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EDITORIAL

AI in Healthcare; Will it Make us Dispensable?

Aneeq Ullah Baig Mirza

Artificial Intelligence (AI) is the virtue of machines like computer systems, which mimics human intelligence in the form of visual perception, speech recognition and language translation.

Machine learning (ML) is a type of AI which gives computers the ability to learn from and improve with experience, without being explicitly programmed[1].

The term "Artificial Intelligence" was first coined by John McCarthy for a conference on the subject held at Dartmouth in 1956 as "the science and engineering of making intelligent machines". The computer performs tasks based upon algorithms which are the building blocks of AI.[1]

They mimic human cognitive functions like experiential learning. Based upon the data fed and the patterns of correlations, AI can make predictions. In machine learning, neural network acts as a classifier while in deep learning, it becomes a feature extractor as well.

There is an argument that AI will replace doctors, especially in diagnostics like radiology and pathology. The merits of AI over the human mind lie in the capacity to store immense data and lack of fatigue. Besides, AI will eliminate the need for unnecessary investigations due to reduction in false positive alarms. AI may improve patient outcomes and reduce treatment costs and time. AI is going to be a game changer.

In radiology, AI carries out automatic segmentation in CT and MRI scans, isolates the pathological sites and performs pre-analysis of a scan before being finally reported by radiologist. Large datasets in AI can help in early detection of breast cancer.

Studies report that, usually, an average radiologist must interpret one image every 3–4 seconds in an 8-hour workday to meet workload demands. Therefore, errors are inevitable, especially under such constrained conditions. The development of AI is driven by the desire for greater efficacy and efficiency in clinical care.[2]

Similarly in pathology, the ever-increasing data related to genome and biomarkers makes it difficult for a pathologist to keep pace with. Overwork and fatigue can lead to judgement errors.

Regarding the diagnostic improvement in clinical specialties, there is significant improvement in prediction of risk for cardiovascular disease with ML which will save the management time of a cardiologist. It improves the sensitivity and specificity of diagnosis. Applications in ophthalmology, dermatology and all other specialties include diagnosis, quantification and progression analysis of various diseases in an efficient manner so that the doctor can treat in time.

As far as patient management in clinical specialties is concerned, newer promising roles of AI include precision medicine, cognitive assisted robotic surgery and AI documentation. AI written notes, investigations and prescriptions reduce the documentation time.

Communication in healthcare, education and research has been revolutionized by Generative pre-trained transformer (CHAT GPT) by providing human-like responses. It delivers text response by its language model, just like humans. It generates precise diagnosis and individual management plan by its deep learning algorithms and helps in medical education. CHAT GPT relieves the burden of memorizing facts and promotes continuous learning and better patient care. Advantages of Chat GPT are diagnostic accuracy, personalized treatment, cost reduction and enhancement of medical knowledge.

CHAT GPT provides health-related guidance by language translation to patients in remote areas, answering FAQs to the patients (thus reducing the OPD burden) and can prioritize and schedule the appointments.

Other uses of Chat GPT are providing research-driven better conclusions and assisting in biomedical research by identifying disease markers, drug interactions, selecting possible topics for future research & creation of hypothesis.

The pressing question is **whether AI is going to make**

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humans dispensable? The answer is complex.

A large part of quantitative job in diagnostics can be covered by AI, but the qualitative part i.e. subsequent management of patient and overall governance will stay with the human mind. These virtues include innovative thinking, ethics, communication with patients, counselling, governance, data feeding and decisions about when to treat and how aggressively to treat (depending upon age, financial constraints and family circumstances).

At one end, AI is easing the diagnostic steps and at the other, it can assist the physician to better focus on management and communication with the patient.

The role of radiologists may elevate to industrial level in the development of newer technologies according to the clinical issues and ethics. In 2018, Liew[3] presented the idea of 'Radiologist-in-the-loop' according to which the radiologist would stay as an authority in the larger picture of diagnostics, managing verification of reports, judgement calls and multidisciplinary approach. Continuous improvement in deep learning is only possible when radiologists in different institutions collaborate[4] to share and enhance the normal and abnormal data to create training sets and practice guidelines. This is going to be a very labor-intensive job involving transformation of the role.

Each set of images is associated with a clinical scenario. The number of potential clinical scenarios and the variety of tasks that each of the image might offer is astronomical and might be impossible to tackle by one organization with any AI algorithm.[5] A similar change in role might be expected for pathologists.

As for cardiologists, ophthalmologists, dermatologists and other specialties, the diagnostic systems are very expensive and lack the normative data for local populations. Feeding that data is a continuous and uphill task. Moreover, considering a holistic picture, the final decision about management stays with the doctor.

Traditional physical examination of patients would still be required by physicians for complex diseases, CNS evaluation, rare problems, drug side effects, tachyphylaxis and any disease were AI lacks precedence.

Overall clinical decision making depends upon a variety of combinations of symptoms, rare presentations and disease patterns (pertaining to one disease or a variety of concomitant diseases) which affect patient agony, treatment misery and life expectancy. This requires the wisdom of the human mind.

As far as the role of Chat GPT in patient management is concerned, it has its own limitations. Chat GPT operates on the basis of statistical pattern of data. The human mind is essential to monitor Chat GPT output and to verify any false positives and negatives. Although ChatGPT can assist in research projects, but human mind is essential for innovative input and project execution. The healthcare professionals can spend more time on the actual research thus saving overall time.

AI poses very serious concerns related to ethical, technical and legal issues. The ethical issues include loss of 'doctor-patient relationship', privacy of patient, security of data and psychological impact of loss of empathy & trust. How will the patients trust the system whether their preferences are being respected?

The technical problems can be in the form of biased information, lack of originality, issues of informed consent for data feeding, cybersecurity, infodemics, reliability, validity of normative/representative data etc. Besides, there are issues of digitalization of healthcare data in poor and developing countries.

A patient comes to a hospital in a vulnerable state and expects protection of his rights[6]. There will be legal issues as to whom to hold responsible and accountable in cases of negligence/malpractice.

An innovative mind will always be required for complex cases and perpetual development of digital systems, data input, program evaluations and legal frameworks to address all these issues. This will be in the form of healthcare professionals, policy makers, IT professionals and patients who will work in unison, in order to achieve better patient outcomes.

Conclusion

Medicine is a science as well as an art and AI will be a partner in medicine. New courses need to be amalgamated in the individual modules by medical schools in AI technology learning and data management . AI would provide a great opportunity to support and augment the physicians. It would

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reduce the element of memorization and fatigue. Bypassing the preliminary routine work and investigations, the physician would spend more precious time with their patients, improving the human touch. That would create a time gain to initiate the management at the earliest.

AI should not be considered a monster created by Frankenstein. However, the medical professionals must make themselves abreast of the advances in modern technology in healthcare, for otherwise, physicians who shun AI may be replaced by those who don't. Have we braced for the game change?

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Assessment of Triglyceride/Glucose Index as a Predictor of Insulin Resistance in Comparison with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR): in a Referral Laboratory

Aqsa Mushtaq, Muhammad Younas, Muhammad Qaisar Alam Khan, Zujaja Hina Haroon, Muhammad Anwar, Muhammad Usman Munir

ABSTRACT

Objective: To investigate triglyceride glucose index (TyG index) as a predictor of insulin resistance (IR) in comparison with homeostasis model assessment for insulin resistance (HOMA-IR) for the screening of DM in healthy adult population

Study Design: Cross-sectional comparative study.

Place and Duration of Study: The study was done at Chemical Pathology & Endocrinology Department, Armed Forces Institute of Pathology, Rawalpindi from 01st June 2022 to 31st May 2023 over a period of one year.

Materials and Methods: The study comprised 307 healthy individuals coming for laboratory investigations to our laboratory after routine annual checkup at Combine Military Hospital, Rawalpindi. Individuals of both genders aged between 18 and 35 years were included and initial history of any previous medical condition was taken. All the participants with previous history of any chronic disease were excluded. Healthy individuals who were disease free were included. Blood sample was taken in clot activator and sodium fluoride tube for lipid profile, serum insulin fasting and blood glucose fasting, respectively. Formula used for estimation of HOMA-IR was:

$HOMA\text{-}IR = \frac{\text{FPG} \times \text{Insulin}}{22.5}$. The equation used for TyG index was natural log of fasting plasma glucose and triglycerides divided by 2 i.e. $\ln\left(\frac{\text{FPG} \times \text{TG}}{2}\right)$.

Results: A comparative analysis was done using SPSS version 29.0 and revealing a significant positive correlation between the TyG index and HOMA-IR with an r value of 0.79 and *p* value = 0.001 where *p* value <0.01 is considered as significant.

Conclusion: TyG index can be used as a surrogate marker of HOMA-IR to predict insulin resistance in healthy adults population.

Key Words: *Diabetes Mellitus, HOMA-IR, Insulin Resistance, Metabolic Syndrome, TyG Index.*

Introduction

In this era of technology where information and services are readily accessible the lack of active lifestyle and increasing trend toward unbalanced diet, our world is developing many diseases which were uncommon before. The most catastrophically spreading non-communicable diseases affecting every single household in this time and age are diabetes mellitus, metabolic syndrome, obesity occurring at a very early age. Many of the ways to fight these wildly spreading diseases are addressing the root cause which is now identified as insulin resistance.[1]

Insulin resistance(IR) with a pivotal role in the development of metabolic disorders, like type 2 diabetes and cardiovascular diseases has become a significant factor to be detected at an early stage.[2] IR can be defined as a condition of decreased sensitivity of target tissues to regularly available insulin in circulation. IR is also an attribute to dyslipidemia, obesity, glucose intolerance and hypertension.[3] Dyslipidemia due to insulin resistance occurs by increased triglycerides levels, decreasing HDL levels and changing the composition of LDL molecules which ultimately leads to obesity and intima changes

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at vascular levels leading to hypertension.[4]

Worldwide the prevalence of IR varies over a range of 15.5 to 46.5%.[5] While in Pakistan, it is reported to be at 26.7% by Azeem *et al.,*[6] accurate assessment of IR is essential for early detection and customized intervention strategies. Hyperinsulinemic-Euglycemic clamp (HIEC) is considered as gold standard for estimation of IR but due to its complexity and extreme cost it is difficult to use in daily life and in smaller setups.[7] Keeping in view of this, the HOMA-IR has been widely used as a substitute indicator for IR. However, recent studies have proposed an alternative and potentially more practical tool for IR assessment which is TyG index.[8]

Among routine risk factors, the fasting blood glucose (FBG) and triglycerides (TG) are well known for their part to foresee the progress of DM. Raised FBG levels in impaired fasting glucose range have been observed to be an autonomous risk factor for type 2 diabetes.[9]

HOMA-IR is determined by fasting glucose and fasting insulin levels, and it provides an estimation of IR by evaluating the ability of insulin to reduce glucose production by the liver.[13] Pakistan is a developing country, as a nation we do not have access to many efficient and gold standard procedures due to lack of resources and high raising inflation.

Moreover, many studies have been done in our region for determination and utilization of TyG index as surrogate marker for IR for developing diabetes mellitus for high risk groups.[15] But a little work has been done on evaluation of this marker in Pakistan for this purpose in adult healthy individuals.[16]

Although HOMA-IR has demonstrated its usefulness in the screening of IR, it requires measurements of insulin, which are not always available in routine clinical practice.[14] Contrary to this, the TyG index requires only the measurement of fasting glucose and triglycerides, which are routinely measured in clinical laboratories, making it a more feasible tool for extensive assessments.

The TyG index is a new index recommended as a replacement of HOMA-IR. The TyG index is an effortless and simply calculated value. The formula to obtain the TyG index is: $\text{TyG index} = \ln\left(\frac{FPG \times TG}{2}\right)$.[10]

Thus, a strong surrogate marker for insulin resistance due to its close association with the gold standard HIEC technique is TyG index.[11] TyG index can be used as marker of IR, not only for DM but also for other diseases like metabolic syndrome.[12] Extensive literature review shows that scanty work has been done to assess the association of HOMA-IR and TyG index in patients with T2DM in Pakistan.

In our study, we not only focused on TyG index but also compared it with HOMA-IR which is a well recognized marker for determination of IR. So, our study aimed to provide some strong evidence for utilization of TyG index as a predictor of IR in comparison with HOMA-IR for the screening of DM in healthy adult population.

Materials and Methods

This cross-sectional study was conducted in the Department of Chemical Pathology & Endocrinology, Armed Forced Institute of Pathology, Rawalpindi from 1st June 2022 to 31st May 2023 after getting ethical approval from the Institutional Review Board of Armed Forced Institute of Pathology, Rawalpindi with letter reference number: FC-CHP-26/READ-IRB/21/659.

Sample size calculation was performed using World Health Organization sample size calculator which came out to be 307. Participants from 18 – 35 years who came for their annual checkup at Combined Military Hospital, Rawalpindi were selected for the study. Individuals of both genders were selected and initial history of any chronic medical condition was taken. All the participants with previous history of any chronic disease like diabetes mellitus, chronic kidney disease, ischemic heart disease and hypertension etc. were excluded. Only healthy individuals who were disease free were included which was confirmed by their history and most recent available laboratory investigations. Any individual with previously diagnosed pre-diabetes, on any special diet, pregnant females and lactating mothers were also excluded. 5ml of venous blood by aseptic technique were collected in yellow top gel tubes and sodium fluoride grey top tube. Serum/plasma centrifuged at 3500 revolutions per minute (RPM) for 5 minutes and analysed for serum lipid profile, serum insulin fasting and plasma glucose fasting.

Spectrophotometric technique was used to measure serum lipid profile and plasma glucose fasting on Siemens ADVIA 1800 Chemistry Analyzer and

chemiluminescence technique was used to measure serum insulin fasting on Advia Centaur XP. Statistical Package for Social Sciences (SPSS) version 29.0 was used for data analysis. Results were mentioned as mean ± standard deviation (SD). Pearson correlation analysis was used to examine the relationship between the TyG index and HOMA-IR. Independent t-test was applied to compare TyG index with the cutoff of HOMA-IR.

Results

A total of 307 healthy individuals with age group 18-35 years irrespective of gender were enrolled in our study. The split between the male and female was 215 (70%) and 92 (30%) shown in Fig. I. The mean age of study participants was 33 ± 6 years.

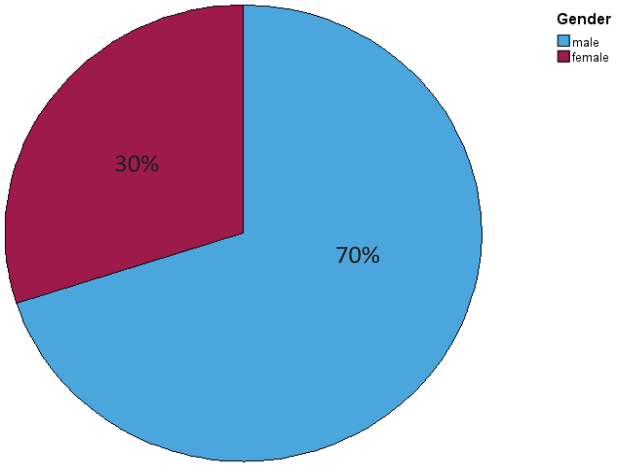

Figure 1: Distribution of Gender between the Participants

Mean and SD for serum lipid profile, serum insulin fasting and plasma glucose fasting were calculated. Mean ± SD for total cholesterol, triglyceride, LDL-C, HDL-C, glucose and insulin were 4.28±0.9 mmol/L, 1.70±0.5 mmol/L, 2.46±0.74 mmol/L, 1.01±0.29 mmol/L, 5.55±0.76 mmol/L, 11.2±4.8 µIU/ml respectively shown in Table I

Table I: Mean Value for Initial Investigations

Parameter	Mean Value
Total Cholesterol (<5.2 mmol/L)	4.28±0.9
Triglyceride (0.4-1.6 mmol/L)	1.70±0.5
LDL-C (<3.2mmol/L)	2.46±0.74
HDL-C (>1.04 mmol/L)	1.01±0.29
Glucose (< 5.6 mmol/L)	5.55±0.76
Insulin (5-25 µIU/ml)	11.2±4.8

HOMA-IR was calculated using formula: $HOMA\text{-}IR = \frac{\text{FPG} \times \text{Insulin}}{22.5}$, and already established cutoff of 2.22 was considered for insulin resistance. While for TyG index, equation used was $\text{TyG} = \ln\left(\frac{\text{FPG} \times \text{TG}}{2}\right)$.[10] The values calculated for each patient for both indices. Shapiro-Wilk test was applied to check the data distribution, which came out to be parametric. For correlation between the two indices, Pearson correlation was applied and r value= 0.79, *p* value= 0.001 (*p* value ≤ 0.01 considered significant) were observed as shown in Table II.

Table II: Pearson Correlation between HOMA-IR and TyG Index

	HOMA-IR		TyG Index	
Parameters	R value	*p* value	R value	*p* value
HOMA-IR	.	.	0.798**	0.001**
TyG Index	0.798**	0.001**	.	.

**Correlation is significant at the ≤0.01 level. HOMA-IR: Homeostasis Model Assessment for Insulin Resistance, TyG Index: Triglyceride glucose index

Individuals were separated in two groups on the basis of HOMA-IR cutoff i.e. >2.22. Both groups were compared with TyG index by applying independent t-test which came out to be significant i.e. *p* value less than 0.05 shown in Table III. TyG index score for Group 1 was 1.17 ± 0.21 and TyG index score for Group 2 was 1.70 ± 0.26.

Table III Comparison of TyG Index with Group 1 and Group 2 of HOMA-IR

HOMA-IR	Group 1* (N=120)	Group 2** (N=187)	*p* value
TyG Index	1.17 ± 0.21	1.70 ± 0.26	0.001***

* Group 1 with HOMA-IR cutoff value of <2.22
**Group 2 with HOMA-IR cutoff value >2.22
****p* value is significant at less than <0.05.HOMA-IR: Homeostasis Model Assessment for Insulin Resistance, TyG Index: Triglyceride glucose index

Discussion

In this study, 307 healthy individuals were included. Mean and SD for total cholesterol, triglyceride, LDL-c, HDL-c, glucose and insulin were 4.28±0.9 mmol/L, 1.70±0.5 mmol/L, 2.46±0.74 mmol/L, 1.01±0.29 mmol/L, 5.55±0.76 mmol/L, 11.2±4.8 µIU/ml respectively. TyG index with HOMA-IR was compared using Pearson Correlation which showed correlation with r value=0.798. This showed that TyG index can be used for determination of IR even if the HOMA-IR calculation is not possible.

A study done at Dow University by Kanpurwala *et al.*,[17] for TyG index evaluation showed its significance in different groups and showed high significance in

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group with higher risk of developing IR i.e. offspring of parents who has DM. In their study, they only used TyG index with lipid profile and no marker for IR was used. While in our study we took only the healthy individual without any family history of DM and we used HOMA-IR for comparison of TyG index.

Many studies have compared the TyG index and HOMA-IR in various populations and have found TyG index to be comparable or even superior in identifying insulin resistance. Kang *et al*.,[18] compared TyG index and HOMA-IR in adolescents and found the correlation to be significant at r value= 0.41, while in our study we compared both indices in adults with a significant correlation at r value=0.79. So, they concluded that TyG index can be used at an early age for the detection of insulin resistance. This goes in accordance with our study which also suggests TyG index usage for screening of IR.[2]

Lee *et al*.,[19] carried out a cohort study in Korea over a period of 4.5 years and suggested the superiority of TyG index in comparison to other indices. In their study, they enrolled 5,354 non-diabetic subjects of middle-age and followed the cases for 4.5 years closely assessing the subjects for developing diabetes. They concluded that TyG index is more efficient in detecting in IR than the other indices available including HOMA-IR with r value= 0.27 and *p* value <0.0001 when compared with non-diabetics and diabetics individuals. While, we only focused our study to comparison of TyG index with HOMA-IR which showed TyG index to be comparable to HOMA-IR.

Locateli *et al.,*[20] used the same indices to compare in South American obese adolescent and adult population and suggested it to be a reliable marker for assessment of IR. He also added another index to improve the efficacy of TyG index i.e. TG/HDL-C index, which also uses the day-to-day profiles to assess the IR risk. In our study, we took all the individuals from general population with different BMIs and did not considered BMI as the major confounding factor in the determination of both indices. Nonetheless, our study showed higher indices as the BMI increases.

Selvi *et al.,*[21] in their study took one step further and estimated utilization of TyG index for assessment of glycemic control in diabetics. In their study, they enrolled 140 patients of T2DM and divided them into 2 groups with good glycemic control of HbA1c value <7.0% and poor glycemic control of HbA1c value >7.0%. They concluded that TyG index can be efficiently used in assessment of TyG index as compared with HbA1c and HOMA-IR with r value= 0.46 and *p* value =0.001. While our study also showed a strong comparison between these 2 markers with r value=0.79 and *p* value <0.001. Thus, TyG index is proved to be a reliable marker, not only for risk estimation, but also management of DM.

Lv *et al*.,[22] performed a cross-sectional study on patients of T2DM and checked utilization of TyG index for estimation of diabetic kidney disease (DKD). For this purpose, they took 1432 patients, and compared their TyG index alongwith microalbuminuria and eGFR. In their study, they showed significant correlation between the TyG index and development of DKD, claiming it to be a potential marker for DKD risk evaluation. Our study lacked the determination of role of TyG index in diabetic population, which can be also be helpful in our region as most diabetic patients donot have access to state of the art labs performing robust techniques.

Many studies were carried out to assess the significance of TyG index in diseases other than DM. One of the studies was carried out by Song *et al*.,[23] for evaluation of non-alcoholic fatty liver disease (NAFLD) utilizing TyG index. In their study, they included 225 patients in their study diagnosed with different grades of NAFLD and TyG and its modified indices were compared in these different grades. TyG index along with its modified indices came out to be useful for evaluation of NAFLD. As we focused on TyG index role in IR we were not able to compare its role in other disease. Thus, TyG index is not only efficient for screening and monitoring of DM but can also be utilized for diagnosis and monitoring of other diseases, proving its utilization for broader spectrum.

Conclusion

The TyG index shows promise as a practical and accessible surrogate marker for insulin resistance in adults, potentially surpassing the limitations associated with the HOMA-IR method. Its strong correlation with insulin resistance and association with metabolic disorders suggests that the TyG index can be a valuable addition to routine clinical practice

and epidemiological studies.

Limitations of study

Multiple other factors like BMI, family history, lifestyle evaluation and activity levels which are considered important for the identification of insulin resistance are important for more focused approach to tackle this havoc. This was single centered study, in which we have used cross-sectional data.

Recommendations

Standardized cut-offs for our population should be established to ensure consistent interpretation and clinical application of the TyG index. So further investigation, validation, and consensus among the medical community are necessary before widespread adoption in clinical practice. For evaluation of cutoff in our region, study should be done with the gold standard test which is HIEC and it is currently not available in Pakistan. Moreover, in future a multi-centric long-term study can be done to confirm the importance of this index in various other ethnic populations. Further studies could investigate the longitudinal predictive value of TyG for various health outcomes or evaluate its utility in guiding interventions for IR and related conditions.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Genotypic Characterization of Macrolides Resistance in Clinical Isolates of Staphylococcus Aureus from Rawalpindi, Pakistan

Iram Manzoor, Muhammad Idrees, Shumaila Naz

ABSTRACT

Objective: To determine the patterns of resistance among different macrolides and to detect macrolide resistance genes in *Staphylococcus aureus* collected from different clinical samples.

Study Design: Cross-sectional observational study

Place and Duration of Study: The clinical samples sourced from the Pathology Labs of Railway Hospital, Tehsil Head Quarter (THQ) Hospital Taxila and Wah General Hospital Wah Cantt, Pakistan was collected from 01 August 2017 to 01 February 2018.

Materials and Methods: One hundred non-repetitive clinical isolates were obtained from different clinical samples (pus, urine, sputum and blood). Each *Staphylococcus aureus* isolate was obtained from only one sample, to avoid repetition of strain. They were selected on the criteria of their growth with bright yellow color colony formation on mannitol salt agar (MSA) media along with the color change of media from red to yellow and coagulase positive results. Kirbey-Baur disk diffusion test was followed for the detection of antimicrobial sensitivity, whereas genotypic resistance drift was determined using PCR.

Results: Highest frequency of *Staphylococcus aureus* was observed in pus samples i.e. 45 (40.2%). Out of 100, 34 isolates of *Staphylococcus aureus* were resistant to macrolides group. Among 34 resistant isolates the frequency of *ermC* gene was 25 and *msrA* was 14 respectively, whereas all isolates were negative for *ermA* gene. Maximum resistance was observed against erythromycin, n=33 (29.5%) and minimum against clarithromycin, n=26 (23.3%). The highest susceptibility trend was seen against Azithromycin, n=62 (55%).

Conclusion: Resistance of *Staphylococcus aureus* may vary with different antibiotics within the same group. A high frequency of erythromycin resistance was seen in this study. The most predominant resistance was for *erm*C, among the resistance genes in isolates.

Key Words: *Drug Resistance; Genes; Macrolides; Microbial; Staphylococcus Aureus.*

Introduction

Excessive use of antibiotics for the treatment of bacterial infections has raised resistance to macrolides and lincosamides. These resistance proportions show variations with different geographical distribution and study periods. Staphylococcus aureus, facultative anaerobic bacteria that usually grows as aerobically but can survive anaerobically.[1] Most abundantly found in the nasal passage, respiratory tract and on the skin.[2] *Staphylococcus aureus causes* the *number of infections to human like scalded skin syndrome, toxic shock syndrome, septic arthritis, bacteremia and endocarditis etc.* Food-borne illness is majorly caused by enterotoxin producing strains of Staphylococcus aureus**.** The most obvious clinical manifestations are acute onset of vomiting and watery diarrhea. *Mode of infection includes two mechanisms, either by invading the tissues or by producing toxins*.[3] Staphylococcus aureus was regarded as main etiological factor for much of hospital acquired and community infections such as bacteremia, surgical attained and skin infections.[4]

Acquisition of resistance occurs either by extra chromosomal elements such as mobile DNA segments, plasmids, transposons and integrons that are attained from other bacteria in the surroundings, or by efflux pumps which releases multiple antibiotics.[5] The prevalence of these antibiotic resistance infections is more common in hospitals and in medical centers. The introduction of new antibiotics to treat the infection of Staphylococcus

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aureus has led to the proliferation in antibiotic resistance.[6]

Macrolides are antibiotics having 12 to 16 membered lactone rings along with some amino sugars. They are considered bacteriostatic but also act as bactericidal at very high concentrations. Resistance to macrolides in Staphylococci may arise through either target-site modification, involving genes such as erm (erythromycin ribosomal methylase) or active efflux, encoded by msrA (methionine sulfoxide reductase A) enabling the bacteria to expel the antibiotics.[7]

Literature shows many studies of macrolides resistance particularly in respiratory pathogens like Streptococcus pneumoniae[8] and Mycoplasma pneumoniae[9]. Antibiotic usage in Asia has shown increasing trend between 2000 -2015. In India, consumption surged from 3.2- 6.5 billion on defined daily doses (DDD's) marking a significant 103 % rise. Likewise, in China increase occurred from 2.3- 4.2 billion DDD's (79%), while Pakistan's antibiotic consumption has grown from 0.8 – 1.3 billion DDD's (65%).[10] Since 2010, the pattern of macrolide resistance has expanded even more, with many studies indicating a resistance rate of more than 92%.[11]

Frequent use of macrolides plays a crucial role in shaping the resistance pattern of this group among different countries. Hsia research highlights the commonly used antibiotic for hospitalized children in China, Japan, and South Korea is azithromycin, with a prescription rate of 11.8%[12] while inappropriate prescription rate of macrolide group in Pakistan is 74.6 %[13]. To the best of our knowledge the resistance rate of macrolide particularly in Staphylococcus aureus is not studied in Rawalpindi region. The present research mainly focuses on the frequency of macrolides resistance in Staphylococcus aureus in Rawalpindi and molecular characterization of macrolide resistance genes in the strains as these antibiotics were chosen because of their common choice of selection by physicians.

Materials and Methods

A cross-sectional observational study was conducted between 01st August 2017 and 01st February 2018, and the data was collected from various hospitals (Railway Hospital, Tehsil Head Quarter (THQ) Hospital Taxila and Wah General Hospital Wah Cantt in Rawalpindi, Pakistan) by using non-probability (purposive sampling technique). Ethical approval for this study was obtained from the University of Wah, Pakistan under Ref# UW/BIS/18/222. Post-operative wound pus sample, urine samples of UTI and sputum samples of individuals with cough and pulmonary disease were collected. Samples were obtained from individuals of both genders aged 10 years and older, individuals with post-operative wound pus samples, with urine samples diagnosed with urinary tract infections and with sputum samples exhibiting symptoms of cough and pulmonary disease were included. Repetitive isolates of Staphylococcus aureus along with those samples which were contaminated or showed signs of improper handling and those isolates that were not purified were excluded from the study.

Hundred non-repetitive isolates of Staphylococcus aureus were purified from different clinical samples (pus, urine, sputum and blood) in Pathology lab of Railway Hospital, Rawalpindi. Purified isolates were then taken to the Lab of Department of Biosciences, University of Wah. Mannitol Salt Agar media was used for growth of Staphylococcus aureus. The purified isolates were Gram's stained and checked for color and morphology. Catalase, oxidase, and coagulase tests were also performed.

Disk diffusion method was used to check the susceptibility of bacterial isolates against commercially available macrolide antibiotics. Disk Diffusion method devised by Kirby-Bauer was used for antimicrobial drug susceptibility. Zone of inhibition were measured according to Clinical and Laboratory Standard Institute (CLSI) guidelines.[14]

Extraction of genomic DNA of resistant strains was done by Geneaid (Cat.# GEE150). Macrolides resistant genes erm(A), erm(B), erm(C), and mrs(A/B) were detected by the PCR amplifications using particular oligonucleotide primers (Table I).

Multiplex PCR assays were performed in 25 µl PCR mixture. Mixture contained a DNA template (20 µg), 2 µl of dNTP's, 0.5 µl of Go Taq DNA polymerase, 2.5 µl green Go Taq buffer (10X), 0.5 µL of each forward and reverse primers were used in concentrations of 25 pM. Primers of ermA, ermC and msrA were selected from different literatures[15,16] (Table I). The PCR was performed with some modifications, initial denaturation at 95 °C for 5 minutes, followed by 30

cycles of 30 seconds at 95°C for denaturation, 58 °C for 30 seconds (annealing of erm), 60°C for 30 seconds (annealing of msr) extension at 72 °C for 1 minute then final extension 72 °C for 7 minutes.[17] Amplicons were analysed on 1% agarose gel and visualized in Syngene InGenius3: gel documentation system. Amplicons size was checked by using 1Kb ladder as a marker.

Data analysis was performed by IBM SPSS version 26.0. Descriptives including frequencies and percentages were reported in a tabular and bar chart.

Results

Frequency and Percentages of Staphylococcus aureus in samples were n=23 (20.5%) in blood, n=18 (16.1%) in urine, n=45 (40.2%) in pus, n=26 (23.5%) in sputum. The highest frequency of Staphylococcus aureus strains was in pus samples. (Figure 1)

Among all the macrolides maximum resistance in bacterial strains was against erythromycin with the percentage of n=33 (29.5 %), and minimum resistance was against clarithromycin with the percentage of n=26 (23.3 %), whereas azithromycin susceptibility was highest n=62 (55.4 %) among the group. (Figure 2)

Thirty-Four strains were found to be resistant, and they were subjected to PCR amplification for macrolides resistance genes detection (msrA, ermC, ermA). Twenty-five (73.5 %) strains were positive for ermC gene, n=15 (44.1 %) for msrA whereas n=11 (32.4 %) strains were positive for both ermC and msrA. While 05 strains were negative for all the three primers. In contrast, ermA gene was not detected in 34 resistant strains. (Figure 3)

Lane M; marker of 10Kb, Lane 1; as Positive control for ermC and msrA , Lane 2 (IM 40), Lane 3; Negative control, 4 (IM 45), 5 (IM 70), 6 (IM 36) , 7 (IM 23), 8 (IM 108), 9 (IM 106), 11(IM 112), 13 (IM 05) and 14 (IM 33). Samples in lane 2, 4, 5, 9, 11, 12 and 14 showed positive result for msrA with product size of 939 bp. Whereas samples in lane 6, 7, 10 and 13 showed positive result for ermC with product size of 321 bp. (Figure 4)

Discussion

The highest frequency of Staphylococcus aureus was recorded in pus sample, n=45 (40.2%) from wound infections. This high incidence was also found in Nepal in 2018.[18]This increase existence in pus sample

Table I : Primers of Macrolides Resistance Gene along with their Sequences

Gene	Primer	Oligonucleotide seq(5'->3')	Product size(bp)	Tm Ċ	GC%
msrA1	msrA1-F	GGC ACA ATA AGA GTG TTT AAA GG	939	55.79	39
	msrA1-R	AAG TTA TAT CAT GAA TAG ATT GTC CTG TT		57.02	28
ermA	ermA-F	AGCGGTAAACCCCTCTGAG	457	57.78	58
	ermA-R	TAGTGACATTTGCATGCTTCAA		55.66	38
ermC	ermC-F	ACTTGTTGATCACGATAATTTCCA	321	58.41	33
	ermC-R	TCTACTTAATCTGATAAGTGAGCTATTCAC		57.21	33

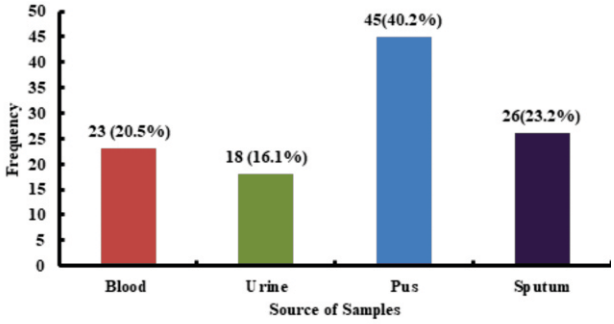

Figure 1: Frequency and Percentages of Staphylococcus Aureus in different Samples

Table II: Susceptibility Patterns of Staphylococcus Aureus to Different Macrolides

Antibiotics	Resistant	Intermediate	Susceptible
Azithromycin	29	9	62
Clarithromycin	26	14	60
Erythromycin	33	32	35
Telithromycin	29	15	56

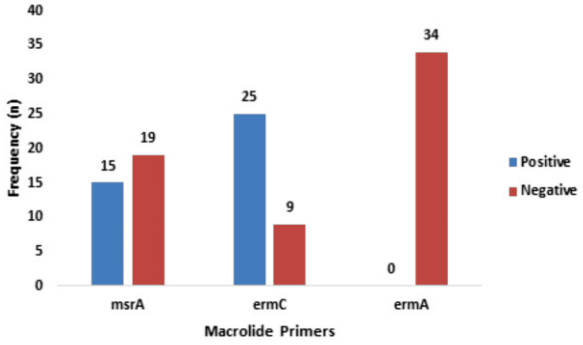

Figure 2: PCR of Different Macrolide Resistance Genes

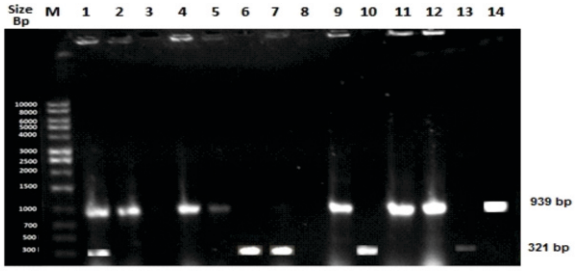

Figure 3: ermC and msrA typing of Gel with Control and Selected Samples

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may occur as Staphylococcus aureus is a habitant of skin when it gets inside the wounds or cut becomes pathogenic in nature. The pattern of resistance of macrolides in Staphylococcus aureus was recorded as erythromycin > azithromycin = telithromycin > clarithromycin and their percentages were 29.5% > 25.9% = 25.9% > 23.2%. The highest percentage of resistance, at 29.5%, was observed for erythromycin. It is notably a lower resistance fraction as compared to the findings of other studies from Pakistan. For instance, previous research in Peshawar[19] recorded a peak resistance rate of 99%, while 72% in Lahore.[20]

Difference may be raised because of advancements in medical facilities in Rawalpindi, a neighbor city of capital of Pakistan, infection control awareness among the medical professionals is high as compared to the peripheral cities. Erythromycin resistance in Pakistan, particularly in the Rawalpindi region is less as compared to other Asian countries like India, Nepal[21] and Iran[22]. The variation in resistance rate may be due to geographical factors and small sample size. This shows Rawalpindi has a better situation, with significantly lower resistance to erythromycin.

This research has highlighted pattern resistance within the macrolide group in which erythromycin has shown its peak as compared to its other group members (azithromycin, clarithromycin and telithromycin). High resistance to the erythromycin or any drug of this class which are commonly used in medical practices for respiratory infections can limit the treatment options and complicate the infection control measures. This can lead to prolonged illness, increased severity of symptoms, and a higher risk of complications as multi-drug resistance in microbes has emerged as concerning global issue within medical community.[23] This increasing resistance of bacteria to various drug poses a considerable threat to the efficacy of antibiotics.

Maximum rate of erythromycin resistance may co-relate with the high fraction of ermC gene (73%) in S. aureus isolates. msrA and erm (A and C) genes were selected for detection of macrolides resistance in S. aureus in recent study. Out of 100 S. aureus isolates 34 were resistant to different macrolides; further on these resistant isolates were subjected to PCR amplification for msrA and erm (A&C) gene finding.

Our study findings indicate that ermC (73%) is the conspicuous factor for erythromycin resistance in contrast to the msrA and ermA. These results are in accordance with the reports from Iran[22] and Japan where ermC gene was attributed for major erythromycin resistance. However, these values conflict with other investigations from several countries for instance a study from Korea, Turkey and Egypt[24], reported ermA gene as a major cause of resistance against macrolides. This high prevalence of ermC gene poses a risk of gene elements transformation to other species as it is transferable. Frequency of msrA in our study was also high 44% which seems to be very similar (43.6%) with study from Iran[25]. Notable results of present research were zero frequency of ermA gene in Staphylocoocus aureus strains. Probably the zero frequency of ermA was responsible for the low percentage of erythromycin resistance as compared to other studies. Another interesting finding of our study is high percentage of co-existence of ermC and msrA 11 out of n=34 (32%) which depicts mechanism of combined resistance is increasing in Rawalpindi. ermC and msrA both genes are linked with resistance to macrolides and lincosamides, and their co-existence may confer the higher level of resistance to both classes of drugs making it more challenging to treat the infections for which they are used. The co-occurrence of resistance genes may suggest their presence on the same genetic elements, can contribute to spread of multi drug resistance through horizontal gene transfer between bacteria.

Limitations

- Antimicrobial resistance (AMR) evolves over the time that's why a short period of 6 months may not highlight the long-term trends of resistance.
- Bacterial resistance is multifactorial so the study of just one factor (resistance genes) may affect the results. More factor like virulence gene study can add effective contribution to the solution.

Conclusion

Staphylococcus aureus is currently exhibiting maximum resistance against erythromycin and minimum against clarithromycin. Azithromycin exhibits the highest susceptibility, emphasizing its effectiveness as a choice of drug for the treatment of infections previously treated with erythromycin. To avoid further rise in erythromycin resistance in

Staphylococcus aureus and its potential transmission to other bacterial strains, both clarithromycin and azithromycin are recommended as alternatives.

Among three genes (msrA, ermA and ermC), ermC has high percentage in resistant isolates. This ermC gene is a key contributor in erythromycin resistance. Concurrently co-existence of ermC and msrA gene is also responsible for increasing rate of macrolides resistance. In future long-term studies to monitor the patterns of resistance against macrolides and other classes of antibiotics are recommended to control multi-drug resistance in Staphylococcus aureus.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Herniotomy to Treat Inguinal Hernia in Children: Analysis of Clinical Outcome of One Decade Experience

Mumtaz H Khan[1], Amna H Khan[2], Naila Yaqub[3]

ABSTRACT

Objective: Evaluation of the clinical outcome of inguinal herniotomy in children at a single center.

Study Design: Retrospective cross-sectional study.

Place and Duration of Study: Department of surgery, Northern Area Armed Forces Hospital Hafer al Batin, Saudi Arabia, from July 10, 2011, to Oct. 10, 2021.

Materials and Methods: A total of 256 patients admitted with inguinal hernia underwent inguinal herniotomy. All the patients were treated by single senior pediatric surgeon. The age ranged from 2 months to 13 years. The data was collected regarding age at operation, gender, location, investigations performed, operative procedure, and complications of the surgical intervention. The follow up was also done in the outpatient clinic for 12 months to assess the complications and outcome of the procedure. The data was analyzed by IBM® SPSS® version 26.0. The Fischer exact test was applied to evaluate the association of site of inguinal hernia with gender. The *p* value less than 0.05 was considered statistically significant.

Results: One hundred and seventeen (46%) patients had right sided inguinal hernia, 124 (48%) had left sided and 15 (6%) were having bilateral inguinal hernia. There was no per-operative and post-operative complication. There was no testicular atrophy. There was no recurrence of inguinal hernia during follow up of 12 months after surgery. All the children had successful clinical outcome on follow up of 12 months period. Fischer exact test was applied to find the association of type of inguinal hernia with gender and the *p* value was 0.166 which is considered statistically nonsignificant.

Conclusion: Early inguinal herniotomy on next available elective list is safe, effective and feasible procedure to treat children with inguinal hernia.

Key Words: *Inguinal Hernia, Inguinal Herniotomy, Recurrence, Testicular Atrophy.*

Introduction

Inguinal hernia is a common pediatric surgical problem which needs surgical intervention.[1]The child usually presents with inguinoscrotal swelling. Thus, in children it is always indirect herniation with contents passing through the deep ring.[2] It occurs due to inability of closure of processus vaginalis.[3] In female children persistence of canal of Nuck is its counterpart.[4] The congenital origin of etiology and its surgical management was described by Ambroise Pare about 400 years back.[5]

The incidence of this condition in full term children is 3% and in preterm babies, the incidence is 30%.[6]

In a simple hernia, differential diagnosis includes hydrocele, undescended testis, retractile testis and lymphadenopathy.[7] Amyand's hernia with appendix as content of sac occurs in 1% of the cases of inguinal hernia. It was described by Claudius Amyand in 1735.[8]

The inguinal herniotomy is the most common elective surgery performed by the pediatric surgeons.[9]The herniotomy is indicated as elective surgery to prevent complications like incarceration leading to strangulation of its contents.

Baird *et al.,* [10] reported increased risk of apnea of prematurity after surgery. The risk of apnea in premature infants with corrected age less than 45 weeks is reported to be 5 times higher after surgery as compared to the infants operated after the corrected age of 45 weeks. Thus overnight observation of premature infants with less than 45

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weeks of corrected age is recommended.

The procedure of herniotomy involves transfixation of patent processus vaginalis at the deep ring. The vas and testicular vessels are at risk of injury during the procedure. Testicular atrophy may also occur after inguinal herniotomy.[11] Recurrence of inguinal hernia has been seen in 0.02 to 2.5 % of patient.[12]This fact prompted the authors to analyze the clinical outcome of inguinal herniotomy in children performed by single pediatric surgeon over a period of past one decade.

Materials and Methods

This retrospective cross-sectional study was conducted at Northern Area Armed Forces hospital Saudi Arabia from July 10, 2011 to Oct.10, 2021. All the children diagnosed as a case of reducible inguinal hernia ranging from 2 months to 13 years of age were scheduled through outpatient clinic for inguinal herniotomy as elective surgery. Moreover, the patients included were only elective cases, without any comorbid condition. The cases presenting with incarceration or strangulation and with associated genital or abdominal wall pathology were excluded from the study. The herniotomy was advised only when the inguinal hernia was clearly evident on clinical examination. The children were admitted through out- patient clinic one day prior to surgery. Complete blood picture, coagulation profile and hepatitis screening tests were done for all the cases. All the children were treated by inguinal herniotomy under general anesthesia by a single pediatric surgeon.

We adopted the policy of not exploring the contralateral side with unilateral inguinal hernia. The surgery was performed through standard small skin crease transverse groin incision. The external oblique aponeurosis was divided only in children more than one year of age. The hernial sac was identified and dissected away from surrounding cord structures saving the vas and vessels with high transfixation at the neck of the sac at the deep ring (Figure 1-3). The hospital stay was 24 to 48 hours. The patients were discharged home on first post-operative day in good health, with a follow up visit in outpatient clinic at one week, 6 months and one year of intervals.

Data regarding age at operation, gender, location of hernia, investigations undertaken, operative procedure, and postoperative complications was collected from electronic hospital record and was analyzed by the operating pediatric surgeon. The results were analyzed to evaluate the clinical outcome of inguinal herniotomy. The IBM® SPSS® version 26.0 was used for data analysis. Fischer exact test was applied to see the association of type of inguinal hernia with gender. The *p* value ≤ 0.05 was considered statistically significant.

Results

There were 98 (38%) infants below the age of one year in our study, whereas 96 (38%) patients were between the ages of one to five years, 56 (22%) patients were between the age of 6 - 10 years and 6 (2%) patients were between the ages of 11 - 13 years. (Table-II). The mean age of patients in our study was 3.5 years.

One hundred ninety-seven (77%) patients were male, and 59 (23%) patients were female. The M: F ratio was 76.95:23.04. (Table I). One hundred and seventeen (46%) children had right inguinal hernia, 124 (48%) children had left inguinal hernia and 15 (6%) patients had bilateral inguinal hernia. Amyand's hernia with appendix as content of the sac was found in 2 (0.8%) patients. Both were treated by appendectomy and herniotomy.

There was no per-operative complication. Only 4 (2%) patients had mild wound infection treated by a short course of oral antibiotic with wound care. Three (1%) patients had mild scrotal hematoma which resolved spontaneously. There was no testicular atrophy (0%). No recurrence of inguinal hernia is seen in this series (0%). All the patients had successful outcome of inguinal herniotomy on follow up of more than one year. Only 5% children developed contralateral inguinal hernia during follow up of 12 months, which were treated as elective cases. Fischer exact test was applied with *p* value 0.166, which is non-significant, inferencing that there is no significant association of gender with the site of inguinal hernia.

Table I: Association of Site of Inguinal Hernia with Gender

Gender	Inguinal Hernia Type			*p* value
	Right (n=117)	Left (n=124)	Bilateral (n=15)	
Male (n=197)	85	98	14	0.166
Female (n=59)	32	26	1	

The *p* value ≤ 0.05 was considered statistically significant.

Table II: Age Range of the Patients

Age Range	Number of Patients
Less than one year	98 (38 %)
1-5 years	96 (38 %)
6-10 years	56 (22 %)
11-13 Year	6 (2 %)

Figure 1. Hernial Sac being Separated

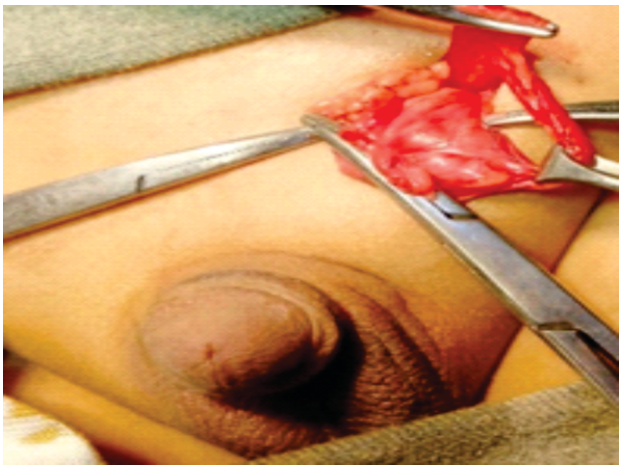

Figure 2. Vas deference being Saved

Figure 3. Testicular Vessels being Separated

Discussion

Our study showed that 38% children present with inguinal hernia before one year of age. Right sided inguinal hernia was present in 46 % and left sided inguinal hernia was seen in 48% cases. Bilateral inguinal hernia was present in only 6 % of patients. In this series, 0.8% patients showed right sided Amyand's hernia with appendix as content of sac found at operation. There was no peroperative complication (0%).There was no recurrence (0%) of inguinal hernia and no case of testicular atrophy (0%) was found in this study during follow up of more than 12 months period.

The male to female ratio is 11.3:1.[13] In our series, male to female ratio was 3.3:1. Most of the hernias occur in males. The difference in ratio may be due to data from a single center. Tan SS *et al.,*[14] reported that 33 % patients present within one year of age. In our series, 38% children presented within one year of age.

Ramachndran V et al.,[15] found that 60 % of inguinal hernias occur on the right side. In our series, right sided inguinal hernia was found in 46 % of the patients. The left sided inguinal hernia was seen in 48% cases and bilateral inguinal hernia was found in 6 % of patients. The inguinal hernia may be unilateral or bilateral. There is variation of data at single centers. Thus, there is need of meta-analysis from different centers.

Contralateral herniotomy has been recommended in the literature.[16,17] We followed the policy of not exploring the contralateral side with unilateral inguinal hernia to avoid unnecessary surgery, and herniotomy was advised only when the inguinal hernia was clear on clinical examination. We found that only 5% cases developed contralateral inguinal hernia during follow up of 12 months. Thus, our study indicates that routine contralateral exploration is unnecessary.

Morini F *et al.,*[18] found that Amyand's hernia occurs in 1% of the cases of inguinal hernia and is more common on right side. In our series, 0.8% patients had right sided Amyand's hernia with appendix as content of sac found at operation.

Walsh CM ., at al[19] reported per-operative complications of inguinal herniotomy including injury to testicular vessels and vas deferens. We didn't have any injury to testicular vessels or vas

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deference in this series. Baird *et al.,*[20] reported 5 times increased risk of apnea of prematurity after surgery in premature infants with post-conception age less than 45 weeks. In this series, overnight observation of infants less than 45 weeks of corrected age was found as a safe practice. Edon O et al.,[21] reported postoperative complications including scrotal hematoma, recurrence of inguinal hernia and testicular atrophy. There was no post-operative complication in this series

Minimal mobilization of cord and floor of inguinal canal is recommended to prevent postoperative complications of inguinal herniotomy.[22,23] This factor was found most relevant in this study to avoid per operative and postoperative complications of herniotomy.

Despite of large sample size, this study was a single centered study. However, this data is reliable as it covers a large population.

Conclusion

Early inguinal herniotomy on next available elective list is safe, effective and feasible procedure to treat children with inguinal hernia. Minimal mobilization of cord and floor of inguinal canal is recommended to prevent postoperative complications of inguinal herniotomy

Conflict of Interest

Authors declare no conflict of interest in publication of this article.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Miscarriage Prevalence and Public Perceptions in Eastern Province of Saudi Arabia

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ABSTRACT

Objective: To determine the prevalence and measure the perceptions of women regarding causes, emotional feelings, and emotional support following a miscarriage.

Study Design: Descriptive cross-sectional.

Place and Duration of the Study: The study was conducted in the eastern province of the Kingdom of Saudi Arabia from 15th May 2023 to 30th August 2023.

Materials and Methods: This cross-sectional study was conducted among women living in the eastern province of Saudi Arabia. A self-administered Arabic questionnaire was sent to the eastern population using Social Media platforms. Data was analyzed in Software Sciences (SPSS) version 26.

Results: A total of 402 women responded, and 32.3% (130) were aged between 26 and 35 years.

57% (229) had a history of miscarriage and 26.2% (60) encountered recurrent miscarriages.

Of the miscarried pregnancies 53.7% (216) were planned pregnancies. Approximately 78.4% (78) of women received medical care and (176) reported a miscarriage less than 7 weeks of pregnancy, The common perceived causes of miscarriage were spiritual 89.1% (358) and lifting heavy objects 60.3% (242). Almost 70.7% (284) had average emotional support after miscarriage, 16.2% (65) had high, and only 13.1% (52) had low emotional support received. Factors that influenced emotional support were the increasing parity, without a family history of miscarriage and repeated miscarriages (p<0.05).

Conclusion: A high prevalence of miscarriage is recorded in Saudi Arabia's eastern province, with perceived causes encompassing destiny, lifting heavy objects, and fetal genetic abnormalities. Identifying causes is vital for improving awareness and effective counseling and support at healthcare facilities.

Key Words: *Healthcare, Miscarriage, Perceptions, Prevalence.*

Introduction

Miscarriage of a pregnancy is a distressing event that can have significant physical and emotional consequences for women and their families worldwide.[1] Miscarriage or Abortion is described as a loss of a pregnancy before the age of viability which is defined as before 20 and 24 weeks of gestation as per the American College and Royal College of Obstetricians and Gynecologists respectively (ACOG and RCOG).[2,3] In Western countries, such as the United States and the United Kingdom the reported occurrence of miscarriage is approximately 11% to 25% of clinically recognized pregnancies.[3] The causes of sporadic and recurrent miscarriages (defined as two or more consecutive miscarriages) are well established and include chromosomal abnormalities, infections, environmental and immunological factors, uterine anomalies, fibroids, and polycystic ovarian syndrome.[2] Public understanding of these causes is often lacking, leading to widespread misconceptions.[4] These misunderstandings, encompass notions like the rarity of miscarriages, the potential link to lifting heavy objects, and the mistaken belief that there are no effective preventive treatments, which can be detrimental.[5,6] Experiencing a miscarriage often leads to psychological effects leading to isolation, with many women opting not to share the loss with family and friends and feeling ostracised.[7] Adequate counseling from healthcare professionals is essential to cope with grief.[8,9]

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Across the globe, several aspects are assessed, taking into account different regions and cultural contexts that may impact perceptions toward miscarriage.[9,10] Additionally in the hospital emergency room (ER), women displaying signs and symptoms of miscarriage are subjected to prolonged waiting, conveying a perception of marginalization.[11] Unfortunately, the demanding schedules at hospitals often hinder health professionals from conducting these awareness sessions adequately. Consequently, proposing an internet-based medical forum emerges as a viable alternative to effectively address and clarify these concerns and rectify their weird perceptions about the causes of miscarriages. Also will provide an effective opportunity for bereavement counseling.[12]

Limited research on miscarriage is available in the published literature from the Kingdom of Saudi Arabia (KSA). A study in the eastern province has primarily focused on the etiology and management of recurrent miscarriages.[13,14] Another study in the western province of Saudi Arabia has assessed women's miscarriage experience and perception.[20]

The prevalence and perceptions of miscarriage probably still have not been searched in all provinces of KSA. The eastern province of KSA, with its distinct socio-cultural characteristics, represents a unique setting to explore the prevalence of miscarriage and the public's perceptions of this phenomenon. The objective of the current study was to determine the prevalence of miscarriage and evaluate women's perceptions regarding the causes and emotional support received during miscarriage in the Eastern Province of Saudi Arabia. This assessment can illuminate cultural norms, and societal and personal perspectives, as well as the adequacy of counseling and support provided at healthcare facilities, facilitating the customization of support services and interventions to better address the needs of affected individuals and communities.

Materials and Methods

This research employed a cross-sectional study design and collected responses through an online self-administered questionnaire from 15th May to 30th August 2023 in the Eastern Province of Saudi Arabia utilizing convenience sampling. The ethical approval for the study was retrieved from the King Faisal University Research Deanship (KFU-REC-2022-NOV-ETHICS348). The minimum 385 sample size was calculated with a 95% Confidence Interval and a 5% margin of error. The inclusion criteria for participation in the study were married women aged 18 years or older who have experienced a miscarriage and reside in the Eastern Province. Females below 18 years old, without miscarriage events, and living in other provinces were excluded from the study. The questionnaire was taken from a published survey in 2015[10] which was modified and developed according to the religious and cultural aspects of Saudi Arabia. Later it was translated to the native Arabic language by the language experts and pilot-tested for its validity. The questionnaire included socio-demographic items, general and obstetric information, emotional support statements after a miscarriage on a 5-point Likert scale, perception statements for a cause of miscarriage on a 3-Likert scale, and feeling statements on a 3-point Likert scale.

The emotional support after miscarriage has been assessed using a 9-item questionnaire, a 5-point Likert scale category ranging from "strongly disagree," coded with 1, to "strongly agree," coded with 5 as an affirmative or positive emotional support. Negative questions have been re-coded inversely to avoid bias in the score. The total emotional support score has been calculated by adding all 9 items. Scores ranging from 9 to 45 points have been generated. The higher the score, the higher the emotional support. By employing 50% and 75% as cutoffs to assess the extent of emotional support. Respondents were considered as having low emotional support if the total score was less than 50%, while 50% to 75% were considered average, and a score of above 75% was considered as high emotional support.

The questionnaire was sent online to the eastern province population using Social Media platforms. The objectives of the study were explained to the participants before responding to the questionnaire. The participants were informed that submitting a response would indicate their consent to participate.

The data were analyzed using the software program Statistical Packages for Software Sciences (SPSS) version 26 (Armonk, New York, IBM Corporation, USA). Categorical variables were presented using

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numbers and percentages in descriptive statistics, whereas mean and standard deviation were employed for the calculation and summary of continuous variables. The differences between the emotional support score and the socio-demographic characteristics of the woman have been conducted using the Mann-Whitney Z-test. The normality test (statistical collinearity) was performed using the Shapiro-Wilk test as well as the Kolmogorov-Smirnov test. According to the results, the emotional support score followed the non-normal distribution. Thus, the non-parametric test was applied. Significance was attributed to values with a *p*-value less than 0.05.

Results

A total of 402 women responded to the questionnaire, 32.3% (130) were aged between 26-35 years old, with nearly 60% (239) residing in Al-Ahsa. Most women were married (92.3%), and about half (49.5%) had more than 10,000 SAR of family monthly income. Unemployed women constituted 44.5%, whereas 66.9% (269) were bachelor's degree holders. Only one woman had no previous pregnancy history, and 19.9% had at least two children. The prevalence of women who had chronic disease was 57% (Table I). Among those who had chronic disease (N=229), the most common chronic disease was anemia 26.5% (61), followed by hypertension 24.8% (57) G6PD 19.7% (45), and Diabetes 17.9% (41).

Table I: Socio-Demographic Characteristics of the Women (N=402)

Study variables	N (%)
Age	
• 18 – 25 years	60 (14.9%)
• 26 – 35 years	130 (32.3%)
• 36 – 45 years	121 (30.1%)
• >45 years	91 (22.6%)
City of residence	
• Al Ahsa	239 (59.5%)
• Dammam	58 (14.4%)
• Khobar	37 (9.2%)
• Qatif	51 (12.7%)
• Jubail	10 (2.4%)
• Abqaiq	07(1.7%)
Marital status	
• Married	371 (92.3%)
• Divorced or widowed	31 (07.7%)
Family monthly income (SAR)	
• <5,000	50 (12.4%)
• 5,000 – 10,000	153 (38.1%)
• >10,000	199 (49.5%)
Occupational status	
• Student	41 (10.2%)
• Employed	163 (40.5%)
• Retired	19 (04.7%)
• Unemployed	179 (44.5%)
Educational level	
• Illiterate	05 (01.2%)
• Less than high school	12 (03.0%)
• High school	78 (19.4%)
• Bachelor's degree	269 (66.9%)
• Master's degree	25 (06.2%)
• PhD or higher	13 (03.2%)
Have ever been pregnant?	
• Yes	401 (99.8%)
• No	01 (0.20%)
Number of children	
• None	25 (06.2%)
• One	60 (14.9%)
• Two	80 (19.9%)
• Three	71 (17.7%)
• Four	64 (15.9%)
• Five	39 (09.7%)
• Six	38 (09.5%)
• More than 6	25 (06.2%)
Chronic disease	
• Yes	229 (57.0%)
• No	173 (43.0%)

In Table II, the prevalence of miscarriage was 57%. Among those who had a miscarriage, 26.2% had encountered repeated (recurrent) miscarriages. Of the miscarried pregnancies 53.7% were planned pregnancies. Approximately 43.7% had reported a miscarriage of less than 7 weeks of pregnancy, 78.4% of women who experienced a miscarriage received medical care and 78.4% had recorded a family history of miscarriage. Furthermore, respondents believed that fate and medical illness 30.1% were the most common causes of miscarriage.

In the assessment of emotional support and feeling after a miscarriage (Table III), the highest ratings were seen in the statement "I received appropriate emotional support from my partner." (mean score: 4.03), followed by the statement "I received appropriate emotional support from those I told." (mean score: 3.98) and "I felt ashamed" (mean score: 3.45). The overall mean score was 28.7 (SD ±

Table II: Obstetric Characteristics and Causes of Miscarriage (N=402)

Characteristics	N (%)
Previous history of miscarriage	
• Yes	229 (57.0%)
• No	173 (43.0%)
Frequency of miscarriage	
• None	173 (43.0%)
• One	127 (31.6%)
• Two	58 (14.4%)
• Three	18 (04.5%)
• More than three	26 (06.5%)
Have there been repeated miscarriages? (two or more consecutive miscarriages)	
• Yes	60 (26.2%)
• No	169 (73.8%)
Was the miscarried pregnancy a planned pregnancy? (N=229)	
• Yes	123 (53.7%)
• No	106 (46.3%)
When did the miscarriage occur? (N=229)	
• Less than 7 weeks	100 (43.7%)
• Between 7 - 14 weeks	96 (41.9%)
• Greater than 14 weeks	33 (14.4%)
Did you get medical care for your miscarriage? (N=229)	
• Yes	175 (76.4%)
• No	54 (23.6%)
Family history of miscarriage	
• Yes	315 (78.4%)
• No	87 (21.6%)
What do you think **one** of the most common causes of miscarriage? (select only one from the following)	
• Fate	121 (30.1%)
• Medical factors (examples include hormones, uterus)	120 (29.9%)
• Genetic and hereditary factors (examples include genetic problems in the fetus and syndromes)	99 (24.6%)
• Psychological problems (examples include a stressful event, depression, the mother not wanting to become pregnant)	41 (10.2%)
• Lifestyle (examples include drugs, alcohol, and smoking during pregnancy)	18 (04.5%)
• Punishment from God	03 (0.70%)

5.13), with low, average, and high emotional support constituting 13.1%, 70.7%, and 16.2%, respectively. Response has a range from "strongly disagree" coded with 1 to "strongly agree" coded with 5.

In Figure 1, based on participants' ratings, the top three most common perceived causes of miscarriage were spiritual cases such as destiny or fate (agree: 89.1%), lifting heavy objects (agree: 60.3%), and

Table III: Assessment of Emotional Support and Feeling after a Miscarriage (N=229)

Statement	Mean ± SD
1. I received appropriate emotional support from those I told	3.98 ± 0.88
2. I received appropriate emotional support from my partner	4.03 ± 1.02
3. The medical facility provided appropriate medical support	3.26 ± 1.68
4. The medical facility provided adequate emotional support	2.41 ± 1.62
5. I felt guilty †	2.81 ± 1.34
6. I felt alone †	2.76 ± 1.30
7. I felt ashamed †	3.45 ± 1.27
8. I feel I did something wrong which caused the miscarriage †	2.98 ± 1.38
9. I feel that I could have prevented the miscarriage	3.00 ± 1.39
Total Emotional Support Score	**28.7 ± 5.13**
Level of emotional support	
• Low	30 (13.1%)
• Average	162 (70.7%)
• High	37 (16.2%)

† Reversed coded question.

genetic abnormalities of the fetus (agree: 58.5%), punishment from God had the least ratings (agree: 3.5%)

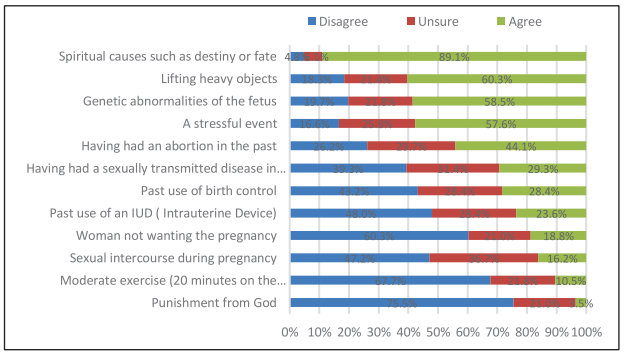

Figure 1: Perceived Most Common Causes of Miscarriage

In the combined Figure 2 responses were recorded on five and three point Likert scales.The first figure showed that 17.9% strongly agreed that they would feel less alone if a friend or family member had suffered the same miscarriage, while 24.9% agreed. When enquired about the emotional impact of miscarriage only 3.1% would feel extremely upset emotionally if they suffered a miscarriage, while 10.5% could be moderately upset shown in the second figure. Also, 79% of women would like to know the cause of miscarriage so that they could do

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something to prevent it from happening in the future, while 72.1% would like to know even if they could not do something to prevent it from happening again. When asked if they would want to know the cause of a miscarriage, regardless of prevention possibilities, 79% of women expressed interest in knowing to take preventive measures, while 72.1% indicated they would want to know even if they could not do something to prevent it from happening again displayed in the third figure.

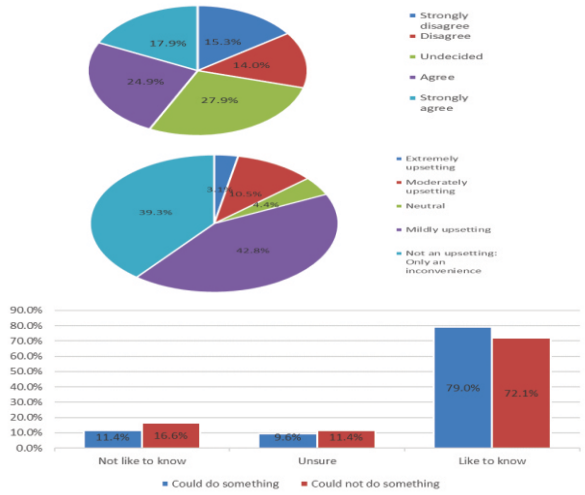

Figure 2: Participants' Response to Three Emotionally Based Questions on Five and Three-Point Likert Scales.

When measuring the association between the emotional support score and the socio-demographic characteristics of the women who had a miscarriage (Table IV), it was found that a higher emotional score was more associated with having more than 3 children (Z=2.013; *p*=0.044), those without a family history of miscarriage (Z=2.030; *p*=0.042) and those who had no repeated miscarriage (Z=2.030; p=0.011). No statistically significant association was retrieved between miscarriages and sociodemographic characteristics, obstetrics features, and chronic diseases.

Table IV: Association Between Emotional Support Score with the Socio-Demographic Characteristics and other Study Variables of the Women who had a Miscarriage (N=229)

Factor	Emotional Support Score (45) Mean ± SD	Z-test	p-value §
Age group			
• ≤35 years	28.4 ± 4.87	0.749	0.454
• >35 years	28.9 ± 5.34		
City of residence			
• Inside Al Ahsa	28.7 ± 5.55	0.380	0.704
• Outside Al Ahsa	28.9 ± 4.64		
Marital status			
• Married	28.8 ± 5.03	0.780	0.435
• Divorced or widowed	27.3 ± 6.39		
Family monthly income (SAR)			
• ≤10,000	28.3 ± 4.98	1.266	0.206
• >10,000	29.0 ± 5.28		
Occupational status			
• Employed/Student	28.9 ± 4.87	0.768	0.433
• Unemployed/Retired	28.4 ± 5.37		
Educational level			
• High school or below	28.5 ± 5.30	0.180	0.857
• Bachelor or higher	28.7 ± 5.08		
Number of children			
• Three	28.1 ± 5.17	2.013	**0.044** **
• More than 3	29.5 ± 4.99		
Chronic disease			
• Yes	28.3 ± 4.70	0.827	0.408
• No	28.8 ± 5.32		
Family history of miscarriage			
• Yes	28.3 ± 4.99	2.030	**0.042** **
• No	30.0 ± 5.43		
Repeated miscarriage			
• Yes	27.3 ± 5.62	2.555	**0.011** **
• No	29.2 ± 4.87		

§ P-value has been calculated using Mann Whitney Z-test.
** Significant at p<0.05 level.

Discussion

The findings of the study revealed a high prevalence of miscarriage among women living in the Eastern Province of Saudi Arabia. Nearly 60% suffered at least one miscarriage. Of them, more than one-quarter (26.2%) experienced repeated miscarriage. This is almost consistent with the study of Taybeh et al.[15] According to reports, 53.1% experienced at least one miscarriage, 27% experienced at least two, and 19.2% had three or more incidences. On the contrary, a study by Arck et al.[16] reported lower miscarriage prevalence at 6.8%. Supporting this report, Strumpf et al.[18] documented incidences of miscarriage between 2003 and 2014 at 11.3%.

According to the study by Alam et al.[18], increasing age and better education were at higher risk for miscarriage. Corroborating these reports in Arck et al. [16] increasing age was also found associated with miscarriage, lower BMI, and repeated miscarriages were linked to higher stress/demands. However, in our study, we did not find a significant association of miscarriages with age, chronic diseases, parity, and all other socio-demographic characteristics of the

women, which did not coincide with aforementioned findings.

One of the hallmark findings of this study was about emotional support received and feelings after miscarriage. In this study, two-thirds of our respondents received an average emotional support score, more than one-third had a high, and a slightly lower proportion had low emotional support post-miscarriage. These findings are comparable with Taybeh et al.[15] findings where more than half had indicated receiving adequate support from their partners and families. In a study by Mayor S.[19], less than half expressed receiving emotional support, 41% thought they had done something wrong, while 38% believed they could do something to prevent it. In contrast with Mayor et al., the current study's findings showed a large number of women received emotional support and were interested in knowing the cause of a miscarriage irrespective of could or could not do anything in this matter. Similar to our finding, the majority of the respondents in a United States survey conducted by Bardos et al.[10] expressed a desire to determine the cause of miscarriage, even if they couldn't take any action to address it. This demonstrates their eagerness to acquire awareness and knowledge regarding the causes of a miscarriage.

Women with more children, no repeated miscarriages, and no family history of a miscarriage were more likely to have better emotional support scores in this study. Banno et al.[7] indicated that married educated females and healthy participants provided significantly higher correct responses to the perception questionnaire whereas in the USA survey,[10] perception and understanding of miscarriage were significantly related to the gender and their level of education.

Regarding the specific details of emotional support, the highest emotional support received based on respondents' ratings was the support provided by their partners, followed by other individual support. However, emotional feelings post-miscarriage were also seen to affect women, particularly feeling ashamed, guilty, and alone. Consistent with our results, Bano et al.[7] and Bardos et al.[10] reported that the predominant emotional responses following a miscarriage were feelings of guilt and loneliness.

Awareness about the different causes of miscarriage is necessary to eliminate different misconceptions about it. In this study, spiritual causes (destiny/fate), lifting heavy objects, genetic abnormalities of the fetus, stressful events, and previous history of abortion were the top five most perceived causes of miscarriage. In a USA[10] survey genetic abnormalities of a fetus were, a stressful event, long stress, lifting heavy, and past sexually transmitted diseases were the top five perceived causes in a USA survey.Genetic fetal malformations were correctly perceived by a heavy majority reflecting a better awareness than our participants due to the adequate availability of health issues-related information in online medical leaflets and forums. However, Mayor S[19] reported stressful events or longstanding stress as the most prominent causes of miscarriage. A study in Jeddah by Rouzi et al.[20] on the perception of causes and feelings almost aligns with the current study findings and concluded that women possessed insufficient knowledge regarding the causes of miscarriage but in contrast to our respondents, women in the mentioned study received better support from healthcare facilities. This divergence might be attributed to the possibility of more effective healthcare delivery in Jeddah.

Present study findings indicate that the emotional and medical management support offered by treating healthcare professionals was not remarkable after a miscarriage. Similarly a study conducted by Bilradi et al.[21] in Australia, the majority of women expressed dissatisfaction with emotional support, counseling services, and follow-up care provided by healthcare professionals following a miscarriage.

The dissemination of information regarding well-established causes of miscarriages is crucial to prevent individuals from engaging in self-blame, self-pity, stress escalation, and ultimately, the development of depression. Effectively delivering such sensitive awareness necessitates comprehensive counseling for those affected. This approach has the potential to elevate awareness about the causes of miscarriages, empowering individuals to navigate their loss with a positive outlook and resilience.

Conclusion

A high prevalence of miscarriage is recorded in the eastern province of Saudi Arabia. Perceived causes of

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miscarriage included destiny, lifting heavy objects, and genetic abnormalities of the fetus. Identifying the potential causes of miscarriage may positively affect the emotional state of the patients and could lead to better prevention. The study provided valuable insights that can contribute to improved healthcare services and community support structures.

Limitation of Study

As an online cross-sectional study, the findings lack generalizability, and there may be a potential for recall bias among some women.

Recommendation

Researches need to be conducted in all other provinces of Saudi Arabia to calculate a valid prevalence and perception of miscarriages which can help to devise awareness and supportive measures post-miscarriages in all health care systems throughout the country.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

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ORIGINAL ARTICLE

Determination of Curve of Spee in Healthy Permanent Dentition and Its Application in Complete Denture Wearers

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ABSTRACT

Objective: To determine the depth of the curve of Spee in healthy permanent dentition for its application in complete denture wearers.

Study Design : Cross-sectional study.

Place and Duration of Study: The study was conducted at Lahore Medical and Dental College from 20th April to 20th October 2023.

Materials and Methods: A total of two hundred patients aged 18 – 32 years were included in this study. Mandibular casts of patients were obtained. Each of the casts had fully developed dentitions except for the third molars. Independent sample t-test was used to determine mean depth of the curve of Spee between females and males. Data was collected, results were then statistically analyzed using SPSS version 25. A p-value ≤ 0.05 was considered significant.

Results: The mean age of subjects was 25.19 ± 3.529 with minimum and maximum age as 18 and 32 years. The depth of the curve of Spee was found to be P=0.380 and t= -1.540, the curve of Spee is not significantly different in both genders. The curve of Spee mean value was 1.990 ± 0.6175 mm.

Conclusion: This study has revealed that the depth of the curve of Spee in natural dentition remains constant irrespective of age and gender. Therefore, the curve of Spee values can be used in the rehabilitation of complete denture wearer.

Key Words: *Balanced Occlusion, Complete Edentulism, Curve of Spee, Dentition, Occlusal Plane.*

Introduction

Human dentition, i.e., the teeth and their supporting tissues is a mutually protected, organized arrangement of maxillary and mandibular teeth.[1] With age and poor oral hygiene, severity of periodontitis (peridontium inflammation) increases, that may be one of the major cause of loss of teeth leading to edentulism.[2,3] Determining occlusal plane is one of the important steps in prosthodontic rehabilitation of edentulous patients.[4] In 1890, Ferdinand Graf Von Spee, defined line of occlusion by using skulls with abraded teeth which is now known as curve of Spee.[5] Curve of Spee is defined "as the anatomic curve established by the occlusal alignment of the teeth. It begins from the cusp tip of the mandibular canine and following the buccal cusp tips of the premolar and molar teeth, continuing through the anterior border of the mandibular ramus and ending at the anterior-most portion of the mandibular condyle".[6] It is viewed from lateral aspect, and it is a curved line that is convex in the maxillary arch and concave in the mandibular arch.[7] The Curve of Spee, exists in the natural dentition, allows harmony to exist between the anterior tooth and condylar guidance. Clinically, the curve of Spee can be determined distally from the marginal ridges of posterior teeth and the incisal edges of the incisors that determine the curve of Spee.[8]

For restoring the natural dentition prosthodontically, the treatment objective is a mutually protected occlusion or canine guided occlusion, whereby the posterior teeth disocclude during eccentric functional movements.[9] The curve of Spee, along with anterior guidance, condylar inclination, and posterior cusp height, plays an important role in the development of the desired occlusal scheme.[10]It may be extremely altered in situations resulting from

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rotation, tipping, and extrusion or intrusion of teeth. Andrews described six keys to normal occlusion and stated curve of Spee as the sixth key to normal occlusion that ranges from mild to flat curve.[11] A study reported that, once established in adolescence, the curve of Spee appears to be relatively stable.[12]

In other studies, curve of Spee, when seen in most of the cases, showed a mean radius of approximately 106.4 ± 7.6 mm in the maxillary arch and 83.4 ± 5.2 mm in the mandibular arch. Radii of the curves of Spee in the maxillary arch were significantly larger than those in the mandibular arch (P<.0001).

It had a mean depth of approximately 1.6 ± 0.4 mm in the maxillary arch and 1.9 ± 0.5 mm in the mandibular arch. The depth of the curve of Spee in the mandibular arch was significantly deeper than that in the maxillary arch.[13]

The current study was designed to assess and determine the depth of curve of Spee in mandibular arches in men and women in local population. As no local data is published and studies on global population are also not widely available, this study will help us to generate baseline data and the results of the study will aid the clinician in developing occlusion in the sagittal plane which would be useful when providing prosthetic rehabilitation for patients with edentulous arch or occlusal derangement. The objective of this study was to determine the depth of COS in healthy permanent dentition for its application in complete denture wearers.

Materials and Methods

A cross-sectional study was carried out at department of Prosthodontics, Lahore medical and dental college for a period of 6 months from 20th April to 20th October 2023. The present research was conducted by following all ethical principles. Foremost, Ethical Committee Approval was sought, which works as an Institutional Review Board (IRB) LMDC/FD/4950/23 Nonprobability consecutive sampling technique was used. Informed consent was taken from the patients. The inclusion criteria were all patients aged 18-32, either gender, complete permanent dentition, including the second molars (at least 28 teeth), bilateral Angle class 1 molar and canine relation. Exclusion criteria were patients with caries, malocclusion, history of orthodontic treatment, history of temporomandibular disorders, patients with cleft lip and cleft palate were recorded in a pre-designed questionnaire that included variables regarding socio-demographic features, questions regarding depth of COS in lower arch.

A total of 200 subjects meeting inclusion criteria were taken. The sample size was calculated using expected mean of depth of curve in mandible as 1.9 ± 0.5 mm.[6] We used 95% confidence level, and 5% margin of error. Basic demographic information (name, age, gender) and contact details was taken. Mandibular casts were obtained from irreversible hydrocolloid impression in modified stock trays for each subject. In order to measure the depth of curve of Spee, a rigid acrylic template was positioned in such a way, that it touches the lower incisal edges and mesio buccal cusp of 1st molar and curve of Spee was measured with the help of periodontal probe from deepest cusp at the 2nd premolar area. All cases were assessed for the measurement of depth of curve of Spee with the help of acrylic template in healthy permanent dentition. All data was entered and analyzed using SPSS version 25. Frequency and percentages were used for qualitative data like gender. Mean ± Standard deviation was applied for quantitative data like age and measurement of depth curve of Spee in healthy permanent dentition. Data was stratified for age, gender, to control the effect of modifiers. Post stratified independent sample t-test was applied to determine curve of spee in healthy permanent dentition and its application in complete denture wearers taking p-value ≤ 0.05 as significant.

Results

The mean age of subjects was 25.19 ± 3.529 with minimum and maximum age as 18 and 32 years. Table -I. The mean age in male was 25.10 ± 3.650 and in female was 25.27 ± 3.420. The maximum and minimum value of depth of curve of Spee in both male and female subjects was 3.5 mm and 1.0 mm. Table -II. The curve of Spee of P-value is 0.380, t= -1.540 for both males and females. Table -III. The mean ± SD depth of curve of Spee in age group 18 – 25 years is 2.08 ± 1.08 and for age group 26 – 32 years is 1.99 ± 0.64. The depth of curve of Spee P- value is 0.481. Table -IV.

Discussion

One of the key clinical steps in the rehabilitation of multiple long span posterior restorations is the re-establishment of occlusual plane.[14] The restoration

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Table I: Descriptive Statistics of Age (Years)

Age(Years)	
Mean	25.19
Std. Deviation	3.529
Range	14
Minimum	18
Maximum	32

Table II: Descriptive Statistics of the Study Sample by Gender

	Gender									
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
	Mean		Std. Deviation		Std. Error Mean		Minimum		Maximum	
Age	25.1	25.2	3.65	3.42	0.36	0.34	18	20	32	32
Depth (mm)	1.92	2.05	0.601	0.629	0.060	0.062	1.0	1.0	3.5	3.5

Table III: Mean Depth of Curve of Spee between Females and Males

Depth	Gender	Independent Sample T test	P - Value
	Male	-1.540	0.380
	Female	-1.540	

Table-IV: Stratification of Depth of Curve of Spee with Respect to Age N=200

	Age groups	Mean	Std. Deviation	P- value
Depth	18-25 years	2.082	1.0802	0.481
	26-32 years	1.994	0.6422	

of compensating curves forms the basis for ideal teeth arrangement.[15] This study was conducted to investigate the curve of Spee in healthy permanent dentition and its implications for complete denture wearers. The mean age of the subjects was 25.19 ± 3.529 years. The maximum and minimum values of the curve of Spee depth were 3.5 mm and 1.0 mm, respectively, for both males and females. The results show no significant difference in the depth of the curve of Spee with respect to age and gender, consistent with several previous studies.[16]

In the current study, our findings indicate that the depth of the curve of Spee does not vary significantly with age. This observation aligns with the results of Paes-Souza et al., who reported no correlation between the curve's depth and age.[17]However, Karani J. found a significant increase in the depth of the curve of Spee with age, suggesting a possible difference in methodology or sample population.[18] This discrepancy highlights the need for standardized measurement protocols in future research.

Similarly, we observed no significant difference in the depth of the curve of Spee between males and females. This result supports the findings of Marshall et al., who also reported no gender-based differences.[7,19] This uniformity across genders simplifies clinical applications, as gender-specific adjustments to the curve of Spee may not be necessary.

The method of measuring the curve of Spee varies among studies, contributing to inconsistent findings. In this study, it was measured from the deepest cusp at the 2nd premolar area. While Veli et al. and another study indicated the deepest point at the mesiobuccal cusp of the first molar, Hasan et al. reported it at the buccal cusp of the second premolar.[8,20] These variations underscore the importance of developing a universally accepted measurement technique to ensure comparability across studies.

Clinically, maintaining the curve of Spee is crucial for functional occlusion and patient satisfaction in complete denture wearers.[21,22] Our study suggests that deviations from the natural curve may lead to interferences during mandibular movements, impacting the masticatory system's health. Therefore, clinicians should carefully consider the curve of Spee during denture fabrication to avoid such complications.

Limitations of Study

One limitation of our study is the narrow age range of 18 to 32 years, which may not fully capture age-related changes in the curve of Spee. Additionally, our study does not account for skeletal morphology, dental arch form, or occlusal relationships, which could influence the curve's depth.

Future research should incorporate a broader age range and additional variables such as skeletal morphology, dental arch form, and occlusal relationships.

Conclusion

In conclusion, the present study contributes to the understanding of the curve of Spee in healthy permanent dentition and its implications for complete denture wearers. The depth of the curve does not significantly differ by age or gender, suggesting uniformity that can simplify clinical applications. However, measurement variability among studies highlights the need for standardization. Clinicians must maintain the natural curve of Spee in denture fabrication to ensure functional occlusion and patient satisfaction.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Depression, Anxiety and Stress using Depression, Anxiety, and Stress Scoring System (DASS-21) Among the Students of Women Medical and Dental College Abbottabad, Pakistan

Amina Malik[1], Maham Bashir[2], Fahad Saqib Lodhi[3], Zahid Gul Jadoon[4], Asya Tauqir[5], Muhammad Akram Khan[6]

ABSTRACT

Objective: To determine the frequency of stress, anxiety, and depression among medical students using DASS-21 scoring system.

Study Design: Cross sectional survey.

Place and Duration of Study: Women Medical and Dental College Abbottabad from 1st February 2023 to 31st July 2023.

Materials and Methods: A sample, containing 140 students, was included in the study after receiving ethical approval from the medical college. Twenty-eight medical students each from the first year to the fifth year were contacted by using simple random sampling technique and were each given a Depression, Anxiety and Stress Scale (DASS-21). The questionnaire used in this study had two parts: a sociodemographic one that asked students about their age, year of study, relationship with family, health status, time they spent on social media, personalities, socioeconomic class, academic performance, and DASS scale, the second part of the questionnaire. The data was analyzed using the IBM SPSS (version 26.0, Armonk, NY, USA).

Results: Anxiety was found in 85% of students (17% mild, 31% moderate, 15% severe, and 22% extremely severe). A total of 52% of students reported having depression (15% mild, 19% moderate, 11% severe, and 7% extremely severe). Forty-two percent of the medical students were stressed (15% mild, 12% moderate, 13% severe, and 2% extremely severe).

Conclusion: A high occurrence of anxiety, followed by depression and stress, was found among medical students, affecting their academic performance and social well-being.

Key Words: *Anxiety, Depression, Medical Education, Student's Mental Health, Stress.*

Introduction

The World Health Organization (WHO) has laid out a compelling case for the importance of mental health, quoting it as a "state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community".[1]

In today's frenetic world where everything is a competition, a race, where everyone is striving to be the best and working hard mental health is often neglected, making people vulnerable to mental illnesses with depression, anxiety, and stress being more prevalent. Healthcare workers, more specifically medical students the aspiring doctors, are more at risk of experiencing depression, anxiety, and stress as medical education is immanently stressful and demanding. Students are expected to acquire a broad range of expertise and skills in a limited time period making them undergo regular pressures and overwhelming burdens. In addition to the academic obligations, students face extremely competitive surroundings that requires social and personal sacrifices, along with disrupted sleep, high expectations from family and the institute, gender

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inequality, and discrimination aiding in considerable mental distress.[2]

Numerous studies have shown that compared to the general population, medical students experience higher levels of stress, anxiety, and depression, with overall psychological discomfort levels that are continuously higher.[3] A recent comprehensive study and meta-analysis estimated that 28% of medical students worldwide experienced depression or one of its symptoms.[4] A meta-analysis of 41 research including medical students from multiple countries reported a high pooled prevalence of depression among the students, at 37.9%, in the study by Jia Q *et al.,*[5] The prevalence of depression among medical students, however, has been estimated to be 39.4% in UK[6], 29% in Malaysia[7], 40% in India[8], and 39.1% in Pakistan[9]. Among medical students worldwide, the incidence rate of anxiety was 33.8%. Middle Eastern and Asian medical students reported anxiety the most frequently.[10] Furthermore, a study conducted in Pakistan concluded that the frequency of stress among Pakistani medical students had been 51.6%.[11]

Despite the growing body of research on this topic, there remains a significant literature gap in our region, where the mental health of medical students has been understudied. The aim of this study was to assess the level of stress, anxiety, and depression among medical students and investigate whether they are more susceptible to mental illnesses than the general population. If this could provide a more representative picture of the mental health of medical students in this region, enabling the development of targeted interventions to address the identified issues. Moreover, this study explored the underlying causes of mental illness among medical students, including academic pressure, social factors, and personal characteristics.

Materials and Methods

A cross-sectional study was conducted on medical students of Women Medical and Dental College for a duration of 6 months from 1st February to 31st July 2023, after the receiving of ethical approval (Reference No: 2023-2 CIMID-ERC-23) from Institutional Review Board to get an estimate of frequency of stress, anxiety and depression. A total of hundred and forty students were selected through random probability sampling. The WHO sample size calculator was used to determine the sample size, with a prevalence of 18.4%[26], a confidence range of 95%, and an absolute precision of 0.08. Participants included were medical students, whereas the general public was excluded from the study.

A self-administered, self-constructed questionnaire with two components was used in the study. This was validated by a pilot study, whose data was not used in the findings. The first part of questionnaire was sociodemographic questionnaire, where in each student was asked to provide their age, year of study, relationship with family, health status, time spend on social media, hobbies/interests, personality type, socioeconomic class, academic performance and the second part was Depression, Anxiety and Stress Scale (DASS-21).[12, 13] The data was entered in an Excel spreadsheet and IBM SPSS (version 26.0, Armonk, NY, USA) was used to for statistical analysis.

DASS-21, which has three self-report scale, was used to measure the emotional states of stress, anxiety, and depression.[12]The range for the depression cutoff score was 9; 10–13 indicated mild depression, 14–20 was categorized moderate depression, 21–27 was labelled severe depression, and 28+ indicated extremely severe depression. The range for anxiety cut off score was 7; 8-9 was considered mild anxiety, 10-14 indicated moderate anxiety, 15-19 indicated severe anxiety and 20+ indicated extremely severe anxiety. The range for stress cut off score was 14; 15-18 indicated mild stress, 19-25 indicated moderate stress, 26-33 indicated severe stress and 34+ indicated extremely severe stress.[12]

The data was entered in Excel spread sheet and for the statistical analysis, IBM SPSS (version 26.0, Armonk, NY, USA) was used. Descriptive statistics were calculated for numerical data, i.e., age, and time spent on social media and categorical data i.e., year of study, relationship with family, health status, personalities, socioeconomic class and academic performance.

Results

Out of 140 students, 40 questionnaires were removed from the analysis due to incomplete response, this left us with 100 questionnaires, resulting in a response rate of 71.4%, 49 hostelites and 51 day-scholars. The mean age of students was 22.5, ranging from 19 – 26 years. The highest incidence of stress, anxiety, and depression was among students of 23-26 years of age. The hostelites

were more prone to anxiety (87.7%) as compared to day-scholars, and all students who had migration from another institute suffered from anxiety as shown in Table I, whereas it was noted that the occurrence of depression (54.9%) and stress (45.1%) was more in day-scholars. Moreover, students who had average or poor relationships with their families, poor health status, introverted and cautious personalities, belonged to lower middle or middle socioeconomic class, and poor academic performance were all more depressed, anxious, and stressed.

The frequency and percentages of the cases, that were diagnosed anxiety, depression and stress on DASS-21 Scale are shown in the Figure 1. Its shows that moderate depression (19%) was most common as compared to mild (15%), severe (11%) and extremely severe (7%) cases of depression. Out of all the reported cases of anxiety, cases of moderate anxiety (31%) were most common among medical students. Whereas mild stress (15%) was highest among students, that were labeled stressed on DASS-21 Scale.

Table I: Demographics showing Descriptive Statistics (n=100).

DEMOGRAPHICS	Frequency (n)	Anxiety DASS-21 > 6 n (%)	Depression DASS-21 > 5 n (%)	Stress DASS-21 > 4 n (%)
Age in years				
19-22	71	33 (46.4)	59 (83.1)	26 (36.6)
23-26	29	19 (65.5)	26 (89.6)	16 (55.1)
Living situation				
Hostelite	49	24 (48.9)	43 (87.7)	19 (38.7)
Day Scholar	51	28 (54.9)	6 (100)	23 (45.1)
Student				
Migration	5	51 (53.6)	80 (84.2)	41 (43.1)
Freshmen	95	1 (20)	5 (100)	1 (20)
Relationship with family				
Good	86	40 (46.5)	72 (83.7)	31 (36.1)
Average	8	6 (75)	8 (100)	5 (62.5)
Poor	6	6 (100)	5 (83.3)	6 (100)
Health Status				
Excellent	28	11 (39.2)	25 (89.2)	9 (32.1)
Good	60	30 (50)	50 (83.3)	24 (40)
Average	8	8 (100)	6 (75)	6 (75)
Poor	6	3 (75)	4 (100)	3 (75)
Social Media				
< 4hrs	64	28 (43.6)	51 (79.6)	22 (34.3)
> 4hrs	34	24 (70.5)	34(94.4)	20(55.5)
Personality				
Introvert	31	24 (77.4)	28 (90.3)	17 (54.8)
Outgoing	28	13 (46.4)	20 (71.4)71.4	12 (42.8)
Adventurous	29	10 (34.4)	2O (68.9)68.9	7 (24.1)
Cautious	12	5 (41.6)	12 (100)100	6 (50)
Socioeconomic class				
Lower middle	1	1 (100)	1 (100)	-
Middle	30	13 (43.3)	25 (83.3)	10 (33.3)
Upper middle	63	36 (57.1)	55 (87.3)	29 (46)
Upper	6	2 (33.3)	4 (66.6)	3 (50)
Academic performance				
Good	74	36 (48.6)	65 (87.3)	29 (39.1)
Poor	26	16 (61.5)	20 (76.6)	13 (50)

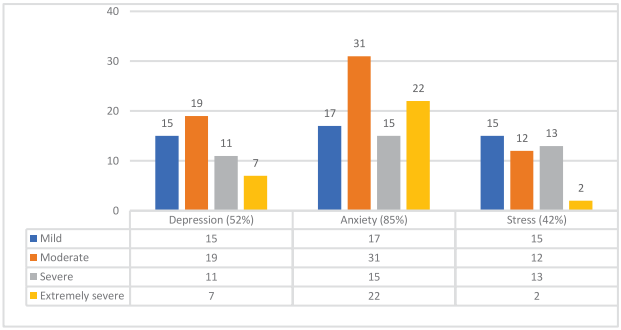

Figure 1: Depression Anxiety and Stress among the Participants

Discussion

As medicine is a demanding profession that requires a lot of sacrifices with a hectic study routine, long study hours, clinical rotations, extensive syllabus, disturbed sleep, increase workload, competitive environment, and gender inequality which can be both physically and emotionally exhausting, which often results in students feeling depressed, anxious, and stressed.

Our study found that anxiety (85%) was most common among medical students as compared to depression (52%) and stress (42%). This was similar to a study conducted by American Psychological Association found that anxiety was the most common mental health concern among college students, followed by depression.[14] But study conducted in a Malaysian Medical College found that 31.1% of the participants were found to be depressed, with the majority falling into the moderately depressed category, 53.9% had anxiety, and 26% had stress.[15] Similarly, Egyptian medical students were found depressed (64.2%), anxious (77.1%), and stressed (70.4%).[16] In Delhi, India stress and anxiety was 32.0% and 40.1% respectively, as compared to depression (43.8%).[17]

Maser B *et al.,*[18] reported that the incidence of mood disorders, anxiety disorders, suicidal thoughts, and psychological discomfort were considerably higher among medical students aged 20–34. Moreover,

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students who are away from their hometowns and families residing in hostels are more anxious than their day scholar colleagues and those who get transferred from some other institutes are at high risk of having anxiety and depression due to change of place, environment, friends and colleagues as perceptible by the study in Northwest England and three overarching themes were identified: "The space between"; "Hotels as vessels for cultivating communities and friendships" and 'The significance of accommodation-based pastoral staff'.[18] This leaves young people vulnerable as they go through a process to re-attach to new people and a new setting, and loneliness and social isolation were vividly felt during this phase. The shift disrupts attachment to place and connections with significant persons.[18]

Loneliness was made worse by locations that hinder social cohesiveness. Since it is typical for students to disconnect both mentally and physically from their flat if they do not make friends there, pastoral professionals that work in accommodations have a crucial role to play.[19] Although these results highlight the value of the human aspect in housing, it is necessary to create spaces that that promotes a sense of community, belonging, and wellness.

It was interesting to note that day scholars appear more depressed and stressed than hostelites attributed primarily to daily commuting between college and their residences, several occurred aspects of commuting were linked to general mental health according to Roberts *et al.*[20]Moreover, there is a linear increase in anxiety followed by depression for each academic level. The increased difficulty with each academic year, may make it difficult for students to keep a balance between their social life and studies, and likewise results were observed by a study conducted by Ishtiaq S *et al.,*[21] and it has also been noticed that low-scoring medical students feel higher levels of stress, anxiety, and depression than high-scoring students.[22]

Several steps can be taken to help students regarding management of depression, anxiety, and stress. This may include mental health societies for students to open up and seek help, counseling services for the students, extracurricular activities, developing healthy coping strategies, and setting realistic expectations and goals.

Conclusion

there is a high frequency of anxiety (85%), followed by depression (52%) and stress (42%) among medical students. Age, year of study, family relationship, health status, personality, social class, and academic performance were all strongly correlated with stress, anxiety, and depression, which can inform strategies to mitigate these triggers and promote the mental and physical well-being of future health care professionals.

Limitations

This study has several limitations that should be evaluated through additional studies. Firstly, this study did not concentrate on additional factors that contribute to depression, anxiety, and stress like drug abuse, family history of anxiety and depression, stressful life events, and childhood traumas. Secondly, the study may not be generalized as the study sample was composed of medical students confined to only one private medical college. Third, a short form of the original DASS-42 version (DASS-21) is used, we noticed that the findings were specific to this version, and we anticipated that the invariance of all versions of the DASS will be tested in future studies.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

The Efficacy of Silver Diamine Fluoride in Arresting Carious Lesions in 6-9 Year Old Children From Peri Urban Islamabad

Sheze Haroon Qazi[1], Rubina Mumtaz [2], Muhammad Sajid [3], Sadaf Humayoun[4], Hajra Shahid[5], Saba Masoud [6]

ABSTRACT

Objective : The present study was done to assess the efficacy of silver diamine fluoride in arresting caries lesions in 6-9 year old school going children.

Study Design : Quasi-experimental.

Place and Duration of Study : The study was conducted from 15th February 2022 till 15th February 2023. The research was conducted by the community dentistry departments of Islamabad Medical & Dental College and Rawal Institute of Health Sciences in school going children from peri- urban Islamabad.

Materials and Methods : A sample size of 384 was calculated using Open Epi software which uses cochran's formula for sample size calculation. Active carious lesions extending to enamel and dentine in primary teeth and first permanent molars were identified using the International Caries Detection System. These teeth were then treated with 38% Silver Diamine Flouride using the standard application protocol. Data was recorded electronically on excel sheets (and later SPSS version 25 for analysis) at baseline and after 6 months to assess if the active carious lesion had been arrested. The data was discrete. Wilcoxon Signed Rank test was used to test the significance of the results.

Results: The participants included 64% males and 36% females. Average age of the study population was 7.7 years. More than half (66.4%) brushed their teeth once a day. The caries arrest in primary teeth and in first permanent molars was 77.5% and 87.7% respectively. Wilcoxon Signed Rank test was applied to check the significance of our results. In both the primary dentition and permanent molars, a single SDF application showed a statistically significant decrease in the mean number of carious lesions (p-value< 0.05).

Conclusion: The present study concluded that a single application of SDF with its ease of applicability can effectively halt the progression of active carious lesions in 6-9 year old children.

Key Words: *Carious lesions, efficacy, Peri-urban, school children SDF.*

Introduction

Oral health related problems in children revolve around dental caries globally.[1] The World Health Organization Global Oral Health Status Report 2022 estimates close to 3.5 billion people are affected by oral disease worldwide, with almost 75% living in middle-income countries.[2]

The prevalence of early childhood caries has been directly associated with limited finanacial resources and access to oral health care.[3] According to the Global Economy survey in Pakistan 62.27% of the population that lives in rural areas has an estimated dentist population ratio of 1: 200,000. Hence, access to oral health care is very limited in these areas.[4,5]

Traditionally, fluoride compounds have been used for stopping and preventing dental caries. In the 1960s Professor Reiichi Yamaga of Osaka University in Japan discovered Silver diamine Flouride (SDF) as an alternative to conventional restorative materials.[6] This material could be used for treating dental caries in young children, root caries in elderly patients, and for the prevention of pit and fissure caries.[7] It is a colourless liquid with a pH of 10, comprising of 62% water, 44,800 ppm fluoride ions, 25% silver, 8% ammonia, and 5% fluoride. SDF solution comes in concentrations ranging from 10% to 38%; the greater

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concentration has been shown to be more beneficial.[8]

SDF works by uprooting the germs that cause dental cavities and causing calcium fluoride and silver phosphate to precipitate. This process remineralizes tooth structure and prevents dental caries.[9] In addition to this, it deters the matrix metallopeptidase increasing the microhardness of dentine and has an antibacterial effect on cariogenic biofilm, averting collagen degradation.[10] SDF does not cause any side effects when applied but causes a lasting black stain on the porous part of the tooth structure hence parental consent is essential. Although instant use of potassium iodide solution (KI) can potentially reduce the intensity of tooth staining. [9] Additionally, due to its easy application it has reduced dental chair anxiety, making treatment easy for both, the patient and the practitioner.[10]

The importance of managing dental caries cannot be overlooked as it is essential for better oral health outcomes in communities. Whatever the level of preventive method adopted, it is imperious that the technique should be tailored to the needs of the population. According to a recent meta-analysis conducted in Pakistan, the prevalence estimate of dental caries was 50.493% in the primary dentition, 61.183% in the mixed dentition, and 57.184% in the permanent dentition.[11]

In Pakistan, SDF is not widely utilized or discussed despite the aforementioned advantages. Only 25% of dental professionals surveyed in a recent Lahore research were aware of SDF, and only 10% had actually used it. This is a worrying discovery, especially considering Pakistan's high dental caries rate.[12] People in rural localities in comparison to urban ones face these constraints to a greater extent.[13.] The present research sets out to explore the efficacy of one such material in arresting dental caries in school going children from a peri-urban locality.

Materials and Methods

This one group pre post quasi expérimental study was conducted in 6-9 year old school children belonging to peri urban locations of Islamabad from 15th February, 2022 till 15th February, 2023. A sample size of 384 using cochran's formula was calculated taking caries prevalence at 50% among 6-9 year old children and 5% margin of error, with 95% confidence interval. A convenience sampling technique was used**.** After approval from the Ethics review Board from RIHS (Appl#Ref#Rawal/RDC/IRB/22/02) a list of schools in Islamabad's peri urban locality generated. The school administration was then contacted for consent to participate in the study. The children from the participating schools were given an information sheet and a consent form translated into Urdu regarding SDF application. Only those who consented and met the inclusion criteria were included in the study. Children aged 6-9 years with active carious lesions extending to enamel and dentine without any pain or infection were included in the study. According to the exclusion criteria children were not counted in the study if they reported to have silver allergy, or had any signs of irreversible pulpitis or peri apical periodontitis. Children likely to exfoliate teeth in the next six months or did not consent to participate were also not included in the study. Children with stomatitis or ulcerative gingival conditions and partially erupted teeth were also excluded from the study.

The age group of the study participants was between 6-9 years as children younger than that are generally non-compliant and would have made the application of SDF challenging. Secondly, a school setting was used for the purpose of convenience and easy follow up. A group of qualified and calibrated dentists were asked to screen the children for any active carious lesions and make sure that they had no signs of any acute oral infection or tooth ache. The extent of caries in primary teeth and first permanent molars was assessed using the International Caries Detection and Assessment System (ICDAS) and carious lesions in teeth with code three (localized enamel breakdown) and five (distinct cavity with visible dentin) was documented.[14]

In this paper, 'enamel caries' and 'dentine caries' refers to ICDAS code three and five respectively. The present research included only those children who had at least one carious lesion in accordance with the International Caries Detection and Assessment System II.[14]

Following the manufacturer's instructions, the teeth to be treated were first isolated using cotton rolls. Then, 38% SDF (Topamine, DentaLife, Australia) solution was dispensed in a plastic dish and applied directly to the lesion using a disposable microtip

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applicator, leaving it in place for 30 to 60 seconds. This procedure was performed by a dentist after recording the baseline scores of caries. Children were advised to avoid eating or drinking for around 30-60 minutes post application.

LA follow-up examination was performed approximately six months later to check if caries had been arrested in the teeth treated with SDF by evaluating the colour and consistency of the lesions. Once more, the examiners noted if pain and infection were present or not. Dark, hard, and black lesions that were free of pain or infection were seen as positive outcomes when evaluating the effectiveness of SDF based on clinical outcomes. The outcomes were recorded on an excel sheet and subsequently, SPSS for Windows version 25.0 was used to statistically evaluate the non-parametric data. As the data was discrete, a test for normality was not used. Wilcoxon signed rank test was used to check the significance of our results and a p value < 0.05 was considered significant.

Results

From the total sample size of 384 only 200 continued to participate in the study for follow up. Out of these 128 (64%) were male and 72 (36%) were female. The mean age of our study participants was 7.7 years.

Brushing frequency data was recorded (Figure 1). Data regarding the use of toothbrush and toothpaste was missing for nine and eight participants respectively. Among those who brushed their teeth, 174 (87%) confirmed using a toothbrush to do so and 170(85%) said they used toothpaste as well. None of the 200 (100%) participants had any acute oral infection.

The number of teeth with arrested caries in primary teeth and first permanent molars was 341 (77.5%) and 64 (87.7%) respectively (Table 1). As the data was discrete no test for normality was required and Wilcoxon Signed Rank test was applied to check the significance of our results. In the primary dentition, the mean number of enamel and dentin caries both showed a statistically significant decrease (p-value< 0.05). In the permanent molars, SDF application led to a statistically significant decrease in both enamel and dentin caries (p-value < 0.05).

Discussion

The results of the present study established that the efficacy of SDF in halting caries in primary and permanent dentition was 77.5% and 87.5% respectively. With more than half of the study participants 67.4% brushing their teeth at least once daily.

Table I : Number of Teeth with Active and Arrested Caries, at Baseline and Six Months

Variables	Number of primary teeth			Number of 1st permanent molars		
	Enamel	Dentine	Total	Enamel	Dentine	Total
Baseline: active caries	236	204	440	60	13	73
6 months: Active caries	29	70	99	8	1	9
Arrested caries (%)	207 (87.7)	134 (65.7)	341 (77.5)	52 (86.7)	12 (92.3)	64 (87.7)
P-value	0.000	0.00	0.00	0.00	0.013	0.013

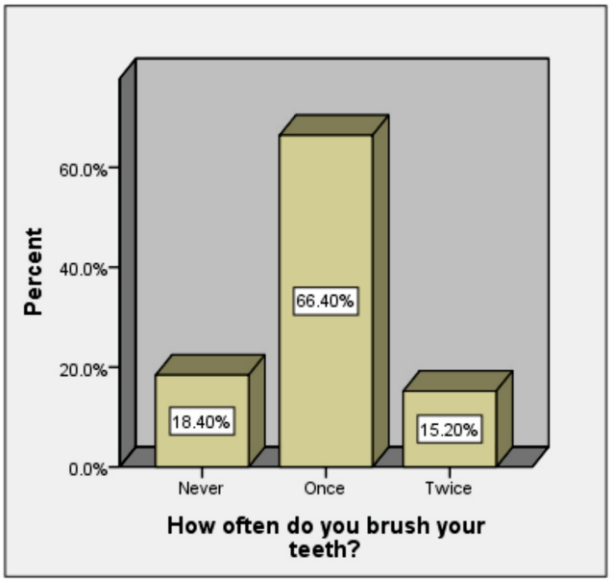

Figure 1: Brushing frequency

The World Health Organization (WHO) states that early childhood caries has an occurrence between 60 to 90% amongst the people in European countries, with 61% of children aged 6 to 12 years having at least one decayed tooth.[15] A recent meta analysis on the existing data in Pakistan showed that approximately 60% of the Pakistani population had dental caries showing it to be at high risk.[15] An alarming high frequency of damaged, untreated teeth in the primary dentition—66.1% of untreated caries in children aged six—was found in a research study carried out in the Rawalpindi district of Pakistan.[16] In the present study as well the participants all had at least one active carious lesion in either their permanent or primary tooth.

In Pakistan the dentist-to-population ratio is

1:10850.[16] The present study was conducted in a peri urban locality where this ratio is even more disproportionate.[4] A recent scopus review indicated that in low and middle income countries, policy makers should focus more on inequality determinants and incorporate practices for impartial dissemination and accessibility of dental facilities.[17] Rural areas of Pakistan have a dearth of dental care programs accompanied by low affordability of rural families, all contributing to the high prevalence of caries in these children.[15] Silver diamine fluoride has been in active use in many countries for arresting caries with an effectiveness ranging from 70-96% since 2009.[18]The present study aslo concluded that a single application of 38% SDF solution was quite effective in halting dental caries in deciduous teeth and permanent molars. Several studies have established its efficacy; a recent one by Chaurasiya and Gojanur with a 12 month follow up concluded that SDF can be utilized for halting caries in primary teeth.[7] As per Azuoru *et al.*, Rady *et al.*, and Chu et al., SDF works well to stop caries in kids.[19] Another study by Duangthip et al. Sihra et al established SDF application was more efficient than NaF varnish.[20]

The results of our study have serious implications in the context of dental caries experience for low socioeconomic status children having limited accessibility to oral health care. SDF with a single application can prove to be effective and efficient as a comprehensive evaluation conducted in 2019 revealed that a single annual application of SDF was significantly more effective in preventing caries than several applications of sodium fluoride varnish.[21] Another systematic review stated that the progression of caries can be stopped by SDF and was safe for children under 18 years of age.[22] About 60% of Pakistani people have dental caries[23], and risk factors for the condition include eating a diet high in cariogenic foods, not practicing good oral hygiene, and having a low socioeconomic status.[21] Apart from ingraining good oral hygiene practices healthy dietary habits SDF can help wrestle the problem at an early stage and prevent the progression of caries.

This research not only recognized the efficacy of SDF in treating enamel and dentinal caries after a single application but also helped us achieve this goal in a timely manner in low resource settings.

A study conducted in Hong Kong concluded that SDF should be incorperated into community dental outreach programs in order to improve access to oral health care and make it more equitable. This is especially important in low and middle-income countries where oral health care is often difficult to obtain.[24] In Pakistan community health workers can be utilized for dental outreach programs especially in rural areas and SDF can be used with its easy applicability. This can prove to be revolutionary in halting the progression of caries among children of our country.

Conclusion

In Pakistan there is grave concern with high prevalence of oral diseases and there is a dire need to devise an approach that is community-based, sustainable, effective and efficient. The present study concluded that a single application of SDF with its ease of applicability can effectively halt the progression of active carious lesions in 6-9 year old children.

Limitations

The present study focused on children only from peri urban locality the results of our study cannot be generalized as the sample size was not sufficient.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Seroprevalence of Herpes Simplex Virus in Females of Childbearing Age in Local Population of Rawalpindi

Muhammad Ali Rathore, Misbah Fayyaz, Eijaz Ghani, Faraz Ahmed, Hina Saeed, Khushbakht Alam

ABSTRACT

Objective: To determine the seroprevalence of Herpes simplex virus among females of childbearing age.

Study Design: Cross sectional study

Place and Duration of Study: Virology department, Armed Forces Institute of Pathology Rawalpindi, from 1st July 2022 to 31st December 2022.

Materials and Methods: A total of two hundred and sixty-seven (267) females of childbearing age (15-49 years) were included in this study. The blood samples were taken for detection of Herpes Simplex Virus (HSV) IgG by enzyme-linked immunosorbent assay of Vircell, Spain. SPSS version 25 was used to analyze the data.

Results: Out of total 267 samples, 213 (82%) were positive and 54 (18%) were negative for HSV IgG. The positivity for HSV IgG was most frequent in the age group-1 (20-29 years) with 111 (50%) positive cases, followed by 87 (32%) in age group-2 (30-39 years) and 15(5.6%) in age group-3 (40-49 years). People with low socioeconomic status had higher positivity of HSV IgG antibodies, while those with high socioeconomic status had a lower positivity of HSV IgG antibodies.

Conclusion: The study concluded that most females of childbearing age had previously been exposed to HSV, as evidenced by the presence of IgG antibodies. However, a significant number of women had not been exposed to the virus, putting them at risk of contracting HSV and potentially facing its complications during a future pregnancy.

Key Words: *HSV, Seroepidemiologic Studies, ELISA.*

Introduction

Herpes simplex virus (HSV) is spread through contact with lesions or mucous membranes. It migrates to nerve tissues where it remains dormant and latent. The human population is susceptible to two types of HSV (HSV-1 and HSV-2), both of which cause latent and chronic infections.[2] HSV-1 causes disease of oral cavity, whereas HSV-2 causes disease of genital tract.[3,4]

HSV-1 is usually transmitted during infancy and adolescence. Infection in persons with decrease immunity can result in severe disease and rarely disseminated infection.[5,6] Neonatal HSV infections can lead to permanent impairments or death. If a primary infection in mother develops in the second trimester of pregnancy, the chance of transmission to fetus are high.[7] Neonatal morbidity and mortality are caused by both primary HSV infection as well as reactivation of disease during pregnancy.[8]

Due to maternal HSV infections in pregnancy, neonatal infections can present as disseminated disease, skin, eyes and mouth (SEM) disease, and central nervous system (CNS) disease. HSV-2 infection is more prevalent in Sub-Saharan Africa than in the United States.[9] Recent research on HSV IgG seroprevalence has revealed that prevalence varies by geographic location. The highest seroprevalence of HSV was found in Africa and America, where as lowest prevalence was observed in Asia[10] According to estimates in 2012, there were 417 million HSV-2 infected people worldwide in the age range of 15 to 49 years. Of these, 267 million of them were women and most of them were from Africa.[11] The proportion of women in the reproductive age infected with HSV-2 varies between 30% and 80% in countries in the Sub-Saharan region countries.[12]

The majority of people become infected with HSV during their early years.[13] Adult population rates of

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HSV 1 antibodies range from 45% to 88%, depending on their gender, age, geography and socioeconomic status.[14] HSV-2 prevalence rises from 35% to 60% by 60 years, however, antibodies to the virus are seldom discovered prior to the age when sexual contact first begins. HSV-2 infection rates are comparatively lower in males than females.[15]

This study was planned to determine the seroprevalence of HSV by detecting HSV IgG antibodies in women of child bearing age in Rawalpindi. This will give us a better understanding of exposure as well as susceptibility of HSV in this population and the measures which include avoidance of oral or sexual contact with infected patients, these can be adopted to mitigate the effect of this disease during the future pregnancies.

Materials and Methods

A cross-sectional study was conducted at the department of Virology, Armed Forces Institute of Pathology, Rawalpindi from 1st July 2022 to 31st December 2022. Informed con sent was taken from all patients and ethical approval for this study was taken from Institutional Review Board (AFIP-IRB No 22/1356). A sample size of 267 was calculated by using WHO sample size calculator.

Clinical history of the patients including any contact with HSV infected person, fever and rash was collected according to predesigned proforma. Samples were collected using aseptic technique. About 5 ml of blood was drawn in a clot activator tube and ELISA was performed to detect IgG antibodies against the herpes simplex virus I and II.

In order to analyze the data, the Statistical Package for the Social Sciences (SPSS) version 25 was used. Standard deviation and the mean of quantitative variables including age as calculated. Frequencies and percentages of qualitative variables including gender, marital status, education and socioeconomic status was calculated.

Results

HSV positivity was highest in women with education status matric or below while lowest in women with a master degree or above. People with low socioeconomic status had higher positivity of HSV IgG antibodies, while those with high socioeconomic status had the low positivity of HSV IgG antibodies

Out of total 267 samples, 213 (82%) were positive for HSV IgG antibody, while 54 (18%) were negative. The positivity for HSV IgG was most distinct in the age group 1 (20-29 years) with 111 (50%), followed by age group-2(30-39 years) with 87(32%), and age group-3(40-49 years) with 15(5.6%)

Table I: HSV IgG Antibody in Different Age Groups

Age	Positive cases (%)	Negative cases (%)
<20 years	5(2.3%)	2(4.2%)
20-29 years	111(50.9%)	25(9.1%)
30-39 years	87(39.9%)	16(33.3%)
40-49 years	15(6.9%)	5(10.4%)

HVS - Herpes Simplex Virus

Table II: Prevalence of HSV According to Different Parameters

Parameters	HSV Positive	HSV Negative
History of past HSV Infection		
Yes	11(5%)	0
No	202(95%)	48(100%)
Education		
Matric or below	74(33%)	20(41%)
Intermediate	55(25%)	14(29%)
Bachelor's degree	56(25.7%)	12(25%)
Master's degree or above	33(15%)	2(4.2%)
Socioeconomi status (Monthly income in rupees)		
<25000	38(17%)	8(16%)
25000-60000	166(76)	37(77%)
60000-150000	13(6%)	3(6.3%)
>150000	1(0.5%)	0
Joint family system		
Yes	196(89%)	47(97%)
No	22(10%)	1(2.1%)

HVS - Herpes Simplex Virus

Discussion

Herpes Simplex Virus (HSV) infection is a global health concern with far-reaching implications, particularly in reproductive health. In Pakistan, where infectious diseases are of significant concern, understanding the seroprevalence of HSV is crucial for designing effective healthcare strategies. Over the past 20 years, the frequency of HSV had considerably increased in both developed and developing countries.[16]

In this study, a total of 267 samples underwent ELISA analysis to detect HSV IgG antibodies. Positive results for HSV IgG were found in 213 cases (82%), while 54 cases (18%) tested negative. The research revealed a higher prevalence of HSV IgG antibodies among individuals with lower socioeconomic status, whereas those with higher socioeconomic status showed a lower prevalence. This difference is

attributed to the poorer nutrition and less hygienic conditions experienced by individuals of lower socioeconomic status.

A study carried out by Anthony *et al.,* in Australia in which a total of 270 samples were tested for detection of HSV-1 and HSV-2 antibodies. The seroprevalence of HSV-1 and HSV-2 was 97.8% and 58.5%, respectively.[17] These results found higher prevalence of HSV in comparison with our study. This difference in HSV seroprevalence could be due to difference in lifestyle, study population, travel, migration and demographic causes.

In another study conducted by Ahmed *et al.,* in Sudan, higher seroprevalence of HSV was reported, reaching a positivity rate of 97.8%.[18] These findings are contrary to the outcomes of our study, in which lower seroprevalence of HSV was found. The disparity between these two studies in terms of seroprevalence could potentially be attributed to regional differences.

The study carried out by Monica *et al*., in United States, reported a seroprevalence of 59.3% for HSV-1 and 21.1% for HSV-2 among the studied population.[19] Seroprevalence of HSV in this study was lower in comparison with the results of our study, possible explanation for this disparity in seroprevalence could be due to geographical and population density variations which could have influenced the prevalence of infections.

Similarly, in a study conducted by Drisu *et al.,* it was found that the seroprevalence of HSV infection among young adults was 74.7%. This study also found increased seroprevalence of HSV infection among young adults which depicts the significance of this age group as a susceptible population.[20] This study had lower seroprevalence as compared to our study

A study conducted by Mahmood *et al.,* in KPK Pakistan, found that seroprevalence of HSV as 13 %.[21] These results showed much lower seroprevalence in comparison with our study. Moreover, accuracy and sensitivity of the diagnostic methods used to detect HSV antibodies can influence the reported seroprevalence. Differences in the quality and type of diagnostic tests employed could lead to differing outcomes.

Limitations

The study was conducted in a single center, so the results may not be generalizable to the entire population of females of childbearing age in Pakistan. The sample size was relatively small, which may have limited the ability to detect statistically significant differences between subgroups.

Conclusion

The study concluded that most females of childbearing age had previously been exposed to HSV, as evidenced by the presence of IgG antibodies. However, a significant number of women had not been exposed to the virus, putting them at risk of contracting HSV and potentially facing its complications during a future pregnancy.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Evaluation of Copper and Zinc Disturbances in the Patients of Alopecia

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ABSTRACT

Objective: To evaluate serum copper and zinc levels in patients with different types of alopecia compared to healthy controls, and to assess the potential relationship between trace element deficiencies and specific alopecia types.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, from 1st June 2021 to 30th April 2023.

Materials and Methods: A total of 250 patients categorized into five groups; Group-1 male pattern hair loss, Group-2 female pattern hair loss, Group-3 alopecia areata, Group-4 telogen effluvium, and Group 5 healthy individuals were enrolled. Serum zinc and copper levels were tested by using atomic absorption spectrophotometer and results were compared with the help of SPSS by applying one-way ANOVA and post hoc test. The *p* value ≤ 0.05 was considered statistically significant.

Results: In Group-3, the mean serum copper was 15.14±3.26 followed by Group-4 (14.99±2.23), Group-2 (14.11±3.83), Group-1 (9.92±2.23), and the control group was 14.97±3.6. As in Group-2, the mean serum zinc was 12.93±2.97 followed by Group-4 (11.13±3.50), Group-3 (10.23±2.91), and Group-1 (8.70±2.08), and the control group was 14.01±1.82. Serum zinc had a statistically significant difference (*p* value ≤0.05) between all groups of alopecia. Whereas statistically significant low copper levels were observed only in male pattern hair loss with *p* value ≤0.001.

Conclusion: Low zinc levels are related to all types of alopecia. Whereas low copper levels are observed only in male pattern alopecia. Hence zinc supplementation can be used to get some beneficial effects in all types of alopecia. Whereas patients with male pattern alopecia should also be evaluated for serum copper levels and supplementation is required only if they have low copper levels.

Key Words: *Alopecia, Serum Copper, Serum Zinc, Trace Element.*

Introduction

Alopecia is a disorder marked by hair loss from the body areas where hair is normally found especially head. The distressing illness lowers sufferers' self-esteem, impacting them mentally and socially. The disorders can be caused by a variety of factors, including stress, inheritance, hormones, diet, certain illnesses, and some drugs such as those used to treat cancer.[1] Nutrition and food can be used to treat hair loss, and this is an active field of research.[2] The FDA has approved just two serendipitous medications (minoxidil and finasteride) for the treatment of alopecia.[3]

There are several forms of alopecia, among them the most frequent are androgenic alopecia, Telogen effluvium, and alopecia areata.[4] Androgenic alopecia is a prevalent form of baldness that can affect both men and women. Males are mainly impacted by it as opposed to females, primarily due to the higher production of testosterone, which is a male sex hormone responsible for triggering the condition.[5]

Alopecia areata is a common localized non-scarring, inflammatory, autoimmune hair loss disease that occurs on any skin-bearing hair. Autoimmune, genetic, and environmental factors are considered to be the possible etiologies of Alopecia areata. Alopecia areata is a disorder characterized by a focally, organ-specific autoimmune disorder.[6] The

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prevalence of Alopecia areata in female individuals is 0.252%–0.271% and in male individuals is 0.145%–0.171%.[7] Telogen effluvium is a condition where hair loss occurs due to hair follicles being pushed prematurely into the dormant telogen stage, without causing any permanent scarring.The disease is widespread among the elderly, persons who are physically and emotionally disturbed, and those who have thyroid or additional hormonal imbalances.[8]

Zinc (Zn) and copper (Cu) which are found in trace quantities in the human body are considered to play a significant role in maintaining the metalloenzyme processes of the body. Cu plays a significant role in the body by assisting in the production of melanin and facilitating collagen cross-linking through its involvement in tyrosinase and lysyl oxidase processes. Zn plays a part in various cellular functions and metabolic pathways. Zn has a very significant role as a trace metal in the human body as it controls many functional activities in the hair follicles. It also speeds up hair follicle regrowth and is a strong inhibitor of hair follicle regression. Some patients having alopecia show significant deficiency of Zn and other trace elements.[9] These trace metals are thought to be engaged in many forms of hair loss. However, this statement that Zn and Cu are the reasons for pathogenesis in hair loss in patients of alopecia is still unresolved and requires further consideration.

To diagnose at the early onset, it is important to conduct routine examinations such as an anemia panel, complete hemogram, erythrocyte sedimentation rate, serum calcium, thyroid function tests, serum proteins, etc to determine proper precautionary measures.[10] In the current study, we evaluate the Zn and Cu serum levels in patients having alopecia. Therefore, assessment of serum Zn levels in patients with alopecia appears to be helpful as a marker of severity, disease duration, and resistance to therapies.[11]

Materials and Methods

This cross-sectional study was conducted at the Department of Chemical Pathology & Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi after taking approval from the Institutional Review Board (IRB) of AFIP vide Ref number FC-CHP-29/READ-IRB/21/657. After a thorough literature search, we calculated a sample size of 8 via the WHO calculator, keeping the margin of error at 5%, a confidence level at 95%, and an alopecia prevalence at 0.252% (0.271% in females and 0.145% - 0.171% in males).[6] Sampling was done using a purposive sampling technique at the Dermatology Department, CMH, Rawalpindi. A maximum number of available participants (250) during the study period were recruited.

Participants from 19 – 60 years, without considering any economical status, were enrolled in this study. To find the serum Zn and Cu concentrations for different types of hair loss, the participants were divided into 5 groups comprised of patients with male pattern hair loss (MPHL) as Group 1, female pattern hair loss (FPHL) as Group 2, alopecia areata (AA) as Group 3, telogen effluvium (TE) as Group 4, and healthy individuals (control group) as Group 5. Case and control groups were matched for age, gender, Zn level, and Cu level. Informed consent was taken about the study and all the patients participated voluntarily. The normal reference interval of Zn is 12 to 18 µmol/L, and Cu is 10-23 µmol/L in our hospital.

Venous blood samples (5mL) were collected from alopecia patients and healthy controls in yellow top gel tubes without any anticoagulant. This serum sample was used to measure trace elements. For Zn analysis, 0.5 mL of serum was mixed with 4.5 mL of deionized water in a test tube. Cu analysis involved adding 0.5 mL of serum to a test tube with concentrated nitric acid (HNO_3), heating it in a thermoreactor at 150°C for 15 minutes, cooling it, and then diluting it with 4.5mL of deionized water to make the total volume of 5mL, and at last injecting the mixture in a new plain tube through a filter. The filtered samples are ready to run on a flame atomizer (atomic absorption spectrophotometer). They are then analyzed using a flame atomic absorption spectrophotometer (Agilent Technologies 200 series AA). Quality control and calibration standards were prepared similarly.

Healthy individuals of 19-60 years with a history of hair loss and normal people without any underlying disease as controls were included in the evaluation study. Individuals taking supplements containing Zn an Cu, individuals already under treatment for hair loss with systemic illnesses diabetes mellitus (DM), trace metal disorders, chronic liver disease (CLD), hypertension (HTN), chronic kidney disease (CKD),

and taking any medication including chelating agents were excluded from the study design.

Statistical Package for Social Sciences (SPSS) version 25.0 was used for data analysis.Mean and standard deviation (SD) were calculated for continuous variables and frequency and percentage were calculated for categorical variables. Shapiro-Wilk test was performed to check the distribution of data. One-way ANOVA and posthoc analysis were for comparing serum Zn and Cu level in hair loss patients (male and female), telogen effluvium patients, alopecia areata patients, And The Control Group. A *P* Value ⩽0.05 Was Considered Significant.

Results

A total of 250 patients were included in the study, out of the total, 125 (50.0%) patients were males and 125 (50.0%) were females. The mean age of participants was 31.63±7.25 years from 19 to 60 years. The mean ages of the patient's group and control group were 33.72±7.40 and 31.13±6.23 years, respectively. The detail of the demographic variables of all groups is shown in Table-I.

Normal reference interval of serum Zn is 12 to 18 µmol/L. Low mean serum Zn levels were observed in group 4 (9.88±2.47 µmol/L), group 3 (10.23±2.91 µmol/L) and group 1 (8.70±2.08 µmol/L). Mean serum Zn levels in group 2 were at the borderline (12.38±2.97 µmol/L) whereas mean serum Zn levels in control group were within normal reference interval (14.01±1.82 µmol/L) . There was a significant difference in mean serum Zn levels among all the groups (*p* value < 0.05) shown in Table II. Post hoc analysis showed significant difference in mean serum Cu levels between group 1 and control group (*p* value < 0.05) where as there was no significant difference in mean serum Cu levels between controls and other groups (*p* value > 0.05). However a significant difference was found in mean serum Zn levels between control group and all four groups of alopecia (*p* value < 0.05) shown in Table II..

Table I: Demographic Variables of the Patients (n=250)

Variables		MPHL* (n=50)	FPHL* (n=50)	AA* (n=50)	TE* (n=50)	Control Group (n=50)
Gender	Male	50 (100.0%)	0 (0%)	25 (50.0%)	25 (50.0%)	25 (50.0%)
	Female	0 (0%)	50 (100.0%)	25 (50.0%)	25 (50.0%)	25 (50.0%)
Age (Mean±SD)		31.64±7.44	33.34±8.26	30.90±6.70	32.12±6.58	31.12±6.08

*Male Pattern Hair Loss: MPHL, *Female Pattern Hair Loss:FPHL, *Alopecia Areata:AA, *Telogen Effluvium:TE.

Table II: Comparison of Mean Serum Cu and Zn levels within Groups Based on Post Hoc Analysis

Variables	Groups	Mean±SD	p-Value
Copper µmol/L	Male Pattern Hair loss	8.74±2.97	0.001*
	Control Group	15.52±4.05	
	Female Pattern Hair loss	14.11±3.83	0.410
	Control Group	15.52±4.05	
	Alopecia Areata	15.14±3.62	0.990
	Control Group	15.52±4.05	
	Telogen Effluvium	13.45±5.29	0.078
	Control Group	15.52±4.05	
Zinc µmol/L	Male Pattern Hair loss	8.70±2.08	< 0.001*
	Control Group	14.01±1.82	
	Female Pattern Hair loss	12.38±2.97	0.011*
	Control Group	14.01±1.82	
	Alopecia Areata	10.23±2.91	< 0.001*
	Control Group	14.01±1.82	
	Telogen Effluvium	9.88±2.47	< 0.001*
	Control Group	14.01±1.82	

*The *p* value 0.05 was considered statistically siginificant

Discussion

Alopecia areata (AA) is an autoimmune disorder that specifically affects hair follicles in the anagen phase. This condition follows an unpredictable pattern of chronic relapses which result in transient non-scarring hair loss.[12] Trace elements such as Zn and Cu play a crucial role as cofactors in multiple enzymes and exhibit significant functional activities within hair follicles. They play a great role in the healthy growth and development of hair.[13] However, many studies suggest that the imbalance of these elements is the main cause of AA.[14]

In the current study, 250 patients were recruited; 125 (50.0%) patients were males and 125 (50.0%) were females with a mean age of 31.63±7.25. The current study states that the serum Zn had a statistically prominent difference in all groups while only the serum Cu in MPHL had a statistically significantly different value from the control group. Serum Cu in the rest of the groups was almost similar to that of the control group.

In comparison to the present study Kil MS *et al.,*[15] showed that hair loss patients have a mean Zn value of 84.33±22.88, which was significantly lower than their control group (97.94±21.05 µg/dl) whereas the mean value of Cu was 96.44±22.62, which wasn't significantly different (*p*=0.975).

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In another study conducted by Farah HS *et al.,*[2] Zn concentration in patients was 110.3 ± 17.8 and in the control group was 109.5 ± 15.3 in the age group of 17-32. In contrast to the present study, no significant changes in the mean serum Zn value of the case and control group were observed as the population belonged to young age and was in good health. The defects, which impair Zn absorption rates were seen in older ages.

In a study by Yavuz *et al.,*[16] 40 subjects with chronic telogen effluvium, and 30 healthy females as controls were recruited. In contrast to the present study, no significant differences in Zn serum levels were noticed in patients than in the controls. However, the patients showed a significant increase in Manganese (Mn), Cobalt (Co), Palladium (Pb), Iron (Fe), Magnesium (Mg), Cadmium (Cd), and Cu (p <0.05) levels. This study is a complete antipode to the present study. Also contrary to the present study, this study only recruited women in their control group.

Gowda D *et a.l,*[17] indicated Zn deficiency in 11.76% of MPHL patients and 8.3% of FPHL patients which was almost similar to the present study. This study also stated that Cu deficiency was seen in 29.41% and 31.48% of MPHL and TE patients, respectively, however, in the present study a significant copper deficiency was only seen in MPHL patients. Cheung EJ *et al.,*[18] showed that 115 subjects were diagnosed with TE (acute and chronic), and had similar results of 9.6% Zn deficiency to the present study. Another similar study conducted by Chen S *et al.,*[19] showed a 21.4% reduction in Zn content and a 42.1% reduction in Cu levels and observed that 11.76% of MPHL patients had Zn deficiency and 29.41% of MPHL patients had copper deficiency which was almost similar to the present study.

According to a study by Bhat YG *et al.,*[20] the majority of the patients were in the third decade of life like this study. All patients with prolonged duration showed decreased Zn levels. Whereas the difference in serum Cu levels was insignificant. This study showed an increased incidence of male pattern hair loss than female pattern hair loss (34:16), comparable to the present study.

Limitations

We didnot consider severe alopecia areata cases like total and universalis because there were no hair samples. Further multicenter studies with more patient series are needed to deepen our understanding of the effects of trace elements.

Conclusion

The results showed that low levels of Zn are related to all four types of alopecia. Whereas low Cu levels are observed only in male pattern alopecia. Hence Zn supplementation can be used to get some beneficial effects in all types of alopecia. Whereas patients with male pattern alopecia should also be evaluated for serum Cu levels and supplementation is required only if they have low Cu levels.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Maxillary Sinus and Nasal Cavity Anatomical Variants Evaluation in Adult Karachi Population, A CBCT Based Analysis

Lubna Faisal, Rizwan Ajmal, Zia ul Islam, Tabina Urooj, Saima Athar, Fatima Rehman

ABSTRACT

Objective: To determine the common anatomical variants of maxillary sinus and nasal cavity on cone beam computed tomography.

Study Design: Retrospective cross-sectional study.

Place and Duration of Study: This study was carried out at Anatomy and Radiology Department of Liaquat National Hospital & Medical College, Karachi, from 11th Nov 2022 till 22nd Nov 2023.

Materials and Methods: Cone-Beam Computed Tomography (CBCT) scans of 353 adults were evaluated retrospectively, who had scan for sinusitis for anatomical variations of maxillary sinus and nasal anatomy were included in study. Data analysis was done by SPSS v27.

Results: There were 52% male and 48% female patients, with the majority (43.5%) being in the 26–35 age range. During the course of our investigation, we discovered that 27.8% of patients had a right deviated nasal septum with chonca bullosa, 25.5% had a left deviated nasal septum, and 19.9% had a nasal septal spine. In contrast, 56.3% of patients had hyper pneumatize maxillary sinuses, and 29.3% had hypoplasia of the maxillary sinuses. Anatomical variations in the nasal cavity were significantly associated with age (p = 0.001) and gender (p = 0.002).

Conclusion: Based on our findings, although there was no significant association detected between the anatomical variations in the maxillary sinus and age (p = 0.641). The anatomical variation from the study's results of the nasal cavity is a deviated nasal septum on the right side, followed by a deviated nasal septum on the left, and that the most common variation in the maxillary sinus is hyper pneumatize maxillary sinus, which was followed by hypoplasia.

Key Words: *Anatomical Variation, Cone-Beam Computed Tomography, Maxillary Sinus.*

Introduction

Paranasal sinuses are air filled chambers separated from orbit and cranial fossae by very thin plate of bone.[1] Maxillary sinuses are bilateral pyramidal shaped structures lateral to nasal cavity. Because the nasal cavity and maxillary sinus have a role in the drainage of the sinonasal region and might cause sinusitis, anatomic variations of these structures are highly significant to be considered.[2] In addition for planning any clinical procedures especially endoscopic surgeries in which accurate evaluation is required for the success and safety of patient. Detailed anatomy of nasal cavity and maxillary sinus is required by surgeons otherwise incomplete knowledge can lead to major complications e.g. visual problems, meningitis, oral cavity pathologies and CSF leakage.[3]

Anatomical variations of nasal cavity and maxillary sinus should be carefully evaluated before performing any surgical procedure. They both are important for two reasons (1) Variants of nasal cavity and maxillary sinus have strong correlation with the nasal drainage and proper ventilation of maxillary sinus. (2) These two sites can be visualized in 3 dimensions by using Cone Beam computed tomography (CBCT) resulting in understanding their anatomical variations which will produce significant impact on surgical procedures.[4] Most common disorder related to nasal septum is nasal septum deviation. Deviated nasal septum has been explained as due to developmental cause (mostly C-shaped deformity or S-shaped nasal septum with

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inclination more related to anterior nasal septum) or traumatic (mostly no proper shape, septal angulation or dislocated in origin). Deviated nasal septum can result in displacement of middle turbinate, limiting the middle meatus, developing difficulty in surgical approach and resulting impedance of normal mucus flow as a consequence infection resulted.[5] Deviated nasal septum can cause infection of all four paranasal sinuses due to poor mucociliary clearance, inappropriate mucus drainage, and airway narrowing.[6]

CBCT is the most progressing modality initially originated in the early decades of 1980's with high standard images. It captures anatomic structures providing the 3-dimensional information with slice thickness of less than 0.4mm regarding the morphology, anatomic variations & pathology for both maxillary sinus & nasal cavity.[7] Over the last few decades CBCT is preferred to traditional CT images because it yields high contrast bone scans.[8] Moreover CBCT provides sufficient knowledge to identify diagnostic problems related to this region as compared to Multidetector computed tomography (MDCT) images due to its flat designed panel and due to its few artifacts and it is cost effective.[9,10]

Literature contains large number of studies detailing paranasal sinuses anatomical variants though not specifically designed to evaluate nasal cavity and maxillary sinus anatomical variations in Karachi population on CBCT. Prevalence of nasal cavity and maxillary sinus were concha bullosa 35.3%, Haller cells 25%, and modifications of uncinated process 5% according to Raluca's study performed on 130 patients in 2016 on CBCT. The present study was planned to determine the common anatomical variants of maxillary sinus and nasal cavity on CBCT.

Materials and Methods

This retrospective cross-sectional study was performed at Liaquat National Hospital and Medical College in Department of Anatomy in collaboration with the Department of Radiology. The period of study was one year after obtaining Ethical Review Committee approval (Ethical ref no: #0848-2022 LNH-ERC). Total 353 patient's medical records and CBCT images were reviewed during the period of 11th Nov 2022 till 22nd Nov 2023. CBCT images (16 slice Toshiba) of both male & female patients with clinical suspicion of sinusitis (all symptomatic patients were included by non-probability convenience sampling technique and were categorized into three age groups 20-25 years, in between 26-35 years and ≥ 35 years of age.[1] Exclusion criteria for all patients included the following (1) Previous history of any trauma or surgery (2) Benign or malignant tumors, (3) Clefts that can cause change in sinonasal mucosa resulting in anatomical change of maxillary sinus and nasal cavity (4) Patients under 19 years of age due to not proper and complete development of maxillary sinus. CBCT scan of all patients were captured with (CBCT Machine: Lightning Aquilion Canon model no C16S). Scanning was done in supine position, in cranio-caudal direction for all patients. Maxillary sinus anatomical variants, such as accessory maxillary sinus, maxillary septa & nasal cavity anatomical variants including deviated septum, any septal spur, were interpreted by an anatomist. At the same time radiological findings, any trauma or pathologic lesions of maxillary sinus and nasal cavity, were evaluated through axial images along with coronal reconstruction by radiologist. All images were reviewed retrospectively on Syngobia workstation and all findings were recorded on predesigned proforma for details of patients including age, gender, maxillary and nasal sinus anatomical variants. Data was entered and analyzed on SPSS version 27. Association of anatomical variations (nasal cavity, maxillary sinus) with age and gender was checked by chi-square test. The *p* value of < 0.05 was considered statistically significant.

Results

CBCT images for anatomical variability of nasal cavity revealed in n = 72 females and n = 114 males respectively. Mean age of patients was 30.40±8.99 years with the majority (43.5%) being in the 26–35 age range. During the course of investigation, we discovered that 27.8% of patients had a right deviated nasal septum with chonca bullosa, 25.5% had a left deviated nasal septum, and 19.9% had a nasal septal spine. In contrast, 56.3% of patients had hyper pneumatized maxillary sinuses, and 29.3% had hypoplasia of the maxillary sinuses as presented in Table I.

Table IIA, shows, right deviated nasal septum was found among 51(39.2%) females and 63(28.3%) males. Among males left deviated nasal septum was found in 43 (19.3%) followed by nasal septal spine in

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4 (1.8%), and right and left deviated nasal septum with concha bullosa both having same number of 2(0.9%). No chonca bullosa revealed on CBCT of males. Table IIA, shows that, in females second most frequently occurring nasal septal defect was left deviated nasal septum among 10 (7.7%) patients, followed by concha bullosa in 4 (3.1 %), left deviated nasal septum with concha bullosa in 3 (2.3%), right deviated nasal septum with concha bullosa in 2 (1.5%) and nasal septal spine in 2 (1.5%) patients.

Right deviated nasal septum was more common in 26-35 years (n = 54, 51.4%), followed by ≥35 years (n = 34, 26.6%) and 20-25 years (n = 26, 21.7%). Left deviated nasal septum was more common in ≥35 years age groups (n = 27, 21.1%) followed by 20-25 years (n = 23, 19.2%) and 26- 35 years (n = 3, 2.9%) as presented in Table II B.

Nasal septal spine found among patients in age group 20-25 years was n =2 (1.7%), in 26-35 years was n =2 (1.9%) and in ≥35 years was n =2 (1.6%). Right deviated nasal septum with concha bullosa was found only in 4 patients in age group ≥35 years. Concha Bullosa was observed in 4 (3.8%) patients in the age group 26-35 years. A total number of 3 (2.5%) and 2 (1.6%) patients were noticed in the age group 20-25 years and ≥35 years respectively. (Table II B). Results were summarized in table III A and table III B for anatomical variations of maxillary sinus association with age and gender respectively.

Anatomical variations in the nasal cavity were significantly associated with age (p = 0.001) and gender (p = 0.002), although there was no significant association detected between the anatomical variations in the maxillary sinus and age (p = 0.641). Detailed results of association by Chi square test is presented Table IIA, Table II B, Table III A and Table IIIB

Discussion

In the present study it was found that deviated nasal septum (right side) is the most common anatomical variation followed by deviated nasal septum (left side), supported by Shahidi S *et al.,*[12,13] and Al-Ani RM *et al.,*[14] which had similar findings. A similar conclusion was reported by another study where nasal septal deviation is reported to be a common anatomical variation for nasal region.[15]

Concha bullosa associated with right or left deviated nasal septum is explained as the pneumatization or

Table No I: Demographic Characteristics, Anatomical Variation of Nasal Cavity & Maxillary Sinus among Adult Urban Karachi Population (n= 353)

	Variable	Frequency, n (Percentage, %)
Gender	Male	223 (63 %)
	Female	130 (36%)
Age years	20-25 years	120 (34.09%)
	26- 35 years	105 (29.7%)
	≥35 years	128 (36.2%)
Anatomical variation of nasal cavity	Deviated nasal septum (Right side)	114 (32.3%)
	Deviated nasal septum (Left side)	53 (15.0%)
	Nasal septal spine	6 (1.7%)
	Right deviated nasal septum with concha bullosa	4 (1.1%)
	Left deviated nasal septum with concha bullosa	5 (1.4%)
	Concha bullosa	4 (1.1%)
Anatomical Variation of Maxillary Sinus	Hyperpneumatize maxillary sinus	94 (56.3%)
	Maxillary Sinus Hypoplasia	49 (29.3%)
	Accessory maxillary sinus	18 (10.8%)
	Maxillary sinus septa	6 (3.6%)

Table II (A): Frequency Distribution of Anatomical Variations of Nasal Cavity According to Gender, (n=186).

Gender	Anatomical variations of Nasal cavity Frequency, n Percentage, %					
	Deviated nasal septum. (Right side)	Deviated nasal septum (Left side)	Nasal septal spine	Right deviated nasal septum with concha bullosa	Left deviated nasal septum with concha bullosa	Concha Bullosa
Male (n=114)	63 28.3%	43 19.3%	4 1.8%	2 0.9%	2 0.9%	0 0.0%
Female (n=72)	51 39.2%	10 7.7%	2 1.5%	2 1.5%	3 2.3%	4 3.1%
Total (n=186)	114 32.3%	53 15.0%	6 1.7%	4 1.1%	5 1.4%	4 1.1%

Table II (B): Association Between Anatomical Variations of Nasal Cavity in Relation to Age, (n=186).

Age Group	Anatomical variations of Nasal cavity Frequency Percentage						*p* value
	Deviated nasal septum (Right side)	Deviated nasal septum (Left side)	Nasal septal spine	Right deviated nasal septum with concha bullosa	Left deviated nasal septum with concha bullosa	Concha Bullosa	
20-25 years (n=54)	26 21.7%	23 19.2%	2 1.7%	0 0.0%	3 2.5%	0 0.0%	0.001*
26-35 years (n=63)	54 51.4%	3 2.9%	2 1.9%	0 0.0%	0 0.0%	4 3.8%	
≥35 years (n=69)	34 26.6%	27 11.1%	2 1.6%	4 3.1%	2 1.6%	0 0.0%	

*The *p* value was considered significant at 0.05 levels.

Table III (A): Frequency Distribution of Anatomical Variations of Maxillary Sinus According to Gender (n=167)

Gender	Anatomical variations of Maxillary sinus Frequency Percentage			
	Hyperpneumatize maxillary sinus	Maxillary Sinus Hypoplasia	Accessory maxillary sinus	Maxillary sinus septa
Male (n=109)	61 56.0%	35 32.1%	9 8.3%	4 3.7%
Female (n=58)	33 56.9%	14 24.1%	9 15.5%	2 3.4%
Total (n=167)	94 56.3%	49 29.3%	18 10.8%	6 3.6%

Table No III (B): Association Between Anatomical Variations of Maxillary Sinus in Relation to Age, (n=167).

Age Group	Anatomical variation of Maxillary sinus Frequency Percentage				*p* value
	Hyperpneumatize maxillary sinus	Maxillary Sinus Hypoplasia	Accessory maxillary sinus	Maxillary sinus septa	
20-25 years (n=66)	37 56.1%	19 28.8%	8 12.1%	2 3.0%	0.641
26-35 years (n=42)	23 54.8%	16 38.1%	2 4.8%	1 2.4%	
≥35 years (n=59)	34 57.6%	14 23.7%	8 13.6%	3 5.1%	

*The *p* value was considered significant at 0.05 levels.

presence of air cells in middle turbinate. The findings of this research study did not coincide with the results of previous studies by Katibe *et al.,* [16] in which it was reported left deviated nasal septum with concha bullosa is more common than right deviated nasal septum with chonca bullosa. According to our findings concha bullosa with right deviated nasal septum (n=2) was found in males as well as in females. Concha bullosa with left deviated nasal septum in males (n=2) and in females (n=3). Concha bullosa alone was found only in females (n=4).

Anatomical variants of nasal cavity and maxillary sinus found in this research are significant because they may be source of complication for sinus surgical procedures or can develop pathological consequences at times. CBCT can provide accurate information regarding maxillofacial anatomy. Most frequently involving sinus according to location is maxillary sinus. Similar results were obtained by Teuku Husni *et al.,* [17]. In our study CBCT scans of 353 patients, maxillary sinus analysis for anatomical variations revealed hyper pneumatized maxillary sinus as the most common in order of frequency (n= 61 males) and (n=33) in females followed by maxillary sinus hypoplasia (MSH), accessory maxillary sinus ostium, and maxillary sinus septa. These statements are not in contrast with Maria A. *et al.,* [18] which revealed maxillary sinus hypoplasia as the commonest anatomical variation. MSH can develop dental problems due to elevation of canine fossa. It was found dehiscent of bone over roots of maxillary tooth both molars and premolars along with mucosal lining between the maxillary antrum and roots. These can result in the formation of oroantral fistula following tooth extraction and it can also predispose to recurrent sinusitis as a consequence of dental infection. Accessory ostium of maxillary sinus is defined as additional aperture rather than single primary ostium and is generally located in nasal fontanelle or hiatus semilunaris. In our study total 9 scans both in male and in female had maxillary sinus ostium which is not in line with the study of Rashi's *et al.,* [19] which found accessory maxillary ostium as the common anatomical variation of maxillary sinus.

Deep understanding of anatomy, anatomical features and anatomic variations of the sino-nasal region is the essence and requirement for constructive and successful functional endoscopic sinus surgery (FESS).[20] Advanced imaging modalities as well as experienced skillful person can discuss in detail the pathology and anatomical variations of nasal cavity and maxillary sinus.[21] Comparing our study results with the study done in Nigerian population, they found that most common anatomical variation was pneumatization of middle

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nasal turbinates (32.3%) followed by agger nasi cells (23.64%), haller's cell (20.9%) and septal deviation (20.16%). In our study, the most common anatomical variation according to three different age groups was deviated nasal septum (right side) (n=26), followed by deviated nasal septum of the left side (n=23), left deviated nasal septum with chonca bullosa (n=3), and nasal septal spine (n=2).[22]

In a study done by Adem Bora on adults and pediatric age groups they found that septal deviation (79.9%), concha bullosa (40.9%) and ethomoid bulla (21.0%) were the most frequently detected variations. It was also observed in same study that nasal septal deviation was more frequently observed in males than in females, which is in line with our study.[23]

The study sample was divided into three groups 20-25, 26-35 years, and ≥ 35years for evaluation of maxillary sinus anatomical variations and their frequencies were evaluated. Hyper pneumatized maxillary sinus was the most regularly experienced maxillary sinus variation in the age group 20- 25 n=37 (56.1%), 26-35 years n= 23 (54.8%) and ≥ 35years n=34 (57.6%) followed by maxillary sinus hypoplasia n= 19 (28.8%) in the age group 20-25 and n=16 (38.1%) in the age group 26-35 years ,n= 14 (23.7%) in the age group followed ≥ 35years by accessory maxillary sinus n= 8 (12.1%) in 20-25 and n=2 (4.8%) in the age group 26-35 years, followed by maxillary sinus septa n=2 (3.0 %) in the age group 20-25, and n=1 (2.4%) in the age group 26-35 years.

A highly significant association was found between gender and anatomical variations of nasal cavity *p* value (0.002) as shown in Table II A. We can conclude that anatomical variations of nasal cavity are more common in females than males, whereas frequency of anatomical variations of maxillary sinus same in both genders according to this study. A significant association was found between patient's age and anatomical variations of nasal cavity *p* value (0.001) as shown in Table II B. However, a significant association was noticed between gender plus age and anatomical variations of maxillary sinus as shown in Table III A & III B.

Conclusion

In the light of results found in our study it can be concluded that deviated nasal septum (right side) is the most common anatomical variation of nasal cavity followed by deviated nasal septum (left side) and in maxillary sinus hyper pneumatize maxillary sinus is the most common experienced variant found in our research study followed by maxillary sinus hypoplasia. CBCT should be done before any sinus surgical intervention.

Limitations

It was a single institution study and mainly urban population was included. Since it was a non-contrast study, it was not beneficial for the diagnosis/ detection of tumors. Contrast enhanced CBCT full study is needed in these situations.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

CASE REPORT

Unveiling a Diagnostic Odyssey: A Case Report on Delayed Diagnosis of Creutzfeldt Jakob Disease

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ABSTRACT

Creutzfeldt Jakob Disease (CJD) is a rare prion infection causing rapid, progressive, invariably fatal neurodegenerative disorder. It is reported in 1 in a million people per year worldwide[1] and only 12 cases have been reported over 21 years between 1994 to 2015 in Pakistan as per Agha Khan Hospital Karachi records.[2] We are reporting the clinical course of such a patient with delayed diagnosis and rapidly worsening symptoms.

Key Words: *CJD, Creutzfeldt Jakob Disease, Delayed Diagnosis, Polyspike Discharges, Prion Infection.*

Introduction

CJD is characterized by accumulation of abnormal, highly stable prion protein isoform aggregates in the brain tissue, causing deranged intracellular protein folding, ubiquitination and trafficking, resulting in astrocyte swelling and degradation leading to rapidly progressive neurodegeneration and inevitable fatal outcomes. Based on mode of transmission CJD is classified as being sporadic or genetic. Its initial presentation includes nonspecific symptoms like personality changes, vertigo, fatigue, headache and sleep disorders, ultimately leading to rapid progressing worsening memory, visual, speech, behavioral, movement and coordination abnormalities in later stages. CJD patients (90%) often die within a six month to one year of diagnosis mostly due to complications.[3]

Case

A 30-year-old previously healthy female, presented in emergency with 3-days history of fever, hallucinations and altered behavior. On initial evaluation, she had no meningeal signs and brain MRI, baseline lab investigations and lumber puncture yielded normal results. However, the patient kept on getting worse clinically. Upon re-evaluation the patient was found to have similar symptoms from past 3-4 months and was being taken as a case of supernatural influence. Subsequent hospitalizations revealed progressive neurological deterioration manifesting as right sided weakness, aphasia, decreased oral intake and altered sensorium. After thorough investigations, ruling out common diseases and receiving medical treatment on multiple lines including meningoencephalitis, Guillain Barre Syndrome, other autoimmune, toxic, psychiatric and metabolic disorders, the patient's condition kept on getting worse, necessitating ICU admission and ventilator support. However, as the disease progressed, the patient developed myoclonic jerks, non-conclusive status epilepticus and septic shock. Multiple complications including hypokalemia, thrombocytopenia, anemia and hypoalbuminemia also ensued.

Throughout her hospital admission, the patient underwent multiple investigations and aggressive treatment strategies including multiple antibiotics, immunosuppressants and immunomodulators, but she remained in a vegetative state without any specific provisional diagnosis.

Table I: Routine Examination of CSF

CSF Routine Examination	Result
Proteins	157 (Normal: 200-450 mg/L)
Globulins	Not increased
Glucose	9.7 (Normal: 2.5-4.5 mmol/L)
Leishmans stain	Occasional lymphocytes seen
Gram Stain	Organisms resembling cocci seen
ZN stain	No acid fast bacilli seen
Cytospin	No abnormal cells seen

CSF: Cerebro Spinal Fluid

In early phases the conventional MRI usually appears normal making it impossible to reach a provisional diagnosis based on a one single investigation. But

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later in the clinical course of disease her MRI showed rapidly progressive brain atrophy and symmetric gyriform restricted diffusions indicating high signal intensities in the bilateral basal ganglia including caudate head & lentiform nucleus and the cortex of

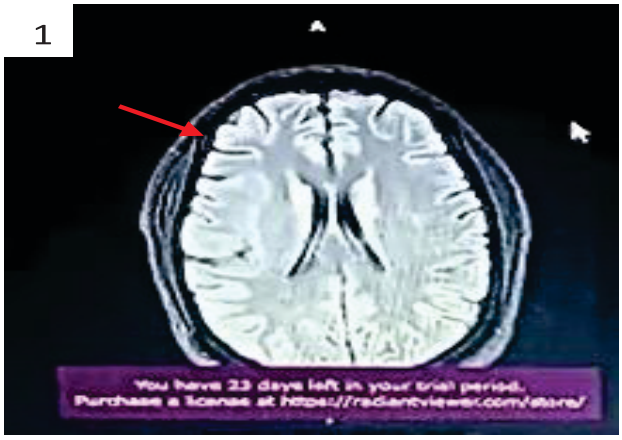

Figure 1: Cortical Ribboning and Deepening of Sulci Showing Cerebral Atrophy.

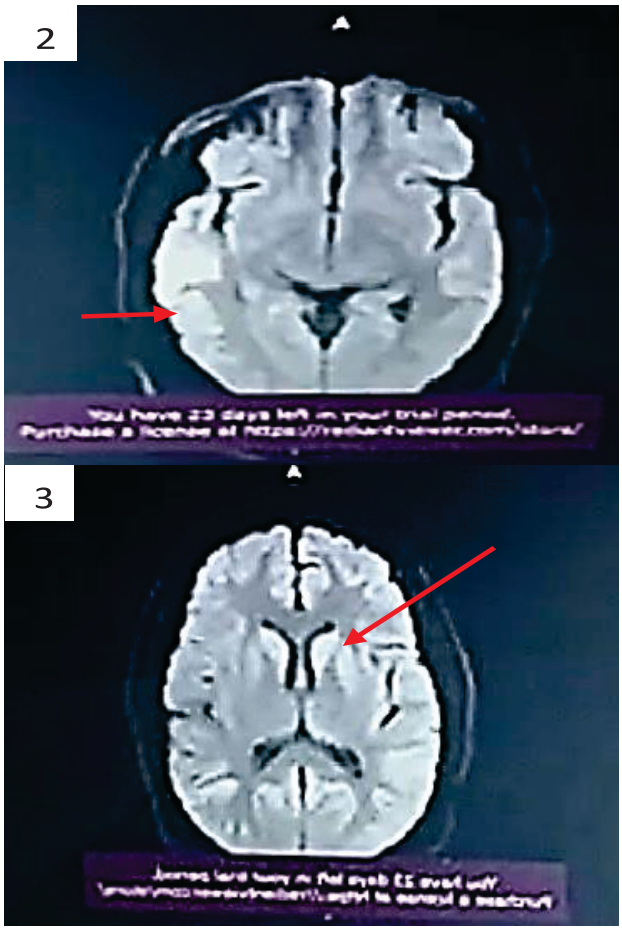

Figure 2 & 3: Gyriform Restricted Diffusions in Bilateral Basal Ganglia and Cortex of Posterior Temporal and Parietal Lobes.

Electroencephalogram showing generalized spike and polyspike discharges.

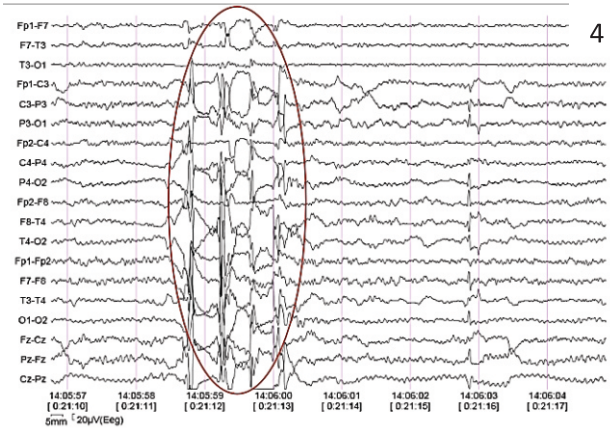

Figure 4: Electroencephalogram (EEG) Showing Generalized Spike and Polyspike Discharges.

bilateral posterior temporal & parietal lobes, which are well known findings of sporadic CJD.

Brain tissue biopsy is the gold standard investigation to confirm the diagnosis which often shows spongiform changes and granular deposits, but it could not be performed in this case due to nonconsent.[4] In line with the CDC criterion for sporadic CJD a diagnosis of probable Creutzfeldt Jakob Disease (CJD) was made.[5] After a total of 92 days in ICU, the patient succumbed to irreversible brain damage.

Discussion

This case was a delayed diagnostic challenge due to its non-specific presenting symptoms coupled with normal baseline investigations, inadequate history and lack of specific investigations and limited resources. Her atypical symptoms mimicked other neurological conditions, which were initially misattributed to supernatural influences and further progressed to more specific neurological signs such as unilateral weakness, altered sensorium and mycolic jerks, unveiling the diagnostic challenges and relentless nature of CJD. The treatment strategy involves supportive care only due to multiple non beneficial drug trials.[6] Despite continuous medical and nursing care the patients often succumb to associated complications such as pneumonia due to impaired swallowing or aspiration, sepsis due to secondary infections such as UTIs or bedsores etc., autonomic dysfunctions such as hemodynamic instability and dysrhythmias, thromboembolic

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events such as deep venous thrombosis (DVT) and pulmonary embolism (PE), malnutrition, dehydration, seizures and neurological impairments.[7]

Conclusion

In conclusion, timely access to diagnostic resources and enhanced interdisciplinary collaborations amongst healthcare professionals should be encouraged to navigate through the diagnostic and therapeutic challenges to decrease mortality and improvising the treatment modalities.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

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SUBJECT AREA: JIIMC is a multi-disciplinary medical journal that publishes scientific research articles related to biomedical sciences.

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  - o CONSORT 2010 flow diagram
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