions held online. Most of the participants were male undergraduate students.[6] Two multi-centric kinds of research conducted in China probed the level of satisfaction with the online education platforms, as both the teachers and students were novices to working full time with them.[3,8] It is worth mentioning that the technical problems encountered during the usage of various platforms influenced their satisfaction.[3, 8]

All the previous literature on students' perception of online teaching covers either the barriers, their experience with the strategies, or how they dealt with the problems. But none covered the satisfaction with the quality of the online teaching strategies utilized. This mandated exploring students' satisfaction, perceptions, and attitudes towards online learning.[6]

METHODOLOGY:

The study was conducted at the Jinnah Sindh Medical University, Pakistan. Permission was taken prior to the conduction of the study from the IRB board letter No. 2021/-407. The design of the study was descriptive cross-sectional. Convenience sampling was done. The sample size was 338, calculated from the total number (2800) of students enrolled in MBBS (5 batches), BDS (4 batches), Pharm-D (5 batches), DPT (2 batches), BSN (2 batches) with a 95% confidence level with 5% chance of error and 50 % hypothesized frequency of outcome in the population. The sample size was calculated through OpenEpi software ver. 3.01.

The inclusion criteria included all the students enrolled in MBBS, BDS, Pharm D, DPT, and BSN programs at JSMU who agreed to be a part of this survey and students with any smart device or computer and internet connection. Exclusion criteria included students with online attendance of less than 50%.

The questionnaire was specifically designed and reviewed by the involved faculty members. It consists of 3 subscales containing teachers review, content review and overall review respectively. It encompasses 16 closed-ended questions. Literature was reviewed for finding the relevant questions to include.[9-18] For every question, the Likert scale was used from strongly agree to strongly disagree. The survey form was checked for reliability by pilot testing on 10% of the sample size population before the commencement of the study. The Cronbach alpha was found to be 0.65. Face validity was also checked.

After seeking permission from the IRB(IRB/2021/-407), an invitation letter to all the Heads of the disciplines was sent requesting them to participate in the study. Upon acceptance, the link to the questionnaire created on Google Forms was shared with the students through their respective Google classrooms.

RESULTS:

A total of 338 responses were received from the students belonging to different programs. The analysis was done through Python 3+. The mean and standard deviation were calculated for each sub-scale, also the frequency of the responses was calculated. The responses were highest on the technical/overall aspect while the standard deviation was highest for content-related questions.

Table 1 contains the sub-section details with each item and the highest and lowest responses they received. For subscale 1, questions related to teachers were asked. The highest positive response was received for the question “The lecture date, time, and topic were conveyed beforehand” was 51.78% agreed. Subscale 2 comprising 6 questions highlights the aspect of quality of content presented during online education. The highest response was for “lectures were focused towards the topic”. The percentage of agreed responses was 71.89. Finally, sub-scale 3 with 5 questions focuses on the overall and technical aspects of online education. The item receiving the highest agreed response was “I was appropriately guided about the technical use of the provided learning platform” which was 49.11%.

Students have different learning styles, which affect their learning capability and satisfaction with the learning process and teaching strategy.[9] Subscale 1 regarding the teacher’s review was positively supported by ambient votes regarding the punctuality of lectures, planned schedules being followed, and the teacher’s ability to hold the interest of the students and make it interactive.

The conversational connections between students and teachers, as well as among students themselves, are an essential component of classroom learning. Online interaction

Table 1: Responses of students in percentage accordingly to instruments in subscale 1, 2, and 3

Sr. No	Question/Instrument	Highest Response	Lowest response
Subscale 1: Teacher			
1	The lectures started on time	Agree 44.08%	Strongly Agree 4.73 %
2	The lecture date, time, and topic were conveyed beforehand	Agree 51.78%	Strongly Disagree 5.62%
3	The teachers were enthusiastic and had command of the subject	Agree 43.49%	Strongly Disagree 5.03%
4	The teachers were taking feedback during the lecture regarding delivery and showed respect towards all the students	Agree 49.41%	Strongly Disagree 5.33%
5	Most of the teachers inspired me to explore the subject further	Neutral 33.73%	Strongly Agree 6.8%
6	The topic and time of lectures were not communicated well before	Disagree 38.46%	Strongly Agree 3.25%
7	The lectures were one-way communication lacking the interaction	Agree 35.8%	Strongly Disagree 2.96%
8	The punctuality of the lecture was not taken care of	Disagree 35.5%	Strongly Disagree 4.44%
9	The lectures were boring and uninteresting to attend	Neutral 28.4%	Strongly Disagree 4.14%
Subscale 2: Content			
10	The lectures were organized and effective	Agree 41.72	Strongly Agree 5.33%
11	The lectures were focused towards the topic	Agree 71.89%	Strongly Disagree 1.78%
12	The pace of lectures was optimal	Agree 40.83%	Strongly Agree 2.96%
13	The teachers were incorporating the given feedback into their delivery	Neutral 35.5%	Strongly Disagree 4.14%
14	Your expectations regarding learning objectives were met	Neutral 31.07%	Strongly Agree 5.33%
15	The presentation and quality of the material were appropriate	Agree 51.48%	Strongly Disagree 3.85%
Subscale 3: Overall & Technical			
16	The teacher's voice was coherent and intelligible	Agree 44.08%	Strongly Disagree 3.85%
17	The learning environment was collaborative	Neutral 32.54%	Strongly Agree 5.62%
18	I was appropriately guided about the technical use of the provided learning platform	Agree 49.11%	Strongly Disagree 4.44%
19	The platform for online lectures was not chosen wisely and was difficult to understand	Disagree 44.67%	Strongly Disagree 7.4%
20	The audio-visuals were disturbing and needed high concentration	Agree 33.43%	Strongly Disagree 1.18%

is less stressful than face-to-face discussions and produces a thorough exchange of views. It is also more student centred, and even the socially shy students feel at ease in conversing with colleagues and teachers.[10]In our survey, more than 35% of the students complained of a lack of interaction. Comparing the results to a previous study held using online instructions showed that, according to the students, effective teaching depended on the teacher`s ability in creating a flexible and structured environment and actively participate in the learning of the students and establish a trust-based relationship.[11]

The second subscale was on the content review of the lecture. There were two issues highlighted in this section. One was the teacher's failure to incorporate feedback in their lecture and the second was a failure to meet the learning objectives. Though the students were satisfied with the content of the lectures regarding the topic, they felt that the defined learning objectives were not met. It creates a gap in what is delivered and what is expected to be learned by the students to be judged at the end of the module or semester. It can also affect the grade of the students which is usually taken as a direct result of the teaching and learning process. Usually, during conventional lectures, we take feedback from students regarding the pace of the lecture and whether they understand or require further clarification. The facial expressions of the students during lectures are informal indicators of both. This is lacking in online lectures for during class, the video and mic were off to decrease the load on the bandwidth. To improve this problem, teachers should ask students either take feedback at the end or take a poll during lectures may improve.[10]To cater for the needs of different kinds of learners it is important to incorporate strategies such as adding pictures and videos in the presentation to gain spark their interest and maintain their attention[9].For this purpose, before the start of the online classes, a training session for Google Meet was held by Professional Development Centre and later "The Basics of Online Assessment and Teaching (BOAT) was arranged by the Institute of Medical Education of the university to support and provide technical training. that was addressed in this section included the voice and video quality of the lecture. The lectures were understandable and coherent, but the quality of the video was poor. Low bandwidth is one of the reasons behind the poor quality of visuals. The lecture recording was uploaded to Google Classroom to inundate the issues of internet connectivity or

Table 2. Summary of Published Articles related to Student Satisfaction with Online Teaching

Author	Venue	Year	Study Focus	Highest Responses/Results
Rafi AM, Pulikkottil VR and Kuttichira P.[17]	Central Kerala, India	2020	Online education Barriers	-Most common barrier was network issue 43.7% -Recorded lectures were preferred 69.2% -Lecture duration preferred 30-40 minutes (47.6%) -Common Platform was Impartus (63.6%)
Hameed T et al.[15]	India	2020	Frequency Organization, Content Preparedness of classes.	-Somewhat satisfied (SWS) with -Amount of syllabus covered (59%) -Frequency of online classes (78%) -Organization and preparedness (96%) -Online mode and methods of teaching (64%)
Verma A et al.[18]	India	2020	Online Teaching	-99% students learning needs were met. -57% felt classes were safe, comfortable, and enjoyable. -92% felt these classes were good utilization of time. -51% felt problems in internal online assessment -47% wants online classes in the future.
Singh K et al.[7]	India	2020	Feedback on Online Teaching	-Previous exposure (73%) -Material shared was relevant (91.8%) -In class questioning was allowed (92.3%) -Interaction with the teacher was poorer than physical classes (43.9%) -Physical classes are better than online classes (50.9%)
Nepal S et al.[16]	Nepal	2020	Learning preparation Means of attending classes Student`s perception	-Mostly mobile were used -Broadband utilized (65.5%) -2/3 rated preferred traditional classes. -76.5% attended online lectures -Utilized notes/books to revise (53.5%) -Use e-books for learning (64%) -Utilized books or e-books before or after classes (55.8%)
Dost S. et al.[14]	UK	2020	Experiences Barriers and benefits	-Time spent online increased during Covid: 23.56% students during the pandemic spending >15 hours per week -BenefitThe benefit of the teaching platform was it's flexibility. -Barriers included distraction from family (26.76%) and poor internet connectivity (21.53%)
Baticulon R et al.[13]	Phillipine	2021	Access to technological resources Study habits Living conditions Self-assessment of capacity for and perceived barriers to online learning, and proposed interventions	-93% owned a smartphone - 79% had a postpaid internet subscription -Only 1505 students (41%) considered themselves physically and mentally capable of engaging in online learning. – Barriers included learning styles, having to perform responsibilities at home, and poor communication or lack of clear directions from educators
Baczek M et al.[12]	Poland	2021	Advantages and Disadvantages of e-learning Comparison of face-to-face and Online teaching Acceptance of e-learning	-Ability to stay at home (69%) -continuous access to online materials (69%) -learning at your own pace (64%) -comfortable surroundings (54%). -Major disadvantage was lack of interactions with patients (70%) and technical problems (54%). -No difference between face-to-face and online learning in terms of opinions on the ability of the learning method to increase knowledge. -E-learning was considered less effective than face-to-face learning in terms of increasing skills and social competencies.

power failure. All in all, the experience with Google Meet was satisfactory.

Several studies conducted in India assessed student`s perspectives on the online learning efficacy, teaching strategies and the barriers to the process of pedagogical shift which are like the studies held in the UK, Ireland, Nepal, Poland, Philippines, and China.[3,8,12-18] These studies are summarized in Table 2 below to compare them.

In comparison, we reported on the various aspects, which are the content, teacher, and technical, as well as other factors that may affect satisfaction with online teaching, whereas none of these studies covered this topic completely. It is vital to contemplate these factors to strengthen the overall learning process for students.

Video conferencing software use was not limited to the lecture delivery; tutorials and case-based discussions were held throughout the pandemic, giving versatility to its usage.[1, 19, 20] Students' satisfaction with online education is affected by several factors, including their prior experience with the software, the workload, including assignments and tests, and their ability to interact and get prompt replies to queries. Also, creating a collaborative, supportive, and motivating environment invigorate the students' online experience. Giving team assignments helps them establish a cohort of friends.[21]

There are some limitations. The study was designed to find out the student`s satisfaction with the online teaching process, and though it covered the different aspects of the process, the emotional/psychological aspect was not included in the survey, which could have impacted satisfaction with the process. A longitudinal study of pre-and post-online teaching sessions would have shown more in-depth pre-session perceptions and readiness and post-session satisfaction with the education delivered during the pandemic.

CONCLUSION:

Although our study reveals that online education is worthwhile, it does not mean that it can substitute for on-campus teaching. We should consider incorporating an optimal proportion of online learning into medical education.

Authors Contribution:
Syeda Zarreen Raza: Study Design, Data Collection, Writing of initial Manuscript
Sanaa Ahmed: Study design, Results formulation, writing of initial manuscript
Ziyad Sanaullah: Data curation, Data Analysis and results compilation
Zuneirah Rais: Writing of discussion and review of manuscript.
Zahid Memon: Writing of introduction and review of manuscript
Saad Saleem: Review and finalization of manuscript

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Assessment of Trends of Consumption of Caffeine Containing Products and their Effects on Medical Undergraduate Students

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ABSTRACT

Objectives: To assess trend of consumption and withdrawal effects from caffeine containing products among medical undergraduate students of Karachi.

Study design and setting: Cross-sectional study conducted via web-based questionnaire, from January 2020 to June 2021.

Methodology: Undergraduate medical, MBBS students aged 18-24 years, studying in 6 different medical universities of Karachi were included in the study. An online survey was conducted. An online questionnaire was designed which consisted of 28 self-made questions that focused on collecting basic sociodemographic information, coffee consumption habits, and any adverse event associated with caffeine intake. The questionnaire was posted online and undergraduate medical students were invited to participate in the study.

Results: One hundred and fifty seven students participated in the study. Out of 157 students 94% admitted to consuming some form of caffeine containing product (CCP), with 42.3% (n = 66) of the total believing that they were addicted to caffeine. A significant number also believed that CCPs helped students deal with their problems. Withdrawal symptoms include migraines, sleep disturbances, and loss of focus, leading to an inability to perform daily tasks. A positive correlation was also found between the daily intake of any CCP and incidence of withdrawal symptoms (p=0.01).

Conclusion: Many students in medical universities of Karachi are moving towards caffeine dependence, due to daily consumption over a prolonged period of time. Promoting responsible consumption habits and spreading awareness over potential adverse effects of CCPs, especially amongst a younger audience could improve the health and lifestyles of students in the long-term.

Keywords: Addiction, Caffeine, Substance Abuse, Withdrawal

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INTRODUCTION:

Caffeine is a widely consumed substance and is ingested in various forms by all age groups.[1] Tea is one forms of caffeine consumed especially in Pakistan, India, China and Britain. It has multiple effects on health, some being controversial such as reduced BMD (bone mineral density). Daily caffeine intake has shown to have some correlation with increased body mass index.[1, 2] It has been seen that the blood chemistry has altered concentrations of AST, ALT, and plasma creatinine in those drinking caffeine.[3] A growing number of clinical studies express that caffeine users develop addiction to the substance and are incapable of reducing their intake despite knowledge of repeated health problems associated with continued use. The World Health Organization (WHO) along with health care professionals identifies caffeine dependence as a disorder.[4] Consequently, with work and productivity there also seems to be an effect on academic performance. Many students use caffeine as a stimulant to increase productivity and work however data would suggest the end result to be the opposite. A previous research study found that excess energy drink drinking is connected to lower academic scores such as grade point averages (GPAs).[5]

The consumption of energy drinks, despite the variation in the reason for choosing these drinks, is quite common among college students. A primary aim of ingesting caffeine is to have more energy and stay awake. [6] Existing literatures prove that caffeine consumption is driven by a number of factors such as taste, withdrawal symptoms such as headaches, keeping alert for longer periods of time, ceasing fatigue, and social factors.[7] Despite this fact, it has been shown that frequent consumption of caffeine has been unsuccessful in enhancing mental alertness and mental performance.[8] A study showed that ''alexithymia, a personality trait characterized by negative moods and deficient emotion regulation", was linked to heavy caffeine intake.[9] The use of coffee has shown poor sleep quality and increased commission errors to combat sleep disturbances can therefore be detrimental in situations requiring inhibitory control. Thus, linking to reduced work productivity and general wellbeing.[10] Given all these reasons and more, it is no surprise that caffeine abuse is progressively being included in the list of potentially harmful substances for the youth in terms of health.[11] However, despite the many risks of excessive and prolonged caffeine intake, many people –especially adolescents and young adults – continue to consume large quantities of caffeine containing products. Therefore, the main objective of our cross-sectional study was to examine the trend of caffeine consumption in Pakistani adolescents and young adult students, and to evaluate its relationship with withdrawal symptoms, thus assessing its addictive ability in this sub-population.

METHODOLOGY:

The study was conducted after Institutional Board Review approval was obtained from Jinnah Sindh Medical University JSMU/IRB/2020/-303. A cross-sectional study was conducted via web-based questionnaire, from January 2020 to June 2021. Undergraduate medical, MBBS students aged 18-24 years, studying in 6 different medical universities of Karachi were included in the study. Students from all the five years were included in the study. Any student who did not complete the survey was excluded from the study. An online survey was conducted. The questionnaire was posted online and undergraduate medical students were invited to participate in the study. A Sample size was 157, was calculated based upon a similar study done previously.[12] It was calculated using the sample size calculator available at: http://www.raosoft.com/samplesize.html considering the confidence interval of 95%.students were selected by using convenience sampling for this cross-sectional study. An online questionnaire was designed which consisted of 28 self-made questions that focused on collecting basic sociodemographic information (age, gender, and education level), coffee consumption habits, and any adverse event associated with caffeine intake. The validity of questionnaire was assessed by carrying out a small pilot test within one university including a small sample size of 50 students. The reliability was assessed by sending the questionnaire to 5 experts on the subject and having research experience of 10 years.

The participants were made aware of their rights in a disclaimer section before the survey, and they were explicitly informed that no monetary compensation would be provided in exchange for participation. The anonymity of all participants remained preserved.

The IBM Statistical Package for the Social Sciences (IBM SPSS version 26; IBM Corp Inc, Armonk, NY) was used to analyse the data. Categorical data was presented in terms of frequencies and percentages, whereas continuous variables were expressed as mean ± standard deviation. Pearson chi-square test of independence was used for comparing continuous and categorical variables wherever applicable. A p-value of <0.05 was considered significant.

RESULTS:

A total of 157 students participated in the study. Out of 157 participants, 123 (78.3%) were females and 34 (21.7 %) males. The mean age of the study population was 20.7 ± 1.7 years. There were 148 participants (94.3%) who admitted that they have taken caffeine, at some point in their life, in the form of coffee, tea, caffeine tablets, or energy drinks. Fifty two participants (33.5%) began consuming tea /coffee in their early childhood (between 2 to 10 years of age).

Different caffeine containing drinks were preferred by everyone. Many preferred more than one drink. Tea was the preferred drink for 134 (85.4%) participants, coffee was preferred by 121 (77.1%) participants, and energy drinks were consumed by 47 (36.3%) participants, whereas 27 (16.6%) participants consumed caffeine in the form of tablets.

Table 1 summarizes the habits caffeine consumption among university students.

Withdrawal symptoms were experienced by 66 study participants (42.3%). They feel moderate to severe withdrawal symptoms, leaving them unable to perform daily tasks without caffeine consumption. Withdrawal symptoms include migraines, sleep disturbances, and loss of focus. Pearson's chi-squared test showed a positive correlation between daily intake and withdrawal symptoms (p=0.01). Figure 1 shows the common withdrawal symptoms reported. The age at which respondents reportedly first tried CCPs was neither significantly associated with the one adverse effect upon excessive consumption ($p = 0.431$), nor was it linked to withdrawal symptoms ($p = 0.710$). Similarly, the initial reasons for consuming CCPs were not significantly linked to adverse effects ($p = 0.387$) or withdrawal symptoms ($p = 0.444$). However, those who reportedly increased caffeine intake when preparing for or taking exams, were found to have a significant relationship with adverse reactions ($p = 0.041$)

Figure 1 shows common reported adverse effects among

Table 1: Caffeine consumption trends among the MBBS students studying in medical universities in Karachi

Consumption Habits	Gender		P - value	Age			P - value
	Males (n, %)	Females (n, %)		<19 years (n, %)	20-23 years (n, %)	>23 years (n, %)	
When did you start taking caffeine? If you do not consume regularly when was the first time you tried it?							
2-10 years old	14,41.2	38,31.1	**0.533**	8,29.6	41,33.1	3,60.0	**0.325**
11-15 years old	13,38.2	57,46.7		12,44.4	58,46.8	0,0	
16+ years	7,20.6	27,22.1		7,25.9	25,20.2	2,40.0	
What's your preferred time of the day to consume caffeine?							
Morning	7,21.2	34,28.1	**0.187**	7,25.9	32,26.2	2,40	**0.875**
Evening	6,18.2	9,7.4		4,14.8	11,9.0	0,0	
Night	3,9.1	4,3.3		2,7.4	5,4.1	0,0	
Anytime throughout the day	14,42.4	56,46.3		10,37	57,46.7	3,60	
Never	3,9.1	18,14.9		4,14.8	17,13.9	0,0	
Which of the following below drove you towards caffeine consumption?							
Peer pressure	6,22.2	12,12.0	**0.264**	2,9.1	14,14	2,40	**0.068**
Studies	7,25.9	32,32		7,31.8	31,31	1,20	
Curious about effects	4,14.8	7,7		1,4.5	8,8	2,40	
Curious about taste	10,37.0	49,49		12,54.5	47,47.0	0,0	
How many cups of caffeine/bottles of energy drinks do you consume in a day?							
0	11,32.4	37,30.3	**0.548**	10,37	37,29.8	1,20.0	**0.737**
1	6,17.6	33,27.0		8,29.6	30,24.2	1,20.0	
2	10,29.4	33,27.0		6,22.2	36,29.0	1,20.0	
3	3,8.8	13,10.7		3,11.1	12,9.7	1,20.0	
More than 3	4,11.8	6,4.9		0,0	9,7.3	1,20.0	
Do you feel caffeine helps you deal with your problems?							
Yes	18,54.5	49,41.9	**0.196**	9,36.0	57,47.5	1,20	**0.304**
No	15,45.5	68,58.1		16,64.0	63,52.5	4,80	
Does your caffeine intake start/increase during exam time only?							
Yes	10,29.4	56,45.9	**0.161**	11,40.7	54,43.5	1,20	**0.783**
No, I consume it all the time	16,47.1	38,31.1		9,33.3	42,33.9	3,60	
I don't take it regardless	8,23.5	28,23.0		7,25.9	28,22.6	1,20	
If someone told you, you were addicted, would you deny or accept?							
Accept	16,57.1	50,52.6	**0.674**	6,31.6	59,59	1,25	**0.045**
Deny	12,42.9	45,47.4		13,68.4	41,41	3,75	

Figure 1: Common withdrawal symptoms reported among the caffeine consuming MBBS students studying in medical universities in Karachi

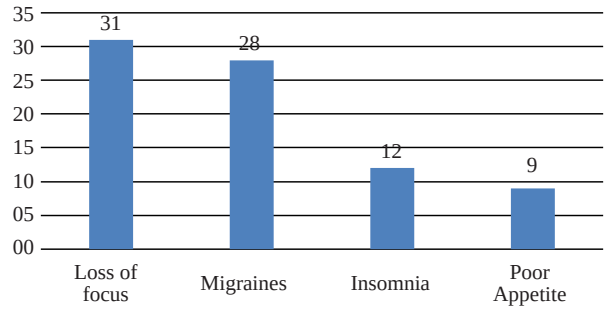
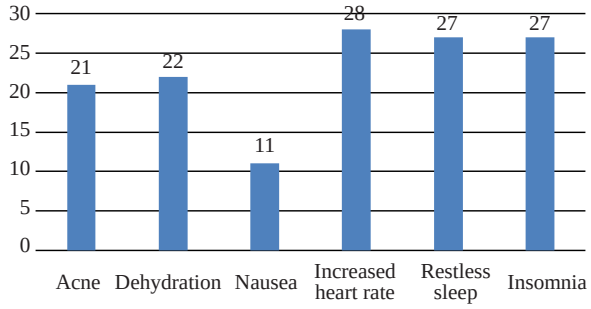


Figure 2: Common adverse effects reported among the caffeine consuming MBBS students studying in medical universities in Karachi



the participants who consumed caffeine. Furthermore, a large fraction of students claimed to have faced some sort of withdrawal symptom upon cessation of the CCP they consumed (n = 61 / 139, 43.9%), though there was no significant relation when stratified by gender (p = 0.350). Additionally, a large fraction of respondents reported that their caffeine intake increased at the onset of exams (n =66 / 156, 42.3%), though no significant relationship could be found with gender (p = 0.161) or current age (p = 0.783). Interestingly, if told that they were addicted to a CCP, a slightly higher fraction of people admitted that they would be willing to accept this information (n = 66 / 132, 54%). When this was further analysed, no significant relation was found with gender (p =0.674), however, the current age showed a significant relationship (p = 0.045)

DISCUSSION:

Our study on caffeine withdrawal is subject to heavy gender biased as the study population is based in medical universities which are known to have an 80-85% female population across Pakistan.[13] Caffeine consumption escalates in the student population during exams. The problem commences when withdrawal headaches are considered as a trigger to take even more caffeine. The headaches are the beginning of more harmful side effects like sleeplessness, insomnia, and lack of mental alertness.

Studies report that the caffeine intake in young adults was 357 ±400 mg/ day and a median intake of 259 mg/ day.[12] Our research shows that college students start taking caffeine at a very early age, and it keeps increasing in amount as they grow. Majority of student population in Pakistan take caffeine in tea, usually starting as young as three years old at teatime with the family.[13] As children consume more caffeine at younger ages (2-16 years), it is potentially detrimental to their growth and development due to caffeine's known consequence of disturbed sleep patterns.[14] There is sufficient evidence in the literature to suggest that children are consuming caffeine and it is a problem.[15]

Multiple studies have shown that caffeine-withdrawal syndrome is clinically significant. Caffeine Use Disorder was added to DSM-5 and requires further research as a diagnosis.[16] This study solidifies that caffeine is a real addiction, and caffeine dependence need to be addressed. There is evidence that a steady caffeine reduction and cessation program may be executed using a manual-only approach. [17]

There is sufficient literature to prove how caffeine disrupts sleep cycles and neurological function.[18] It has been shown to disrupt sleep quality typically, patterns, and durations.[19] A study, in particular, describes that high doses of caffeine extended stage 1 sleep in young adults.[20] Despite the growing trend of adverse effects to caffeine, no 'safe limit' has been determined for said stimulant particularly in South Asia, though there have been proposed values. [21]Health Canada has proposed a limit of 2.5mg/kg/day, however additional data is required.[22] It is widely known that college students often resort to substance abuse in times of severe pressure due to academic and other responsibilities that come with adulthood particularly during and after the COVID19 pandemic. [23]However, there is little to no information available to the public regarding caffeine dependence or its adverse effects.[24] Lack of this knowledge leads to further consumption of caffeine.

There are few limitations to this study. One of the limitation is that a limited number of university students responded, and study is limited to only Karachi. Few male students participated in the study which raises the question of gender bias. Quantitative assertion of caffeine cannot be done as this survey is based on the word of the participants. Majority of students enrolled in the universities of Karachi are female especially medical and dental colleges, heavy gender bias is present in the study.

Further research on the harmful effects of caffeine as an addictive substance is required to be conducted so the harmful effects of caffeine could be highlighted. Study regarding the awareness of harmful effects, dependence and addiction to caffeine containing products among different populations can help highlight the knowledge regarding the issue among the targeted populations.

CONCLUSION:

Many students in medical universities of Karachi are moving towards caffeine dependence, due to daily consumption over a prolonged period of time. Promoting responsible consumption habits and spreading awareness over potential adverse effects of CCPs, especially amongst a younger audience could improve the health and lifestyles of students in the long-term.

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Review Article **Open Access**

Cranial Ultrasound: A Novel Approach of Neuroimaging in Preterm Infants Suffering from Perinatal Birth Injury

Saba Fatima, Amber Goraya, Abid Ali Qureshi, Hina Azhar

ABSTRACT:

Introduction: Preterm birth is a common cause of neonatal mortality with an additional burden of adverse neurodevelopmental outcomes. It is caused by different factors that can be either perinatal, natal or postnatal leading to white matter injury/intracranial hemorrhages. These lesions can be readily assessed by cranial ultrasound which provides cost-effective, radiation-free, bedside imaging.

Conclusion: Cranial ultrasound is an innovative method to assess brain injury in preterm infants. Ultrasonographic evaluation of preterm brain is recommended as early as possible after birth with interval follow up. Three distinct patterns of brain injury can be seen in preterm infants: Periventricular leukomalacia (PVL), Germinal Matrix-Intraventricular hemorrhage (GMH-IVH) and cerebellar hemorrhages. Germinal matrix hemorrhage is found to be most common pattern with cystic PVL being next among three patterns of brain injury. Ultrasound is an operator-dependent technique with poor visualization of few abnormalities on two-dimensional images. The limitation of conventional ultrasonography opens up new aspects of 3 D scanning with better imaging outcomes.

Keywords: Germinal Matrix-Intraventricular hemorrhage, Preterm birth, Periventricular leukomalacia.

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INTRODUCTION:

Preterm birth is defined as neonatal birth less than 37 weeks of gestation.[1] It is divided into extremely preterm (less than 28 weeks GA), very preterm (28-32 weeks GA) and late preterm birth (more than 32 weeks GA).[2] Epidemiologically it causes an annual birth rate of 11% globally with an estimated 15 million preterm births.[3] It is one of the major causes of childhood mortality and causes almost one million deaths each year and overall accounts for a risk factor in about 50% of neonatal deaths.[1] Economic burden caused by preterm birth was studied to be more than 2.9 billion pounds in terms of neonatal admissions, health care and educational assistance.[2]

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These premature neonates are prone to develop multiple problems because of immature organ systems like respiratory, gastrointestinal, cardiac and neurological complications. Premature brain is more prone to injury from multiple pre, peri and postnatal causes due to ischemia, infection or inflammation. The common maternal causes include maternal hypertension, maternal diabetes and anemia while the common fetal causes include birth asphyxia, chorioamnionitis, respiratory distress and sepsis.[4] Perinatal injury causes neurological damage by cumulative effects of hypoxic-ischemic, inflammatory and metabolic processes, which lead to immature auto regulation of cerebral vasculature to hypoxia and thus results in cellular damage.[5]

Damage to premature brain causes intellectual and psychiatric disabilities, like development of cerebral palsy in 15% and behavioral disturbances with impaired academic performance in 30 to 50% of patients.[6] Another study depicts that 10% of patients develop CP with hearing and visual problems while 40% develop cognitive defects, language and educational difficulties.[7] Because of this high incidence of neurodevelopmental problems, prompt and accurate neuroimaging is indicated in preterm neonates. There are multiple techniques for brain imaging with cranial ultrasound being the first-line modality for imaging of neonatal brain as it provides fast, radiation free, cost effective, bedside screening method of imaging. Cranial ultrasound also helps in serial imaging to look for progression of disease process.[8] Three dimensional ultrasound is a new technique of performing cranial imaging which helps in visualization of the brain

parenchyma in multiple planes along with reduced scanning time.[9]

In this review article, we will discuss the basic physical aspects of ultrasound, technique of performing cranial ultrasound with normal anatomical description of neonatal brain and anatomic variants. Various patterns of brain injury in preterm neonates with their ultrasound manifestations will be discussed along with indications for further imaging evaluation

DISCUSSION:

Cranial ultrasound is an important tool that is used for the evaluation of normal and abnormal brain in preterm infants. As it is a bedside screening tool and does not require long sedation as compared to MRI, it is being increasingly used for neuroimaging in neonatal intensive care units.[8]

Technique of cranial ultrasound:

High-frequency sound waves are used to produce images in cranial ultrasound.[10] Sector scanning is the most common mode of imaging in cranial ultrasonography[11] however an article published in AJR recommends the use of linear array transducer.[11] An acoustic window is needed to transmit sound waves from the scan head and the most commonly used window is anterior fontanelle.[12,13] Scanning is performed with a scan head/transducer of 7.5 Hz frequency in sagittal and coronal planes with scanning from frontal to occipital regions and from right to left side of the head.[12] Studies recommend taking 6-8 coronal views with 5 sagittal views.[13,14] Supplemental acoustic windows have also been described to aid in the visualization of the preterm brain like posterior and mastoid fontanelles.[15] Posterior and mastoid fontanelles allow accurate visualization of occipital lobes, atria of ventricles and infra-tentorial structures.[16]

There are many recommendations on timings of cranial ultrasound in preterm infants for early recognition of any brain injury but controversies exist in these recommendations. Perlman et al. gave a scanning protocol based on the weights of preterm infants described in Table 1.

In 2001, the American Academy of Neurology reviewed this protocol and recommended routine cranial ultrasound in preterm infants of <30 weeks gestational age at between 7 and 14 days after birth with repetition of scan between 36 and 40 weeks postmenstrual age.[18] Another study devised scanning protocol based on the gestational age of infants as described in Table 2.

Table 1. Timing protocol for cranial ultrasound based on birth weight [(17)]

<1000 grams	1000-1250 grams	1250 and 1500 grams
Days 3-5	Days 3-5	Days 3-5
Days 10-14	Around day 28	Pre discharge
Around day 28	Pre discharge	Pre discharge

Table 2. Timing protocol for cranial Ultrasound based on gestational age[19]

Gestational age < 32 weeks	Gestational age >32 weeks
Shortly after birth	Third day of life
Third day of life	Weekly thereafter until discharge
Seventh-day of life	
Weekly thereafter until discharge	

Normal anatomy and anatomical variants on cranial ultrasound:

In the coronal plane, most anterior section passes through frontal horns of lateral ventricles and it reveals frontal lobes separated by falx cerebri and fluid-filled cavum septum pellucidum which is a normal structure in preterm infants. Corpus callosum is also seen at this level above the frontal horns. Posterior to the frontal horns, there are septum pellucidum, frontal horns indented by the head of caudate nuclei which are separated from the lentiform nucleus by internal capsules with Sylvian fissures and temporal lobes more laterally. Vascular anatomy at this plane includes the bifurcation of internal carotid arteries into anterior and middle cerebral arteries. Moving posteriorly, there are bodies of lateral ventricles, thalami, tentorium and brainstem with the lateral part being occupied by basal ganglia, internal capsule and deep white matter of parietal lobes. Further posterior plane of imaging includes trigone and atria of lateral ventricles filled by choroid plexus, cerebellar vermis, quadrigeminal cistern and splenium of the corpus callosum. The most posterior image reveals occipital lobes and optic pathway. In the sagittal plane, midline imaging reveals pulsatile branches of anterior cerebral artery coursing over the cavum septum pellucidum, inferior to which lies the third ventricle, the aqueduct of Sylvius and 4th ventricle. All components of the brainstem with cerebellar vermis can also be visualized at this level. Parasagittal images reveal lateral ventricles with thalami lying at their floor and brain parenchyma of frontal and occipital lobes. The most parasagittal images reveal occipital and temporal horns of lateral ventricles with temporal lobes seen bilaterally. Echogenic choroid plexus is seen filling the ventricles in all sections.[20]

Various anatomic variants are commonly found due to improvement in technique and technology of ultrasound and these variants are important to know to avoid misinterpretation as pathologies.[21] Persistent fetal fluid spaces are commonly found and to name as added cavum septum pellucidum, cavum verge and cavum interpositum.[21] Most of these spaces are close by birth in full-term infants while 85% of cavum septum pellucidum closes by 3-6 months of age.[22] These spaces are differentiated from their anatomical location, space anterior to the foramen of Monro and between frontal horns is cavum septum pellucidum while one posterior to foramen of Monro and fornices is cavum verge.[23] Smaller choroid plexus cysts less than 1 cm are commonly found in a neonatal autopsy but are insignificant[20] while multiple,

bilateral and larger cysts have significance due to association with chromosomal abnormalities.[24] Lenticulostriate vasculopathy is a nonspecific finding which can both be a normal variant and pathological with later due to thickening of walls of arteries secondary to TORCH infections, chromosomal abnormalities and metabolic disorders.[25]

Patterns of brain injury in preterm neonates and their ultrasound features:

Various patterns of acquired perinatal brain injury have been described in preterm neonates with three types of structural abnormalities including white matter injuries, intracranial hemorrhages and cerebellar injuries.[26] White matter injury is the most common of brain injury and according to a study, it encompasses periventricular leukomalacia, punctuate white matter injury, intraparenchymal hemorrhage, ischemia and ventriculomegaly with volume loss.[27] While a particular terminology has been devised by Joseph Volpe in 2009 to cover the neuropathological spectrum of preterm infants called "Encephalopathy of Prematurity". This entity consists of periventricular leukomalacia (PVL) and severe germinal matrix-intraventricular hemorrhage (GMH-IVH) with its complications.[28] Out of these defined patterns, PVL with its associated neuronal/axonal diseases is the most common pattern found in 50 %or more of preterm infants while GMH-IVH is only found in 5 % of infants born prematurely.[29] Another important component of preterm brain insult is cerebellar injury which accounts for 19% of the cases as proved in a study.[30]

1. Periventricular leukomalacia: Periventricular leukomalacia (PVL) relates to the injury to cerebral white matter in preterm infants. It consists of two components: 1) a focal necrotic component which is further of two types and 2) a diffuse gliotic component which is due to astrogliosis and microgliosis. Macroscopic necrotic components in combination with gliotic changes evolve into cystic lesions hence referred to as cystic PVL while microscopic necrotic foci with surrounding diffuse gliosis change into glial scars and known as non-cystic PVL.[28,29] The overall incidence was proved to be 26.4%[31] and 16.3 %[32] in two different studies. The former study was based on the preterm African population with the role of genetic and environmental factors leading to higher incidence and hence making it a less reliable study than later.

Cystic PVL is easily seen by cranial ultrasound however it is present in only 3% of preterm infants[33] while the EPIPAGE study demonstrates it in 5% of infants.[34] The later EPIPAGE study is a better one as it includes a large sample size with more accurate results. Non-cystic PVL is difficult to assess on ultrasound however its incidence is reportedly high as compared to cystic PVL. Cystic PVL progresses from areas of in homogeneously increased echogenicities on ultrasound to evolve into complete cystic lesions.[35] These commonly occur along the distribution of long penetrating arteries particularly in watershed areas alongside trigone of lateral ventricles. They appear as multiple small variable-sized cysts having anechoic fluid.[36] Generally, cystic PVL is categorized by four grades described in table 3.

Table 3. Ultrasound grading for Cystic PVL[35]

GRADE	ULTRASOUND APPEARANCE
I	Increased echogenicity areas in the periventricular region
II	Increased echogenicities evolving into small frontoparietal cysts
III	Periventricular frontoparietal and occipital lobe cysts
IV	Extensive subcortical cysts

Non-cystic PVL also called as diffuse PVL is difficult to image on ultrasound however it is found in the majority of cases as proved to be 69%[33] and 80%[37] in two different studies. It is difficult to assess on ultrasound however its incidence is reportedly high as compared to cystic PVL. Miller et al concluded that non-cystic PVL is present in 69% of patients[33] while Leijser et al in their study proved it to be present in 80% of infants.[37] However both these studies had various limitations, like small and limited sample size with timings of performing ultrasound not following any established protocols.

It can be seen as periventricular echogenicities with no progression into cystic lesions.[38] However several studies demonstrate that diffuse white matter injury can progress into brain atrophy which manifests in the form of enlarged ventricles and subarachnoid spaces, widening of Sylvian fissure with reduced gyral folding. Brain atrophic changes had been described in particular in 18% of patients by Horsch et al[39] while Skiold et al proposed these changes to be found in 4.8% patients.[40] The work done by later is more reliable as it provides a quantitative scoring system for different features of brain atrophy.

Generally, the diagnostic accuracy of ultrasound for PVL is variable as proposed to be 68 % by Debellion et al[41] and 90% by Trounce et al[42]. The later study appears to be more appropriate as it compared the ultrasound findings with histopathological sampling at autopsy while in the former study MRI brain was used as a reference standard tool.

2. Germinal matrix – intraventricular hemorrhage and its complications:

Germinal matrix hemorrhage is one of the common abnormalities in the preterm brain which are diagnosed on ultrasound. Germinal matrix itself consists of proliferated neurons and glial cells having vessels of single-cell origin. It starts involution by the end of second trimester and only a small amount remains till 32 weeks in the region of caudothalamic groove. By term age almost complete involution occurs causing decreased risk of hemorrhage in term infants. Germinal matrix hemorrhage has been divided into 4 different grades by Papile et al described in table 4.

Table 4. Grading for Germinal Matrix Hemorrhage[43]

Grades	Description
Grade I	Subependymal hemorrhage
Grade II	Intraventricular hemorrhage without dilatation
Grade III	Intraventricular hemorrhage with dilatation
Grade IV	Intraventricular hemorrhage with parenchymal extension

The overall incidence of hemorrhage was proved to be 44.6 % and 64.4 % in two different studies. These studies also documented individual incidences of different grades which were 52.4 and 40% for grade I, 30.9 and 11 % for grade II, 11.9 and 25.7 % for grade III, 4.7 and 2.8% for grade IV.[44,45] The ultrasound picture of grade I hemorrhage is echogenicities noted in caudothalamic groove on sagittal scans and inferolateral to frontal horns on coronal scans. Grade II hemorrhage is seen as echogenicities filling the part or whole of ventricles while in grade III there is associated ventricular dilatation. Grade IV is ventricular hemorrhage associated with adjacent infarction.[46]

Cumulative incidence of germinal matrix-intraventricular hemorrhage was proved to be 44.6 %[44] and 64.4 %[45] in two different cohort studies which also mentioned individual incidences of different grades with grade I being most common and grade IV being least common in both studies. However the former study appears to be better due to its large sample size and description of the number of hemorrhages with relation to the gestational age of born infants. Ultrasound appearance is of echogenic material in caudothalamic groove and within the ventricular system according to different grades.

3. Cerebellar Haemorrhages:

Cerebellar injury is one of the frequent findings in neonates born prematurely. Germinal matrix present along the fourth ventricle adjacent to the cerebellum can undergo injury with a similar pathogenic mechanism as that of the lateral ventricle germinal matrix. Conventional sonograms with anterior fontanelle are less accurate in the determination of cerebellar hemorrhage however mastoid fontanelle view allows optimal visualization and assessment of this pathology. Sonographically it is seen as echogenicity involving cerebellar hemispheres or vermis with abnormal size or shape of the fourth ventricle. The incidence of cerebellar hemorrhages on cranial sonograms is low as proved to be 9 %[47] and2.8 %[48] in two different studies. Limperopoulos et al in the former study used a big sample size for a case-control study making it a better incidence predictor than latter.

Disadvantages and future perspectives of cranial ultrasound:

Despite being highly sensitive for diagnosing most of the brain injuries in preterm infants, cranial ultrasound still has uncertainty concerning its use. The uncertainty is based upon two factors, one is inter-observer reliability and accuracy because it is an operator-dependent technique. Second, there are forms of brain injury not readily determined on ultrasound using conventional or even supplemental views, like non-cystic diffuse PVL, neuronal-axonal injuries and cerebellar hemorrhages as already described.[38]

Considering these disadvantages of conventional ultrasound, it is the need of hour to work on new aspects of three dimensional ultrasonography which will help in opening new horizons for prompt imaging of neural elements in preterm neonates.[49] It will allow the imaging of entire brain in single volumetric sweep with reconstruction of images in multiple planes thus helping in visualization of parenchymal changes not easily visible on 2 D ultrasound. It also helps in rapid bed side scanning along with storage of data for later manipulation in form of multi planar displays, volume calculations and tomographic images.[49] It was proved in a study performed in California that the scanning time with 3D ultrasound was less than conventional 2D imaging along with better imaging results with three dimensional ultrasound.[50]

Limitations:

The literature used for this article consisted of mainly review articles with few being randomized control trials and cohort studies. Further, the sample size for most of the studies was small and limited to a population of some specific area making them region biased studies and less accurate for epidemiological analysis. Another major limitation was the lack of any standardized quantification in most studies with the use of subjective ultrasound findings for describing various abnormalities which led to vivid interpretation of results.

CONCLUSION:

Cranial ultrasonography is a radiation free screening method for imaging of neonatal brain which helps in assessment of anatomical variants as well as major pathological imaging patterns. Considering inter observer accuracy difference and limitations of two dimensional imaging, 3-D ultrasound is a new aspect of prompt bed side neonatal brain imaging.

Authors Contribution:
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Amber Goraya: Concerned with concept, data collection, analysis and article writing
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Hina Azhar: Concerned with review of article

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Case Report **Open Access**

Sigmoid Volvulus Necessitating Total Colectomy

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ABSTRACT:

Sigmoid volvulus is a well-known cause of large bowel obstruction. Its management includes urgent endoscopic decompression or emergency laparotomy. The gangrenous sigmoid colon is resected with either end to end anastomosis or Hartmann's procedure. Here we present a rare presentation of sigmoid volvulus causing gangrene of the whole colon. It was probably due to double closed loop obstruction caused distally by the volvulus itself and proximally by the competent ileo-caecal valve. It was managed by total colectomy with terminal ileostomy and Hartmann's procedure. To our knowledge only one such case report has been published in the literature so for.

Keywords: gangrene, ileostomy, laparatomy, volvulus.

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INTRODUCTION:

A volvulus of colon is defined as twisting of a part of colon on its mesentery. The two most frequently encountered types are sigmoid and caecal volvulus.[1] The incidence of volvulus presenting as a cause of large bowel obstruction (LBO) is almost 15% in USA[2]. The patient presents with severe pain abdomen, abdominal distension and absolute constipation. Diagnosis can be made with X-Ray abdomen, contrast studies and CT scan abdomen. Prompt treatment is required in order to prevent ischaemic injury to the bowel wall that will lead to gangrene of the involved loop of sigmoid colon. Here we present a rare case report of sigmoid volvulus which caused gangrene not only of the sigmoid, but also involved the caecum and rest of colon up to the volvulus. To our knowledge this will be the second case report of a sigmoid volvulus causing double closed loop LBO leading to gangrene of whole colon.

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CASE:

A 32 year- old soldier was evacuated to a field hospital from a post near Afghanistan border with complaints of severe colicky pain abdomen for three days. The pain had gradually increased in intensity for one day and would not relieve with even intravenous nalbuphine or ketorolac. He also complained of absolute constipation and abdominal distension for two days. He had anorexia and nausea but denied any history of vomiting. On examination he had tachycardia and was dehydrated. His blood pressure was 100/70 mm of Hg. The abdomen was distended and tense. He had guarding and tenderness all over the abdomen but there was no rigidity. Bowel sounds were sluggish. X-Ray abdomen showed distended large gut loops with air fluid levels in both the limbs of volvulus as well as caecum (Figure. 1). The diameter of the caecum was more than 8 cms suggestive of an impending perforation. CT scan was not available. Complete blood counts showed haemglobin of 12 G/dl and neutrophilic leukocytosis. Serum electrolytes were normal. Nasogastric tube was passed, intravenous fluids and antibiotics strarted and he was prepared for emergency laparotomy. On exploration, there was gangrene of the sigmoid volvulus (Figure.2). But there was also distension and full thickness gangrenous patches on the large gut from caecum to descending colon. Detorsion of volvulus was done after decompression and the whole large bowel was packed in hot saline packs for 15 minutes. Patient was also administered 100% oxygen. The colour of gut from caecum to descending colon improved but the full thickness gangrenous patches remained the same (Figure.3). Total colectomy was carried out. End ileostomy was made in right lower quadrant and the distal end was closed as Hartmann's procedure. Patient

had uneventful recovery and was evacuated to tertiary care hospital on 1st post-operative day. He was discharged on the 10th post-operative day and followed up in OPD. He had reversal of ileostomy after three months at the same tertiary care centre and had an uneventful recovery.

DISCUSSION:

Sigmoid volvulus is the third most common cause of colonic obstruction.[3] The exact aetiology is still unknown. However, it occurs due to the redundant and elongated sigmoid based on a narrow mesentery[4]. Constipation and high fibre diet are also considered as important predisposing factors.[5] It is usually considered a disease of the elderly age but can occur in children even. Our patient was a young soldier. Constipation could have been a predisposing factor in our condition because soldiers are deployed at remote posts with poor access to safe and potable water and moreover, it was in the month of July, thus predisposing them to dehydration. Patients present with the classical signs of LBO with pain, distension and absolute constipation. Our patient had severe continuous pain probably due to delayed presentation and gangrene of the involved loop. The diagnosis can be made on plain X-Ray abdomen, CT scan abdomen or contrast studies. The diagnosis can be done X-Rays alone.[6] We had only this facility available at our set up. Different procedures like rectal tube deflation, sigmoidoscopic deflation, laparoscopic detorsion and sigmoidopexy are carried out in the management of sigmoid volvulus. The American Society of Colon and Rectal Surgeons guidelines suggest that endoscopy (rigid or flexible) should be carried out first in order to rule out gangrene of the gut as well as initial decompression of the colon.[7] Once there is gangrene or failure of the endoscopic detorsion then urgent resection is indicated. Sigmoid colectomy shall also be carried out later on in cases managed successfully with endoscopic decompression. When there are signs of gangrene of the bowel then emergency surgery is mandatory but it carries high morbidity and mortality.[8] Resection and anastomosis as well as Hartmann's operation can be done. Hartmann's procedure is to be preferred in complicated cases.[9]

Figure 1. X-Ray Plain abdomen in standing position showing air fluid levels in sigmoid loops as well as distended caecum and ascending colon

Figure 2. Distended and gangrenous loop of sigmoid Colon

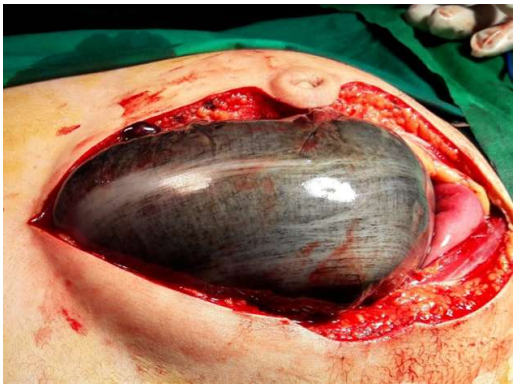
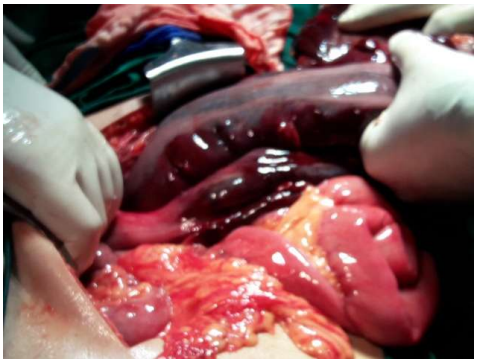


Figure 3. Gangenous sigmoid as well as transverse colon



In our case there was not only gangrene of the sigmoid loop but it involved the complete colon. We assume that there were simultaneously two closed loop obstructions. One was the volvulus and the other obstruction was due to the competent ileocaecal valve. A competent ileocaecal valve is found in about 75% of the population.[10] A literature search was carried out on from 1980 to 2017 on PubMed and pakmedinet using the terms "sigmoid Volvulus", "Colectomy" and "Hartmann's Operation". We could find only one similar case report published so for by Sali PA et al in the International Journal of Case Reports.[11] They also operated on a 27 year-old young male patient. It can be assumed that young patients presenting with sigmoid volvulus need prompt treatment to avoid such a catastrophe.

CONCLUSION:

Sigmoid volvulus is not an uncommon condition. Gangrene of the involved loop of sigmoid is also frequently associated; however, gangrene of the entire colon due to double closed loop obstruction is un-heard of. A high index of suspicion is needed to diagnose it especially in a young patient. An early diagnosis can avert the catastrophe of gut gangrene and septic shock.

Authors Contribution:
Asrar Ahmad: Design, writing the final draft, data collection and analysis
Irum Saleem: Research conception
Mahwish Mahboob Bhutta: Data collection and analysis
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Namra Sohail Raja: Research conception, design,
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Case Report **Open Access**

A Case of Amyand's Hernia Variant

Aun Ali, Daleep Kumar, Madeeha Shahid, Ammara Salam, Summaya Saeed, Khursheed Samo

ABSTRACT:

The presence of vermiform appendix as the content of inguinal hernia is termed Amyand's hernia (AH). It is a very rare entity as most of the time contents of hernia are omentum and small bowel. Very often AH is asymptomatic and diagnosed intra-operatively. Amyand's hernia (AH) is classified into four sub-types depending on clinical features and the status of the appendix. But this time we encountered per-operatively entirety different findings of Amyand's hernia. Treatment of Obstructed inguinal hernia is only surgery, but dealing with Amyand's hernia (AH) is based on the patient condition and type of Amyand's hernia. So, treatment of this hernia remains controversial, different strategies should be applied to different case.

Keywords: Amyand's hernia, Appendix, Inguinal hernia, Omentum

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INTRODUCTION:

The appendix as an inguinal hernia content is termed Amyand's hernia, named after a French surgeon Claudius Amyand who first-ever removed the perforated appendix in 11 years old boy while performing incarcerated inguinal hernia repair on, 6 December 1735.[1] The incidence of it is 1% and is further dropped to 0.08% when it has a complication like acute appendicitis or appendicular abscess.[2]

CASE REPORT:

A 25-year-old male, security guard by profession who had a history of right-sided reducible inguinal hernia for the last 2 years, came to the emergency department (ED) with complaints of painful irreducible right-sided groin swelling for a few hours. The pain is periumbilical and colicky associated with bilious vomiting. He had no known comorbidity. The patient had never taken any medical advice before and was not using any medications. He had no prior surgeries or hospitalizations. He smoked occasionally.

On examination, general physical examination was unremarkable. On focal examination, 4 x 4 cm irreducible tender swelling on the right inguinal region. No cough impulse was noted. He has been diagnosed with a right-sided incomplete obstructed inguinal hernia. After initial resuscitation in the emergency department (ED), all baseline laboratory investigations were sent and the patient was admitted for emergency inguinal hernia repair. A nasogastric tube was passed for small bowel decompression. Half an hour later hernia reduced spontaneously and the patient became symptom free so it was decided to go for elective hernia repair the next morning, rather than emergency repair. All laboratory parameters were within normal range. Unfortunately, no radiological investigation was advised.

Per-operatively we found an indirect hernia sac and a tubular structure lying close to the spermatic cord arising from the deep ring not as a content of the sac, as shown in Figure 1&2.

We carefully dissected and further identified it as an appendix having mesoappendix but couldn't reach up to its base. As it was not inflamed so pushed back inside and the deep ring was tightened with suture (Lytle's repair). Also, there was a risk of weakening of the posterior wall by dissection, increasing the chances of hernia recurrence. So sac was ligated and tension-free Lichtenstein mesh repair was done. Postoperative recovery was swift and event free. The patient was discharged on 2nd postoperative day.

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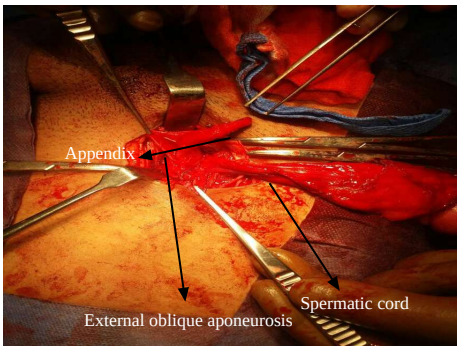
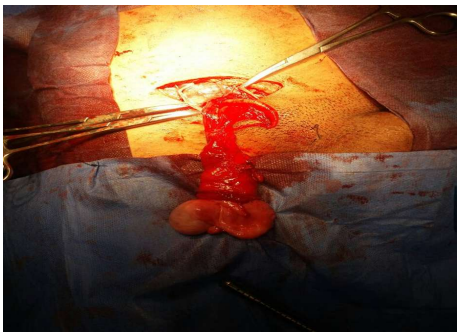
In this case, we did mesh repair as the appendix was not inflamed. Our case is somehow unique in that, the appendix was coming through a deep inguinal ring, not as a content of sac. We can label it as a variant of Amyand's hernia.

DISCUSSION:

The most common surgical problem, an inguinal hernia, is caused by a weakness in the abdominal wall. The Omentum and/or small intestine are frequently found in hernial sacs. But infrequently, other organs have reportedly been observed, including the ovary, fallopian tube, bladder, and large intestine.[3] Males are more likely than females to experience AH on any side. Due to the processus vaginalis' inability to completely disappear during growth, the rate of AH diagnoses in children is three times higher than it is in adults.[4] Though inguinal hernia is one of the commonest surgical procedures, surgeons often encounter different variations of normal anatomy. It has a very low incidence of complications like acute appendicitis <1%.

Fig 1 and 2: Intraoperatively, clearly seeing appendix and indirect hernia sac coming through the deep ring. The appendix was not inflamed





Losanoff and Basson 2008 classified AH into four types that are important in surgical management (table 1).[5,6] The status of the appendix determines hernia repair. Type I has a normal appendix. The management of this type is debatable. Some surgeons prefer mesh repair along with appendectomy while others perform mesh repair without appendectomy.[7,8] They are of opinion that why someone adds risks to mesh infection as appendectomy is a clean-contaminated procedure. Besides that reaching up to its base by enlarging the hernia defect or distending the neck of the hernia sac adds risk to hernia recurrence.[9,10]

Type II has acute appendicitis. The treatment, in this case, is appendectomy and hernia repair not by mesh but by some other technique Shouldice, Bassini etc.[11,8,12]

Type III has acute appendicitis along with abdominal sepsis, in this type, Appendectomy is recommended with primary hernia repair. Mesh placement is avoided because of the risk of mesh infection.

Type IV has acute appendicitis associated with related or unrelated abdominal pathology in this type appendicectomy through hernia or laparotomy plus diagnostic workup is routinely advised.

The "Rikki Modification" is a new category that has been added. It deals with situations when there is an incisional hernia; in these situations, the appendix is addressed as type I; acute appendicitis is managed by appendectomy through the hernia and subsequently followed by hernia repair with primary closure; and peritonitis with sepsis is managed as type IV.[13]

CONCLUSION:

Inguinal hernia repair that frequently presents difficulties to the surgeon. Imaging, laboratory testing, and physical examination are not very helpful for pre-operative diagnosis of Amyand's Hernia. To prevent the potential side effects of AH, such as the development and perforation of an appendicular abscess, early clinical suspicion is essential. The decision to undertake an appendectomy and tension-free Liechtenstein mesh repair at the same time is complicated.

Table: 1 Losanoff–Basson classification of Amyand's hernia (AH) and their management

Types	Features	Suggested Management
1	Normal appendix.	Hernia repair by mesh placement
2	Acute appendicitis with no abdominal sepsis.	Laparoscopic appendicectomy with primary hernia repair.
3	Acute appendicitis with abdominal sepsis.	Open appendicectomy with primary hernia repair
4	Acute appendicitis with concomitant intra-abdominal pathology.	Open appendectomy with primary hernia repair, along with appropriate intra-abdominal pathology investigation and management.

Authors Contribution:
Aun Ali: Design, writing the final draft, data collection and analysis
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Madeeha Shahid: Data collection and analysis
Ammara Salam: Data collection and analysis
Summaya Saeed: Research conception, design,
Khursheed Samo: Research conception, data collection and analysis

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Letter to Editor **Open Access**

Simulation Based Inter-Professional Education – Integrating Theory, Practice and Healthcare Professionals

Khadija Farrukh

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Simulation based learning refers to the representation of an artificial environment similar to a real one to students for achieving learning objectives through experiential learning instead of apprenticeship. The use of simulation for professional training has a well-established history in many professions including military, aviation and health professional education.[1,2] Healthcare workers can learn in a safe environment without fear of harming patients. In Pakistan, approximately 500,000 people, including women and children die annually due to medical errors according to local newspaper report. According to a research study done in Pakistan the medical errors rate reported was 5.5% out of which medication errors were 2.6%, one study reported medical errors rate of 39.28% in tertiary care hospital annually. There is limited research on exact incidence of medical errors in Pakistan, but medical errors are one of leading cause of death in tertiary care hospitals of Pakistan. Common root cause of medical errors are communication gap, inadequate information flow, lack of coordination between healthcare workers, inappropriate patient identification, insufficient patient education, inadequate staff and technical failure.[3,4] Most of root causes of medical errors can be controlled by implementation of simulation based interprofessional education in undergraduate and post graduate health professional education. Simulation-based interprofessional medical education is future of health professional education and will help overcome challenges of patient safety and improve patient outcome.[5]A major concern regarding implementation of simulation-based interprofessional education is limited resources and deficiency of research in Pakistan on simulations. But medical errors adds a huge amount of cost to healthcare which should instead be utilized in training healthcare professional through simulation based learning, to decrease frequency of medical errors. Initiative should be taken to develop and introduce curriculum of simulation based interprofessional education in health professional education to achieve educational outcome which will improve patient outcome. There is also need to collect data and analyze patient reported outcome and patient experience outcome in tertiary care setting by simple questionnaire or electronic software. To implement simulations, the cost is usually main factor under consideration. However, cost of simulator vary according to degree of fidelity and, if used properly can be cost-effective. So attitude towards simulation need to be changed in order to implement it.[6] To design cost effective low and medium fidelity simulators content experts and simulation analyst should work in collaboration. Simulation technology should be developed by consulting all stakeholders especially end users. There are three main concepts which should be taken under consideration during designing simulation: system design process, conceptual framework or philosophy, and specification of the simulator. Simulations are usually based on clinical or hospital environment but majority of population of Pakistan lives in rural settings. To educate students for community setting, a community simulated environment can be created with village model containing houses and other living spaces.[7] Majority of studies demonstrated effectiveness of simulation to improve procedural skills, communication skills and teamwork. However, simulation-based interprofessional education is step ahead, incorporating these features with understanding other professional's role and responsibilities as well as creating ethical values. Failure to perform desired task in clinical practice leads to feeling of discontent in the students; disapproved by the, supervisor in front of patients and colleagues. There is great possibility to encounter difficulty, lack of confidence with same task if performed later on. Educators also face challenges with patients getting aware of students working as a trainee in settings.

Dental simulations are very important as dental procedures incorporate mainly motor skills. However dental simulations are task specific. In dentistry computer aided and augmented reality simulation are being widely used now a days.[8,9] Virtual clinical simulation in nursing education provides immersive self-regulated training to nursing students, reproducing real-life experiences and feedback, in a virtual environment that is safe, interactive, active and pleasant.[10] These learning activities should be integrated with medical students to enhance learning and create high- fidelity simulation activity, usually it is advisable to integrate first year nursing students with third year medical student.

It is important to conduct research on medical errors,

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interprofessional education and simulation to create awareness among health care professional on its importance. Simulation-based interprofessional education provides an environment to learn from experiences of facilitators and students during simulation-based learning and improve patient outcome and healthcare practices. Healthcare simulation community also needs mutual research project and integrated simulation designs to enhance simulation development.

Authors Contribution:
Khadija Farrukh: Design, writeup

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