A Holistic and Innovative Approach to Postgraduate Medical Education

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The field of medical education in Pakistan is undergoing a significant transformation, with an increasing emphasis on innovation to address the changing requirements of the healthcare sector. Postgraduate medical education plays a crucial role in shaping proficient and competent healthcare professionals. Considering this, various innovative measures can be explored to improve the quality of postgraduate medical education in Pakistan. A learning objectives-based self-directed study plan can serve as the basis for the professional development of residents right from the commencement of their residency program [1].

Competency-based medical education (CBME) represents a paradigm shift in postgraduate medical education and has sparked considerable discussion and debate [2]. Unlike traditional assessment tools, CMBE focuses on measuring the actual skills, knowledge, and attitudes that are essential for effective clinical practice. By employing this method, the Association of American Medical Colleges (AAMC) unveiled the Core Entrustable Professional Activities for Entering Residency (Core EPAs) in 2014. This initiative outlines 13 tasks that encompass various competencies, and students are expected to be capable of performing them with minimal supervision upon entering residency. Numerous medical schools in the United States have since embraced, adapted, and extended these EPAs. These EPAs have now been expanded and are extensively employed in postgraduate medical training globally [3]. With the global adoption of CBME approaches, there is a need to redirect attention towards elucidating the implementation of CBME frameworks, understanding their functioning in our clinical practice, and assessing their impacts on our postgraduate medical education system [4].

Embracing digital tools and artificial intelligence, educational institutions are revolutionizing the traditional methods of teaching and learning. Virtual simulations, online lectures, and interactive multimedia resources have provided postgraduate trainees with dynamic and engaging educational experiences. Incorporating a technology-driven approach in postgraduate medical education not only enhances accessibility to educational resources but also cultivates adaptability and proficiency in utilizing modern tools like 3D printing and artificial intelligence [5]. As Pakistan's postgraduate medical education system continues to evolve digital healthcare-based learning stands out as a catalyst for innovation and excellence.

Another strategy for enhancing postgraduate medical education encompasses the substantial enrichment of the learning experience through exposure to global medical practices and collaborations with esteemed institutions. Through exchange programs with international medical centers, residents gain valuable insights into diverse healthcare systems, research opportunities, cultural perspectives, and advanced medical technologies. This exposure not only broadens their horizons but also enhances their understanding, maturity, and proficiency in safe clinical practices [6]. There should be a focus on promoting innovative initiatives such as the PIONEERS (Pakistan Italy, Oncology Network Experiences) exchange program for postgraduate trainees [7, 8].

One often overlooked aspect of enhancing the postgraduate medical education system is the impact of leadership skills. While much attention is rightfully given to the acquisition of medical knowledge and clinical skills, the importance of leadership abilities cannot be overstated. Effective leadership is integral in navigating complex and dynamic healthcare systems, where skills like team building, decision-making, emotional intelligence, and effective communication are paramount [9]. Therefore, the integration of leadership skill development into the postgraduate medical education curriculum is important for preparing healthcare professionals for the multifaceted challenges of their roles. Beyond acquiring medical knowledge, fostering leadership skills ensures that individuals can effectively lead and collaborate within healthcare teams which will result in better patient care [10].

Nevertheless, the role of a mentorship program in postgraduate medical training is instrumental in cultivating the professional and personal development of aspiring healthcare professionals. A well-structured mentorship initiative provides a supportive framework where experienced mentors guide and advise

postgraduate trainees through the complexities of their medical journey, while the mentee remains in the driving seat. Effective mentorship can help mitigate the rates of burnout among residents while simultaneously enhancing their performance and improving patient care [11].

The adoption of innovative approaches in postgraduate medical education in Pakistan is essential for developing versatile and proficient healthcare professionals. Incorporating structured study plans, utilizing technology for learning, executing competency-based assessments, advocating for global collaborations, and endorsing research initiatives collectively elevate the standards of postgraduate medical education. Furthermore, the integration of leadership skill development *via* mentorship programs is equally essential. These holistic measures not only improve the quality of medical education but also play a pivotal role in advancing patient-centered healthcare delivery throughout the nation.

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Impacts of Educational Interventions on the Enhancement of Knowledge of Breast Cancer and Breast Self-Examination among Young Females

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Abstract

Background: Breast cancer is one of the most common malignancies after cervical cancer. Prevention and prognosis depend on earlier detection. Breast self-examination may be a good technique, where facilities are inadequate for mammography and clinical breast examination.

Objective: To assess the knowledge regarding breast cancer and breast self-examination, and to determine the impact of educational intervention among young females.

Methods: A quasi-experimental study method was utilized to conduct this study. A total of 30 participants were selected through a nonprobability convenient sampling technique. An adopted questionnaire was utilized to collect data. The questionnaire consisted of two sections, demographic characteristics and knowledge-related items (21 Items). An additional checklist (13 Items) was prepared to assess knowledge. Maximum points were 86, 01 points each for the item related to the knowledge section of the questionnaire, and 5 points for each of checklist-related items (Total = 65). Those who obtained ≤43 points had poor knowledge, and those who obtained > 43 points were regarded to have good knowledge. Data were collected before the educational session (presentation, video, demonstration), and after the intervention. Wilcoxon test was used to compare pre and post-intervention data.

Results: A total of 30 females participated in the study. In the pretest, 21 (70%) participants had poor knowledge and 9 (30%) had good knowledge. In the post-test, 4 (13.3%) had poor knowledge while 26 (86.7%) had good knowledge. The results were statistically significant ($p<0.001$) using the Wilcoxon sign test.

Conclusion: The findings of the current study reveal that the young female population possesses poor knowledge about breast cancer and breast self-examination. However, educational interventions can be used to enhance knowledge regarding breast cancer and breast self-examination.

Keywords: Breast cancer, breast self-examination, female, knowledge, malignancy.

INTRODUCTION

Breast cancer is the second most common malignancy after cervical cancer and is the most commonly diagnosed cancer among females worldwide, also the fifth leading cause of death estimated at 685,000 in 2020 [1, 2]. In addition, globally 2.3 million new cases of breast cancer were diagnosed in 2020 and it has been estimated as the most common malignancy in low and middle-income countries [3, 4]. Moreover, it affects 1 in 9 females in Pakistan and it is documented that almost 4,000 deaths occur on account of it which puts Pakistan at a higher mortality rate in Asia [4, 5]. The five-year data of cancer incidence (2017-2021) in Karachi revealed breast cancer as the leading cancer among females, documenting 11548 cases of breast cancer for the age of ≥20 years which is touching an alarming proportion [6].

Massive screening programs for early detection may help reduce the incidence of breast cancer given such a high burden in Pakistan [7]. The previous research studies recommend three methods for timely diagnosis of breast cancer, namely Breast Self-examination (BSE), Clinical breast examination (CBE) by a physician, and mammography [8]. Although mammography is a universally accepted screening method for breast cancer, self-breast examination may serve as a useful technique where facilities for mammography and clinical breast examination are deficient [9]. Additionally, the researchers believe that through self-breast examination a malignant tumor as small as one centimeter can be detected by the patient [10]. Therefore, the World Health Organization has strongly recommended BSE for reducing the mortality rate in those regions where facilities for mammography and CBE are not sufficient [11].

On account of the scarcity of facilities, resources, and low awareness, 9.5% of the urban and 4.8% of the rural population of regions like Pakistan go through clinical screening for breast cancer [12]. Furthermore, researchers have argued that an increase in knowledge of breast cancer promotes the behaviour regarding BSE and awareness increases the performance of BSE [8]. Ultimately education among females may result in higher detection of breast cancer as a study has demonstrated that 65% of breast lumps were detected by the patients themselves [11].

Given the huge health problems stemming from a lack of knowledge and awareness regarding breast cancer and breast self-examination, it is imperative to assess the knowledge and identify interventions to improve awareness among females. Educational programs are required to boost awareness and level up knowledge among females in the population of Pakistan [13]. Locally no study was identified to be carried out in this context. Therefore, the findings of the current study may be utilized by health professionals and health administration to create awareness among local females. So, the objective of the current study was to assess knowledge regarding breast cancer (BC) and breast self-examination (BSE) and determine the impact of educational interventions among females.

METHODS

A pretest-posttest quasi-experimental study design was applied to conduct this study from July to November, 2021, in Wah Cantt, Taxila. The study population consisted of 30 young females belonging to Wah Cantt, Taxila, selected through a nonprobability convenient sampling technique. Young females of 16 to 20 years from Wah Cantt were included in the study. Those belonging to medical professionals and having surgical trauma were excluded from the study. Ethical approval was obtained from the Institute of Nursing Wah Medical College. The purpose of the study was explained to all the participants and were assured that their identity would remain confidential and they could withdraw from the study at any time. A written informed consent was obtained from all the participants. An adopted questionnaire was utilized to collect data from the participants with Cronbach's alpha α = 0.78, determined by the principal author [14]. The questionnaire consisted of two sections, the first section was related to demographic characteristics, and the second section was composed of 21 knowledge-related items about breast cancer and breast self-examination. An additional checklist was prepared of 13 questions to assess the demonstration of BSE. One mark was awarded to the correct answer in 21 knowledge-related items while a 0 mark was awarded to the incorrect answer (correct = 1, incorrect = 0). Five marks were given to the correct answer in the checklist for the BSE demonstration while 0 was awarded to the incorrect answer of 13 items (correct = 5, incorrect = 0). So, the total marks were 86. Those obtaining 43 and less marks were considered as having poor knowledge and those above 43 marks were having good knowledge. Pretest data were collected from all the participants. An educational session was arranged for the participants to aware them of breast cancer and breast self-examination.

After giving them 8 hours to relax the post-session date was collected.

A Statistical Package of Social Sciences (SPSS 23) was utilized for analysis. Frequency and percentages were calculated for demographic variables like qualification, family history of cancer, marital status, and residence. Mean and standard deviation were calculated for age, pre-test, and post-test knowledge score. Shapiro-Wilk test was applied to find out the test of normality. A Wilcoxon sign test was calculated to compare the pre-test and post-test knowledge of the participants. For non-parametric Wilcoxon test, a p-value of ≤ 0.05 was considered significant at 95% CI.

RESULTS

The total number of participants included in the study was 30. The mean age of the participants was 18.36 ± 1.40 years. All of them were Punjabis by race and belonged to Wah Cantt, Taxila. The response rate was 100%. Table **1** shows the demographic characteristics of the participants.

Table 1: Demographic characteristics of participants.

Demographic Variables	Frequency (%)
Qualification	
Matric	10 (33.3)
Intermediate	18 (60)
Graduated	2 (6.7)
Marital Status	
Unmarried	21(70)
Married	9(30)
Family History of Cancer	
Yes	4(13.3)
No	26(86.7)
Location	
City	11(36.7)
Town	12(40)
Rural	7(23.3)

Significant findings were obtained when the Shapiro-Wilk test was applied. Moreover, significant difference were obtained when the non-parametric Wilcoxon sign test was applied to the result of pretest and post-test data presented in Table **2** and **Fig. (1)**.

DISCUSSION

The current study was conducted to assess the level of knowledge regarding breast cancer (BC) and self-breast examination (SBE) and the effectiveness of educational interventions among young females residing in Wah Cantt, Taxila. In the current study, most of the participants demonstrated poor knowledge regarding self-breast examination and breast cancer. In one of the previous

Table 2: Comparison of pretest and post-test.

Knowledge Level		Test Statistics	Standardized Test Statistics	p-value
Pre-test				
Minimum	16			
Maximum	76			
Mean	42.167±20.83	411.30	4.205	0.000
Post-test				
Minimum	41			
Maximum	86			
Mean	64.60±12.85			

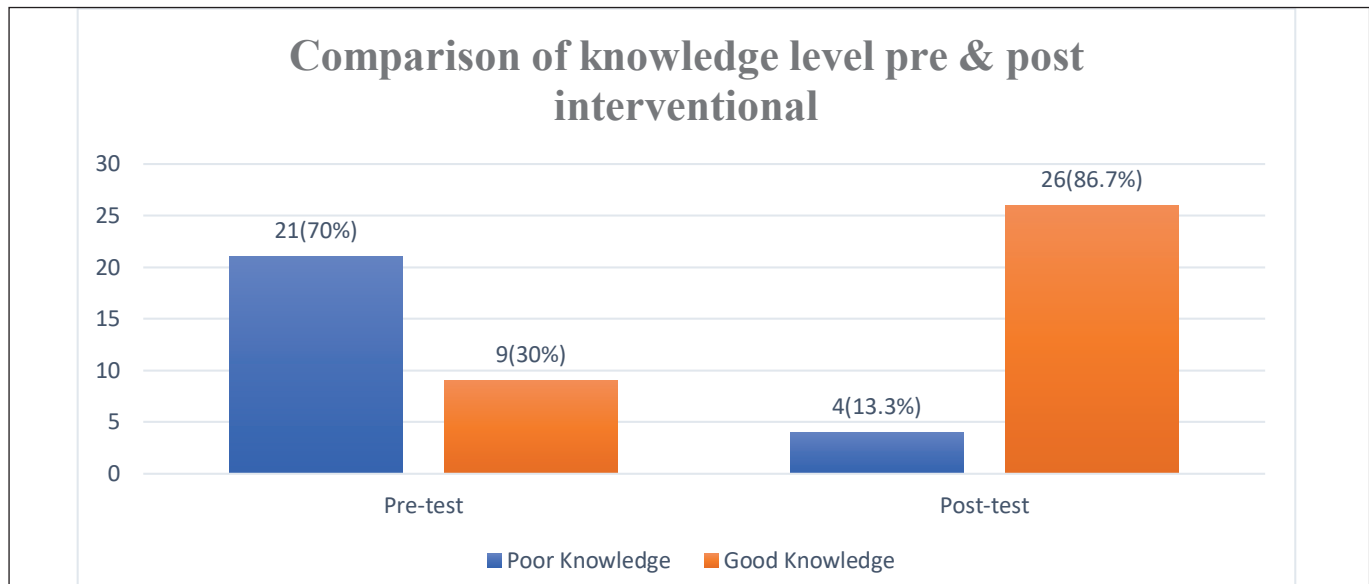*The Wilcoxon test was applied, p-value of < 0.05 was taken as a significant.*

Fig. (1): Comparison of knowledge level pre & post interventional.

research projects, the respondents who did not perform the SBE claimed that it was due to a lack of knowledge/ skills and called for continuous education regarding breast cancer and SBE [9]. Similarly, other studies conducted in Nigeria and Saudi Arabia also revealed poor knowledge in nearly half of the participants [15, 16]. On the other hand, the current findings contradicted the previous findings where 79.8% had good and acceptable knowledge [17]. The huge contradiction is because the previous study was carried out on female health workers in Iran. A study conducted in Ethiopia found more than half of the participants (56%) to have adequate knowledge [18]. This difference in findings is because the previous study was conducted where the participant's age was between 20 to 70. In the same way, a study conducted in Indonesia showed that nearly half of the participants had previously performed BSE, the practice was attributed to maturity in age and education level [19]. It is of paramount importance to enhance

the knowledge of females, so that we may prevent the negative health impact of breast cancer among females in our country. Consequently, training and educational sessions are needed to be arranged which will help reduce the burden of disease in this context. A previous study conducted in Pakistan documented that 14% had poor knowledge, 59% had fair knowledge and 27% had good knowledge [20]. The latter study was conducted among the participants of the educational institutions where most of the participants were students. Their current study may be responsible for the findings of the study.

Our findings showed significant improvement (p-value = 0.002) in the knowledge level among females when pre and post-test data were compared. This finding is in line with the previous quasi-experimental study where the mean score of knowledge was enhanced (p<0.001) in the experimental group [10]. In line with the same findings, another study also showed a drastic improvement

(p<0.05) between the baseline data and post-intervention data [14]. A study carried out on adolescents in Nigeria also improves significantly regarding breast cancer and BSE [21]. Similarly, another quasi-experimental study was conducted on female university students where they found inadequate knowledge which was improved significantly after educational interventions [22]. The research findings are adequate to support that educational interventions and training sessions are the tools through which knowledge and awareness can be leveled up. Consequently, the earlier and timely detection of malignancy will be possible and treatment will be initiated on the spot which will reduce the morbidity and mortality among females.

The study is limited in its sample size, generalizability would have been improved if the sample size was large. The findings are only generalizable to young educated females in Pakistan.

CONCLUSION

The findings of the current study revealed that our female younger population possesses poor knowledge regarding breast cancer and breast self-examination. Furthermore, educational interventions are the best tool to enhance knowledge regarding Breast cancer and breast self-examination.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Review Committee of the Institute of Nursing, Wah Medical College, Wah Cantt, Taxila (REF letter No. IoN/WMC1786/008/Admin). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

Declared none.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

AUTHOR'S CONTRIBUTION

All the authors contributed equally to the publication of this article.

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ORIGINAL ARTICLE

Frequency of Non-Alcoholic Fatty Liver Disease among the Non-Obese Population Presenting to the Gastrointestinal Outpatient Clinic

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Abstract

Background: It has been reported that Asian males with BMI ≤ 23 kg/m^2 have considerably higher content of fat and visceral adipose tissue as compared to their Western counterparts. Multiple studies have reported variable frequency of Non-alcoholic Fatty Liver Disease (NAFLD) in lean population. However, the data is scarce regarding the prevalence of NAFLD in the lean Asian population.

Objective: To determine the frequency of NAFLD among the non-obese population presenting to gastroenterology outpatient clinics.

Methods: This cross-sectional study included all the lean individuals with BMI≤ 23 kg/m^2 presenting to the gastroenterology outpatient clinic from November 2020 to March 2022. Ultrasound abdomen was performed for the presence or absence of fatty liver which was diagnosed based on hyperechoic liver texture. The analysis of continuous variables was performed using the student t-test while the Chi-square test was applied for the analysis of categorical variables. A p-value ≤ 0.05 was considered as statistically significant.

Results: Among the 283 individuals presenting to the gastrointestinal clinic with BMI < 23 kg/m^2 is superscript, the majority were females [150 (53%)]. Out of 283 patients, 118(41.7%) had hypertension, 114(40.3%) had hypertriglyceridemia while 86(29.7%) patients had diabetes. On ultrasound abdomen, fatty liver was observed in 92 (32.5%) patients including 59 (64.1%) females and 33 (35.9%) males. The statistical analysis documented a significant association of NAFLD with female gender (p=0.006), hypertension (p<0.001), hypertriglyceridemia (p=0.130), high total lipids (p<0.001), and serum cholesterol levels (p=0.005). However, no statistically significant association of fatty liver was observed with body mass index (p=0.823), age (p=0.169), and diabetes (p= 0.522).

Conclusion: The presence of hypertension, hypertriglyceridemia, raised total lipids and serum cholesterol levels and female gender were the factors significantly associated with the presence of fatty liver in the lean population. However, to validate our results, multicentered studies on a larger scale are required.

Keywords: Fatty liver, Non-alcoholic fatty liver disease (NAFLD), Pakistan, non-obese, hypertriglyceridemia.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a well-defined condition that is characterized by hepatic steatosis, established based on either radiological tests or tissue biopsy, after excluding the other etiologies associated with increased accumulation of fat in the liver such as alcohol consumption, intake of certain drugs causing fatty liver or genetic disorders [1]. NAFLD is divided into three stages; steatosis, steatohepatitis with and without fibrosis (NASH); and lastly, cirrhosis [2]. Approximately, 25% of the world's population is suffering from fatty liver disease, while its prevalence in Asian countries ranges from 15% to 45% [3, 4]. In Pakistan, the prevalence of NAFLD ranges between 14-47% [5-8]. It is a multifactorial disorder that is frequently linked with other conditions like diabetes mellitus (DM), obesity, dyslipidemia, and metabolic syndrome (MS) [9, 10]. The parameter for measuring obesity is body mass index (BMI). Hence, it is considered an important predictor of NAFLD [11]. Generally, the patients with high BMI are at increased risk of developing NAFLD due to increased visceral fat accumulation.

The high risk of metabolic syndrome in the Asian population can be attributed to the increased body fat leading to increased visceral fat accumulation in this population as compared to the Western population [12, 13]. Previously, studies have revealed a proportionally increased percentage of body fat in the Asian population even with a low BMI [14, 15]. This can be explained by the lower height of Asians as compared to the Western population [16]. Hence, in the Asian population, BMI is an inaccurate tool for the quantification of adipose tissue.

In South Asia, large data is available regarding the obese NAFLD. However, the data is scarce regarding the incidence and frequency of fatty liver in non-obese individuals. Das and his colleagues reported a 5.1% incidence of NAFLD in the non-obese population in a community-based study; but, BMI<25 kg/ m^2 was set as a cutoff [17].

To the best of our knowledge, the exact frequency of non-alcoholic fatty liver disease in the non-obese population is unknown in a densely populated developing country like Pakistan. Abbas *et al*. [5], reported a prevalence of NAFLD in 15.3 % population (n=142) in a hepatitis awareness program in which 22.5% population had a BMI <25 kg/ m^2. Although this above-mentioned study was carried out in the Pakistani population, it

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utilized a high cut-off of BMI (< 25 kg /m^2) as opposed to the current Asian population standard.

Therefore, our main objective was to evaluate the estimated frequency of fatty liver among the non-obese population presenting to our outpatient department (OPD). This study will be helpful for the community to estimate the burden of the disease in this group of patients which can help us in planning timely treatment and prevention of the NFLD related complications.

MATERIALS AND METHODS

This cross-sectional study was carried out at the Department of Hepato-gastroenterology, Sindh Institute of Urology and Transplantation between November 2020 to March 2022. Patients of either gender or ages ranging from 18-70 years presenting with abdominal pain and having BMI <23kg/m^2 were included in the study. The sampling technique used was non-probability consecutive sampling. While, those patients with current or prior history of viral hepatitis including Hepatitis A, Hepatitis B, Hepatitis C, and Hepatitis D (positive anti-HDV antibody), those with a history of significant alcohol consumption (>20 g/day or 14 standard drinks per week in women and 21 standard drinks/week in men) or space-occupying lesion in the liver, those with presence of fluid in the abdomen (ascites) or any history of recent abdominal surgery within past 4 weeks were excluded from the study.

Based on the previous studies, the estimate of NAFLD among the non-obese (BMI < 23 kg/m^2) was 15% to 21%. Taking a margin of error of 8% and a 95% confidence interval, an estimated sample size of 94 patients was proposed for this study.

After the approval from the ethical review committee, consecutive lean patients (BMI ≤23 kg/m^2) visiting the gastroenterology outpatient clinic of Sindh Institute of Urology and Transplantation for upper abdominal pain, were enrolled in this study as per inclusion criteria. Informed consent was taken from all the patients before the enrolment in the study. Ultrasound abdomen was carried out by a consultant radiologist; with more than 3 years post-fellowship experience; using US (TOSHIBA-apleo 50 Model MCM17545TS. Ultrasound abdomen was performed after 8-10 hours of fasting. Nonalcoholic fatty liver was labeled on percutaneous ultrasound based on the presence or absence of hyperechoic liver. Depending upon sonographic findings patients were divided into:
1) Presence of fatty liver
2) Absence of fatty liver

All the demographic information including the age, gender, body mass index, presence or absence of

diabetes (FBS >126mg/dl), hypertension (systolic BP >140 mmHg), hypertriglyceridemia (>150 mg/dl), and findings on ultrasound abdomen were entered in the predesigned proforma.

Statistical Package for the Social Sciences (SPSS) version 24.0 was utilized for the data analysis. Mean ± standard deviation was computed for the continuous variables including age, duration of abdominal pain, weight, height, and body mass index (BMI); while categorical variables including gender, diabetes, and hypertension were expressed in terms of frequencies and percentages. The outcome was observed in terms of the presence or absence of fatty liver on ultrasound abdomen. Effect modifiers like age, gender, diabetes mellitus, and hypertension were controlled through stratification. Student t-test was used for the analysis of continuous variables while comparative analysis of categorical variables was performed using the Chi-square test. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 283 patients presenting to the gastrointestinal clinic with BMI ≤ 23 kg/m^2 were included in the study. Among them, the majority were females [150 (53%)] (**Table 1**). The population had a mean age of 39.1 ± 9.8 years and the mean BMI was 21± 1.6 kg/m^2. Out of 283 patients, 118(41.7%) had hypertension, 114(40.3%) had hypertriglyceridemia while 86(29.7%) patients had diabetes.142 (50.2%) patients had regular eating habits while 109(38.5) and 32(11.3%) patients had irregular and binge eating habits respectively. On ultrasound abdomen, fatty liver was observed in 92 (32.5%) patients including 59 (64.1%) females and 33 (35.9%) males. Among the 118 patients with hypertension, 57 (50%) had fatty liver while 78(66.4%) patients with hypertriglyceridemia and 25(29.8%) patients with diabetes had NAFLD.

Stratification concerning age, gender, BMI, diabetes, hypertension, hypertriglyceridemia serum cholesterol, and total lipids was performed to assess the associated factors with nonalcoholic fatty liver disease.

The statistical analysis documented a significant association of NAFLD with female gender (p=0.006), hypertension (p≤0.001), hypertriglyceridemia (p=0.13), high total lipids (p≤0.001), and serum cholesterol levels (p=0.005) (**Table 2**). However, no statistically significant association of fatty liver was observed with age (p=0.169), eating habits, and diabetes (p= 0.522) in our study.

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is stated as the deposition of fat within hepatocytes in the absence of significant alcohol consumption (> 21 g/day in males

Table 1: Demographics of the studied population (n-283).

Study population(n=235)		n (%)
Mean age(years±S.D)		39.1 ± 9.8
Gender	Male	133(47)
	Female	150(53)
Height(m²)		1.63 ± 6.8
Weight(Kg)		56±6
Body Mass Index(BMI)(kg/m²)		21± 1.6
Diabetes		86(29.7)
Hypertension		118(41.7)
Hypertriglyceridemia		114(40.3)
Eating Habits	Regular	142(50.2)
	Irregular	109(38.5)
	Binge Eating	32(11.3)
Fatty liver on ultrasound	Yes	92(32.5)
	No	191(67.5)
Total Bilirubin(mg/dl)		0.7±0.3
Alkaline Phosphatase(IU/L)		135±109
Aspartate Transaminase(AST)(IU/L)		37.8±55.5
Alanine Transaminase(ALT)(IU/L)		47.4±31.8
Serum Cholesterol		360±155
Serum LDL		105± 31
Serum HDL		42.6± 9.3
Total Lipids		672±150
Serum Triglycerides		158±74

Abbreviations: LDL: low density lipoprotein; HDL: high density lipoprotein.

Table 2: Stratification of Non-alcoholic fatty liver disease (NAFLD) concerning age, gender, diabetes, hypertension, and hypertriglyceridemia (n= 283).

Variables		NAFLD (n-92) N(%)	Without NAFLD (n-191) N(%)	p-value
Age(years)		38.4±8.4	40±10.6	0.169
Gender	Male	33(35.9)	102(53.4)	0.006
	Female	59 (64.1)	89(46.6)	
BMI(Kg/m²)		21± 1.9	21± 1.4	0.823
Diabetes	Yes	25(27.2)	61(31.9)	0.522
	No	67(72.8)	130(68.1)	
Hypertension	Yes	56(60.8)	60(15.7)	≤0.001
	No	36(39.2)	161(84.3)	
Hypertriglyceridemia	Yes	78(84.8)	36(18.8)	0.013
	No	14(15.2)	155(81.2)	
Serum Cholesterol		737±267	173± 38	0.005
Serum Lipids		154±11	129 ± 14	≤0.001

Abbreviation: BMI: Body Mass Index.

and > 14g/day in females), viral serology, steatogenic drugs, and hereditary disorders. The diagnosis of NAFLD is established on the presence of hyper-echoic liver on ultrasound abdomen or > 5% steatosis on liver biopsy [1]. Many factors such as metabolic syndrome, cardiovascular disease, obesity, and dyslipidemia are risk factors for NAFLD [9, 10]. Globally, one of the emerging causes of chronic liver disease is NAFLD. The reported prevalence of NAFLD worldwide is 25% [3, 4]. However, in Pakistan, the estimated prevalence of NAFLD is 14.8%-20% [5-8]. It is more common among the obese population, but it has also been documented among the lean population in both the developing as well as the developed countries [3-9]. Das *et al*. [17] reported the prevalence of NAFLD in India as 8.7 %, with 5.1% of these including non-obese (BMI < 23 kg/m2). In the United States, NAFLD prevalence in lean subjects (BMI < 25 kg/m2) was found to be 9.67% [18]. Kwon *et al*. showed that among the Korean population, non-obese NAFLD was found to be 12.6% [19].

In the Asian population, the people have more visceral adiposity as compared to the overall body fat. Visceral obesity is not only an important predictor of NAFLD but also a risk factor for cardiovascular and metabolic disease [20]. Visceral obesity cannot be defined by BMI as the latter measures the amount of fat and has different cutoffs in different populations. Wang *et al*. [14] and Deurenberg *et al*. [15] found higher body fat content in the Asian population as compared to that in the Western population even with low BMI. Xu *et al*. [21] reported that NAFLD prevalence among the non-obese lean Chinese population was 7.27%, and raised BMI and waist circumference (WC) were significantly linked with the development of NAFLD during the follow-up period. In our study, 92 (32.5%) lean patients had NAFLD on abdominal ultrasound. This can be attributed to the paradigm shift in the lifestyle of our population in recent years *i.e*., from a healthy to a sedentary lifestyle and the intake of food products with high glycemic index and saturated fats along with low physical activity.

A cross-sectional survey of the United States reported that the frequency of fatty liver was higher in females as compared to males (30.7% *vs.* 15.3%, *P* < 0.001) [18]. Similar to Younossi *et al.* [4], NAFLD was observed mostly in females in our population. Zheng *et al*. [22] documented that the mean age of NAFLD patients was 37.32 ± 10.19 years and non-NAFLD was 36.60 ± 11.14 years (p=0.62). Younossi *et al.* [23] reported patients with NAFLD were younger and were more commonly females. Similarly, our patients diagnosed with lean NAFLD were also young and had a mean age of 39.1 ± 9.8 years.

This increased prevalence of lean NAFLD in our young population can again be attributed to certain factors like a sedentary lifestyle and genetic predisposition. However, the pattern of genetic inheritance of NAFLD in the local population is yet to be defined.

WHO expert consultation report stated that Asians have more chances of developing insulin resistance, Type 2 diabetes (T2DM), and cardiovascular disease than Europeans at any given body index [24]. This is because intraabdominal fat and body fat in Asians are comparatively greater than in Europeans [14, 25]. Younossi *et al*. [23] documented that fatty liver in the non-obese population was associated with diabetes and hypertension. Similarly, in our study population, eighty-six participants (29.7%) were diabetic, out of which 25(27.2%) had fatty liver on ultrasound abdomen. This shows that lean NAFLD is more prevalent in diabetics, although this does not show a statistically significant association with lean NAFLD (p = 0.522).

Previously, studies have shown a statistically significant association of hypertension with NAFLD. A study done by Donate *et al*. [26] reported hypertension in 30.9% of patients diagnosed with NAFLD. Furthermore, he also stated that insulin resistance and plasma insulin levels were higher in hypertensive patients as compared to the normal population [26]. Similarly, a study done by Lankarani *et al.* showed approximately 34.1% prevalence of lean NAFLD in the Iranian population [27]. In our study, hypertension showed a statistically significant association with NAFLD with 56(48.2%) hypertensive patients diagnosed with NAFLD (p≤0.001) which can again be attributed to the recent change in the lifestyle of our population. The other reason for such a high percentage of NAFLD in hypertensive patients as compared to the other studies can be due to the high prevalence of hypertension in our population.

Limitations of this study include that liver biopsy was not performed in our study population, considering this as a gold standard. The ultrasound abdomen demonstrated a varied sensitivity ranging from 89-91% along with specificity between 82-93% in diagnosing NAFLD [28, 29]. However, in our study ultrasound abdomen was performed by an expert radiologist with high expertise and skills with a special interest in NAFLD. Furthermore; other limitations can be attributed to this study including a small sample size and a single-centered study. Therefore, our results might not be generalized to the larger populations. Thus, multi-centric studies are required not only to validate our results but also to establish the true frequency of fatty liver in the non-obese population.

Our study also has strengths, as non-obese (Lean) NAFLD is a major but neglected issue in our population. This is the pioneer study showing the frequency of NAFLD in the lean population. The early diagnosis of NAFLD can be done by ultrasound abdomen which is readily available, non-invasive, and easy to perform investigation for diagnosing NAFLD. By identifying NAFLD in our population in the early stage, we can estimate the burden of the disease in this group which will help us in planning timely treatment and prevention of the related complications. *i.e.*, liver cirrhosis.

CONCLUSION

This study demonstrated that a significant proportion of the population with BMI$\leq$ 23kg/m^2 had NAFLD. The lean NAFLD population has a statistically significant association with the female gender along with the presence of hypertension, hypertriglyceridemia, increased total lipids, and serum cholesterol levels. As risk factors and biological behavior of the disease are not determined hence this study opens the door for further exploring the disease in a large population.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethical Review Committee of Sindh Institute Of Urology And Transplantation, Karachi (REF letter No. SIUT-ERC-2022/PA-221, ERC No.: 216). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

Declared none.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

AUTHOR'S CONTRIBUTION

All the authors contributed equally to the publication of this article.

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ORIGINAL ARTICLE

Severe COVID-19 Pneumonia Treated with Tocilizumab in a Pakistani Population: Variables Impacting Outcomes

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Abstract

Background: The association of severity of COVID-19 with raised Interleukin-6 (IL-6) levels led to Tocilizumab (TCZ) approval for treatment based on its IL-6 inhibiting mechanism of action. Treatment outcomes reported have been variable, with little data from Pakistan.

Objective: To identify demographic, clinical, and laboratory variables impacting outcomes (recovery or death) of patients with severe COVID-19 pneumonia treated with intravenous tocilizumab in a Pakistani hospital setting.

Methods: A single-center, retrospective, descriptive case series was conducted at the National Hospital Postgraduate Training and Medical Centre, Lahore from April to December 2020. Severe COVID-19 pneumonia (oxygen saturation below 90%, chest HRCT severity score more than 15) administered intravenous tocilizumab was included. Not fulfilling the above inclusion criteria. Data was analysed to identify significant differences between expired patients and those discharged after recovery.

Results: Forty-nine patients were admitted to intensive care/ high dependency units (ICU/HDU) with severe COVID pneumonia and treated with intravenous tocilizumab during the study period. The mean age was 60.8 years, with male predominance. Of the 49 patients, 23 (47%) expired. In the expired group lactate dehydrogenase (LDH), and neutrophil to lymphocyte ratio (NLR) were significantly higher throughout the admission course, while D-Dimers plus the last available white blood cell (WBC) count, were significantly higher post-TCZ, as was odds of co-infection evidenced by positive blood cultures.

Conclusion: Mortality correlated with increased inflammatory markers LDH and NLR ratio. Post TCZ raised D-Dimers may be indicators of fibrin microthrombi and prophylactic anticoagulation with TCZ may benefit such patients. High odds of secondary bacterial infection post-TCZ had a significant negative impact on recovery.

Keywords: *CoronaVirus-19, COVID-19, COVID-19 Pneumonia, Tocilizumab, Microthrombi, IL-6, Anticoagulation.*

INTRODUCTION

COVID-19 is a term used by WHO for illnesses caused by SARS-CoV-2 [1]. At the end of 2019, this novel coronavirus was identified as the cause of a cluster of cases of atypical pneumonia in Wuhan, China. It rapidly spread and was declared a global pandemic, by the WHO, on March 11, 2020 [2].

At the start of the pandemic, management of COVID-19 in hospitalised adults was based on limited evidence and evolved as clinical data emerged. Interim guidance was issued by the World Health Organisation (WHO) [3]. In severe COVID-19 patients, pathogenic white blood cells with high IL-6 secretion may enter the pulmonary circulation causing an inflammatory storm, which refers to an excessive inflammatory response, resulting in an out-of-control and dysfunctional immune system [4]. Tocilizumab (TCZ), the first Food and Drug Administration (FDA) approved IL-6 blocking agent, with proven safety and effectiveness for use in rheumatic diseases and cytokine release syndrome (CRS), was hypothesised to deter disease progression

in severe COVID-19 pneumonia with acute respiratory distress syndrome (ARDS) [4]. Its use in COVID-19 patients was described in observational studies [4], and later evaluated in clinical trials for the treatment of COVID-19, which showed its effectiveness [5, 6]. The United States of America (USA) FDA issued an emergency use authorization (EUA) in June 2021 [7] and WHO added it to its list of prequalified treatments for severe or critical COVID-19 in Feb 2022 [8]. FDA fully approved TCZ for intravenous treatment of severe COVID-19 hospitalised patients in the same year [9]. It remains an approved in-patient treatment for severe COVID-19 infections to date [10]. In Pakistan, TCZ was approved by the Punjab government for treating critically ill patients in May 2020 [11]. Most physicians were unfamiliar with this drug other than rheumatologists, who have been using it for rheumatoid arthritis since 2010 [12]. Hence, the rheumatology department in our hospital was consulted for most of our study patients.

Notably, the pandemic continued into 2021, 2022, and 2023, only being taken off as a health emergency by the WHO on 5th May 2023 [13]. However, cases are still being recorded in Pakistan to date [14, 15].

This study was designed to look at outcomes of patients with severe COVID pneumonia treated with tocilizumab

in a tertiary care hospital in Lahore and to identify the demographic, clinical, and laboratory variables impacting the outcome *viz* recovery/discharge or death.

METHODOLOGY

This was a single-center, retrospective, descriptive case series. After approval from the hospital's ethical review board, patient data was gathered from April to December, 2020 and included all severe COVID-19 pneumonia patients (diagnosed clinically plus chest HRCT with or without positive COVID PCR) [16] admitted in the ICU and/or HDU of National Hospital and Medical Centre, Lahore, and treated with intravenous tocilizumab. Severe COVID-19 pneumonia was defined as oxygen saturation below 90% and, a chest HRCT severity score of more than 15 [17, 18]. The dose of intravenous tocilizumab used in our study patients was 8mg/kg) [19]. Patient data regarding demographics, comorbidities, presenting complaints, diagnostic data, treatment modalities used, and the development of co-infection was obtained from hospital files. Data for laboratory tests included blood cell counts, inflammatory markers, namely, C - reactive protein (CRP), Ferritin, Procalcitonin, LDH, IL-6, and NLR, and the coagulation marker D-Dimer. Data for each patient was entered into a spreadsheet, with the laboratory values tracked over several days to assess any changes over time. Statistical analyses were conducted using SPSS Version 23.0.0.2 and Jamovi Version 1.2.22.

Patients were then characterised, based on outcomes, into two groups *viz*., death or recovery/ discharge.

A comparison of demographic variables and laboratory parameters was done between the two groups. Continuous variables were presented as Mean ± Standard Deviation where normally distributed (as determined by the Shapiro-Wilk test for normality) and as median (interquartile range) in the absence of normal distribution.

The differences between expired and discharged patients were compared as follows: 1- independent samples t-test in the case of normal distribution and homogeneity of variances (as determined by Levene's test) 2- Welch's T-test in the case of normal distribution but heterogeneity of variances 3- Mann-Whitney U test in the absence of normal distribution. Categorical data was compared using the Chi-square test or Fisher's exact test (where at least one of the values was < 5).

In the case of a significant p-value for Chi-square or Fisher's exact test, the odds ratio (OR) was calculated to assess the odds of an event in the expired group compared to the discharged group. A p-value<0.05 was considered statistically significant (2-tailed) for all the tests mentioned above.

RESULTS

A total of 49 patients were included in the study. The mean age of patients was 60.8 years with 31 (63.3%) of them being male. A significant proportion of them had comorbidities; 31 (63.3%) had hypertension, 25 (51%) had diabetes and 16 (32.7%) had chronic heart disease, with no significant differences between the two groups. Demographic variables, as well as the type and number of comorbidities, were compared between the expired and discharged groups, as shown in Table **1**.

There was a clear pattern when it came to presenting complaints; 42(85.7%) had a fever, 41(83.7%) had shortness of breath and 27(55.1%) had a dry cough, but with no significant differences between the two groups. These were recorded at the time of presentation in the emergency department. The median number of presenting complaints (limited to those mentioned in **Table 1** below) was also recorded and found to be three in both groups (p=0.301).

The median number of days from the onset of the first symptom till hospital admission was 7 (IQR: 3 - 7) with no significant difference between expired and discharged patients (p=0.713). The median day of admission on which tocilizumab was started was 3 (2 - 5) with no significant difference between expired and discharged patients (p=0.271).

The median number of days patients spent in the hospital was 10 (8 - 14), with a significant difference (p=0.008) between expired [9 (7 - 11)] and discharged patients [12 (10 - 16.75)]. Statistically, a significant number of patients required non-invasive ventilation (p=0.003, OR=6.25) and invasive ventilation (p<0.001, OR=57.1) in the expired group as compared to the discharged group. Finally, vasopressors were administered to eight expired patients (34.8%), which was significantly higher (p=0.009, OR=12.8) than discharged patients (1 patient; 4.0%). There was no significant difference between expired and discharged patients concerning the other treatment options, as shown in Table **1**.

A positive COVID PCR was found in 35 patients (71.4%, p=0.125). Bilateral pulmonary infiltrates were found in all patients on chest X-ray and chest HRCT.

Procalcitonin is commonly used as a marker of infection in a hospital/ICU environment. In COVID, however, it has limited utility as an indicator of co-infection since it is found to be raised in most if not all severe COVID pneumonia cases [20]. As expected, in our study procalcitonin was found to be raised in all the patients with no statistical difference between the two groups. Blood cultures were sent for all patients and a positive result was used to confirm

Table 1: Demographics and categorical data.

Demographics and Comorbidities			
Parameter	**All Patients N=49 n (%)**	**Expired N=23 n (%)**	**Discharged N=26 n (%)**	**p-value**
Mean Age in Years ± SD	60.8 ± 14.9	61.7 ± 13.1	59.9 ± 16.6	0.683
Age Groups:				
20-29 years	2 (4.1)	1 (4.3)	1 (3.8)	
30-39 years	2 (4.1)	0 (0.0)	2 (7.7)	
40-49 years	6 (12.2)	2 (8.7)	4 (15.4)	
50-59 years	13 (26.5)	7 (30.4)	6 (23.1)	0.772
60-69 years	10 (20.4)	6 (26.1)	4 (15.4)	
70-79 years	11 (22.4)	5 (21.7)	6 (23.1)	
80-89 years	4 (8.2)	2 (8.7)	2 (7.7)	
90-99 years	1 (2.0)	0 (0.0)	1 (3.8)	
Sex:				
Male	31 (63.3)	14 (60.9)	17 (65.4)	0.744
Female	18 (36.7)	9 (39.1)	9 (34.6)	
Diabetes Mellitus	25 (51.0)	13 (56.5)	12 (46.2)	0.469
Hypertension	31 (63.3)	14 (60.9)	17 (65.4)	0.744
Chronic Heart Disease	16 (32.7)	6 (26.1)	10 (43.5)	0.357
Chronic Pulmonary Disease	1 (2.0)	1 (4.35)	0 (0)	0.469
Chronic Kidney Disease	2 (4.1)	1 (4.35)	1 (3.85)	1.000
Dementia	0 (0.0)	0 (0)	0 (0)	-
Asthma	2 (4.1)	1 (4.35)	1 (3.85)	1.000
Malignancy	1 (2.0)	1 (4.35)	0 (0)	0.469
Rheumatic Disease	3 (6.1)	0 (0)	3 (11.5)	0.237
Chronic Neurological Disease	1 (2)	1 (4.35)	0 (0)	0.469
Smoker	5 (10.2)	2 (8.70)	3 (11.5)	1.000
Liver Disease	0 (0.0)	0 (0)	0 (0)	-
Presenting Complaints on Hospital Admission				
Parameter	**All Patients N=49 n (%)**	**Expired N=23 n (%)**	**Discharged N=26 n (%)**	**p-value**
Fever	42 (85.7)	20 (87.0)	22 (84.6)	1.000
Shortness of Breath	41 (83.7)	20 (87.0)	21 (80.8)	0.706
Dry Cough	27 (55.1)	11 (47.8)	16 (61.5)	0.336
Productive Cough	5 (10.2)	2 (8.70)	3 (11.5)	1.000
Fatigue/Malaise	1 (2.0)	0 (0)	1 (3.85)	1.000
Altered Consciousness	3 (6.1)	2 (8.70)	1 (3.85)	0.594
Diarrhoea	8 (16.3)	2 (8.70)	6 (23.1)	0.254
Nausea/Vomiting	2 (4.1)	1 (4.35)	1 (3.85)	1.000
Sore Throat	9 (18.4)	3 (13.0)	6 (23.1)	0.472
Anosmia	0 (0.0)	0 (0)	0 (0)	NaN
Nasal Congestion	1 (2.0)	0 (0)	1 (3.85)	1.000
Chest Pain	4 (8.2)	3 (13.0)	1 (3.85)	0.330
Headache	3 (6.1)	1 (4.35)	2 (7.69)	1.000
Muscle Aches	9 (18.4)	2 (8.70)	7 (26.9)	0.145
Joint Pain	0 (0.0)	0 (0)	0 (0)	-
Treatment Modalities				
Parameter	**All Patients N=49 n (%)**	**Expired N=23 n (%)**	**Discharged N=26 n (%)**	**p-value**
O2 at Home	14 (28.6)	8 (34.8)	6 (23.1)	0.365
Low Flow O2	13 (26.5)	3 (13.0)	10 (38.5)	0.057
High Flow O2	36 (73.5)	18 (78.3)	18 (69.2)	0.475
Non-invasive Ventilation	21 (42.9)	15 (65.2)	6 (23.1)	0.003
Invasive Ventilation	17 (34.7)	16 (70.0)	1 (3.85)	<0.001
Remdesivir	9 (19.1)[a]	2 (9.1)[b]	7 (28.0)[c]	0.144
Hydroxychloroquine	9 (18.8)[d]	7 (30.4)	2 (8.0)[e]	0.068

Azithromycin	40 (83.3)[d]	19 (82.6)	21 (84.0)[c]	1.000
Systemic Steroids	46 (95.8)[d]	21 (91.3)	25 (100.0)[c]	0.224
Antibiotic (Other than Azithromycin)	46 (95.8)[d]	21 (91.3)	25 (100.0)[c]	0.224
Vasopressors	9 (18.8)[d]	8 (34.8)	1 (4.0)[c]	0.009
Anticoagulation	46 (95.8)[d]	21 (91.3)	25 (100)[c]	0.240
Convalescent Plasma	6 (12.5)[d]	3 (13.0)	3 (12.0)[c]	1.000
Renal Transplant	1 (2.1)[d]	0 (0)	1 (4.0)[c]	1.000
Tracheostomy	0 (0)[d]	0 (0)	0 (0)	-

Abbreviations: *SD = Standard Deviation, [a]Percentage was out of 47 because treatment data for 2 patients was missing, [b]Percentage was out of 22 because treatment data for 1 patient was missing, [c]Percentage was out of 25 because treatment data for 1 patient was missing, [d]Percentage was out of 48 because treatment data for 1 patient was missing.*

the presence of a co-infection. Co-infection was observed in a total of 12 patients, 10 of whom expired and 2 were discharged, with a significant difference between the two groups (p=0.008, OR=8.21).

Lab values for all patients were assessed on multiple days. Baselines were collected from Day 1 of TCZ administration, Day 3 of TCZ administration, and the last available labs before discharge on expiry. The p values (expired *vs.* discharged group) of all the assessed labs can be found in Table **2**. Of those labs, the medians of the ones with significant p values have been graphed in **Fig. (1)**.

DISCUSSION

The mean age of the patients in our study was 60.8 years with a male predominance, similar to a study by Docherty *et al.* which showed a higher disease incidence in the middle-aged and older population with a male-skewed pattern [21]. However, their mortality rate was associated with invasive/mechanical ventilation only, whereas we saw high mortality in both invasive and non-invasive ventilation. Notably, the increased mortality seen associated with various comorbidities in their research, such as chronic cardiac disease, was in line with other studies including a local study from Lahore [22] but was not reflected in our study. Additionally, we found that the duration of symptoms pre-hospital did not correlate with mortality.

LDH and D-Dimers were consistently higher in the expired group, similar to Han *et al.* who found both to be higher in severe illness compared to mild illness and concluded that LDH in particular could allow for early recognition of lung injury and disease severity [23]. Ferner *et al.* analysed multiple case series and found that both micro and macro thrombotic events occurred in COVID-19 patients [24]. The cytokine storm may damage the endothelium at an early stage, leading to microthrombosis, especially in the lungs, resulting in high D-Dimers, high LDH, and mortality. A study by Wadowski *et al.*, published in January 2023, discusses this and describes how COVID-19 disturbs

the equilibrium between platelets and the vessel wall, leading to microthrombi formation and being a possible major factor driving the deterioration of patient disease course in severe COVID-19 [25]. This is supported by postmortem reports of COVID patients [26, 27].

A recent study by Bhoopat *et al.* found that the use of therapeutic doses of heparin had a survival benefit in COVID-19 patients, with no incidence of major bleeding events [28]. This was expanded upon by preliminary results from three international, multicenter clinical trials which posited that full-dose anticoagulation reduced mortality if administered early, when patients were moderately ill, but could potentially be harmful if started in ICU patients [29].

In our study expired patients had high LDH both pre and post-TCZ, however a significant difference of elevated D Dimers between the two groups, even without major overt thrombotic events, occurred post-TCZ suggesting that microthrombosis may have been their cause of death possibly due to ongoing disease activity non-responsive to TCZ. A transient elevation of D-dimer in COVID-19 patients who received TCZ and a trend towards increased death secondary to thromboembolism has been reported by Chan *et al.* [30]. This, in conjunction with our findings on significantly elevated D-Dimers, post TCZ in the expired group, strongly suggests that further research on early D-Dimer guided thromboprophylaxis may be the key to reducing mortality in patients with COVID-19 receiving TCZ.

Expired patients in our study had a higher WBC count, which is in line with other studies such as Peng *et al.* (2020) and Sun *et al.* (2020) which found patients with severe disease have higher WBC counts than those with mild-moderate disease. Based on these findings leukocyte differential count may provide more details and may serve as a predictor for the degree of disease severity and prognosis of the patient [31]. High NLR was associated with mortality, and shown as a poor prognostic marker, as has been shown in existing data [32, 33].
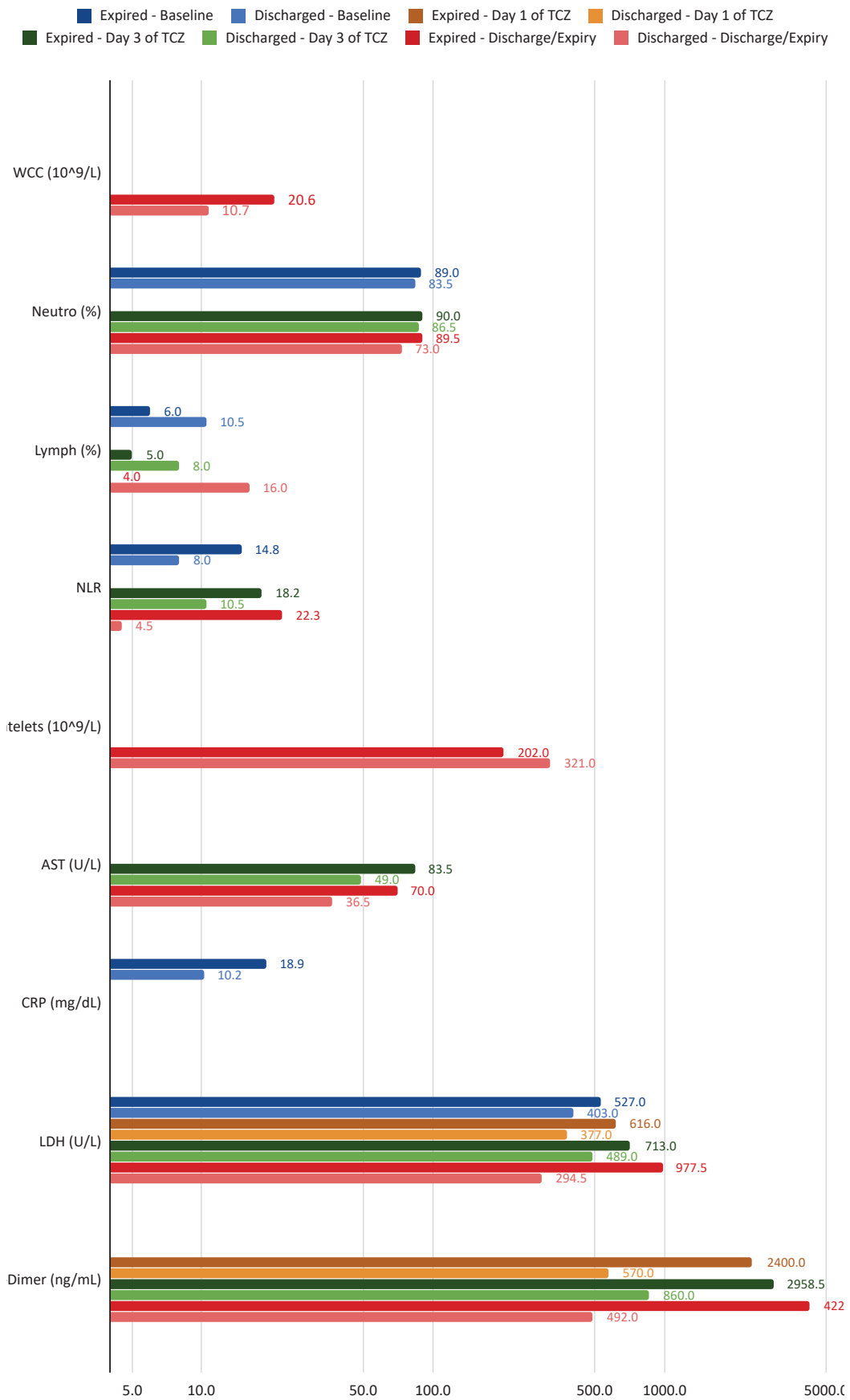
Fig. (1): Median lab values for expired and discharged patients with $p<0.05$.

Table 2: Labs - statistical comparison of laboratory parameters between expired and discharged patients.

Parameters (Normal Range)	Baseline (Mean ± S.D)			Day 1 of TCZ (Mean ± S.D)			Day 3 of TCZ (Mean ± S.D)			At Discharge or Expiry (Mean ± S.D)		
	Dis-charged	Ex-pired	p-value	Dis-charged	Ex-pired	p-value	Dis-charged	Ex-pired	p-value	Dis-charged	Expired	p-value
Haemoglobin (12.1-17.2 g/dL)	12.99 ± 1.55	12.76 ± 1.68	0.625	12.90 ± 1.53	12.72 ± 1.69	0.714	13.20 ± 1.71	12.52 ± 1.99	0.228	13.18 ± 2.12	12.86 ± 1.92	0.597
WBC (4.5-11 x 10⁹/L)	10.14 ± 5.60	9.94 ± 5.50	0.992	12.95 ± 5.18	14.65 ± 6.81	0.336	11.75 ± 4.46	15.18 ± 7.01	0.056	11.35 ± 4.13	21.35 ± 8.70	< 0.001
Neutro % (40-60%)	80.35 ± 10.65	86.50 ± 6.13	0.023	86.44 ± 7.30	89.23 ± 3.91	0.274	84.04 ± 8.72	88.85 ± 5.35	0.007	71.68 ± 17.84	89.23 ± 4.65	< 0.001
Lympho % (18-45%)	14.38 ± 9.50	9.00 ± 5.27	0.027	8.44 ± 4.95	6.23 ± 3.87	0.101	10.38 ± 7.34	5.95 ± 4.26	0.002	15.12 ± 8.26	5.55 ± 3.99	< 0.001
NLR (1-2)	8.93 ± 6.70	13.35 ± 7.26	0.022	14.32 ± 8.46	20.61 ± 12.9	0.135	11.94 ± 9.49	20.87 ± 11.20	0.003	7.61 ± 9.30	26.1 ± 20.43	< 0.001
Platelets (150-450 x 10³/ml)	254.5 ± 110.4	238.7 ± 85.69	1.000	322.4 ± 105	285 ± 126.8	0.127	343.3 ± 101.7	289.4 ± 128.3	0.128	329.1 ± 120.9	228.9 ± 113.9	0.006
INR (≤1.1)	2.76 ± 3.88	1.20 ± 0.25	0.617	3.80 ± 3.81	1.18 ± 0.19	0.469	2.35 ± 1.76	1.13 ± 0.11	0.508	0.65 ± 0.91	1.40 ± 0.20	0.451
Creatinine (0.6-1.3 mg/dL)	1.29 ± 1.63	1.26 ± 0.67	0.273	1.23 ± 1.53	1.39 ± 1.05	0.444	1.38 ± 2.00	1.22 ± 0.66	0.448	1.45 ± 1.69	1.62 ± 1.14	0.388
ALT (19-33 IU/L)	59.38 ± 59.0	39.42 ± 19.77	0.633	56.50 ± 48.61	45.80 ± 61.91	0.080	69.30 ± 55.95	69.63 ± 51.37	0.824	72.71 ± 62.99	80.67 ± 49.43	0.345
AST (8-33 U/L)	69.58 ± 56.40	78.26	0.441	48.95 ± 23.40	79.15 ± 98.98	0.252	54.70 ± 34.29	107.3 ± 89.87	0.024	40.25 ± 15.15	106.5 ± 72.12	< 0.001
Total Bilirubin (0.1-1.2 mg/dL)	0.58 ± 0.200	0.65 ± 0.58	0.398	0.68 ± 0.33	0.76 ± 0.57	0.885	0.80 ± 0.57	0.75 ± 0.37	1.000	0.64 ± 0.27	0.61 ± 0.48	0.078
Troponin I (0-0.04 ng/mL)	0.09 ± 0.227	0.68 ± 1.43	0.404	1.51 ± 2.46	0.99 ± 1.68	0.548	NaN	17.20 ± 29.28	NaN	NaN ± NaN	17.14 ± 26.23	NaN
CK-MB (5-25 IU/L)	44.57 ± 43.55	26.60 ± 15.8	0.626	48 ± 2.82	56.7 ± 42.91	0.804	48 ± NaN	36 ± Nan	NaN	22.50 ± 6.36	124 ± NaN	NaN
Pro-BNP (≤125 pg/mL)	4626 ± 9429	1006 ± 997.7	0.186	104.3 ± 97.53	2453 ± 4160	0.071	37.85 ± 8.27	17896 ± 24191	0.486	99.29 ± 80.20	12977 ± 16663	0.376
CRP (≤0.3 mg/dL)	11.32 ± 8.81	17.73 ± 9.09	0.019	9.14 ± 8.40	12.58 ± 8.17	0.114	2.88 ± 3.48	4.48 ± 4.63	0.084	1.25 ± 1.94	3.02 ± 5.05	0.080
IL-6 (≤18 ng/mL)	127.8 ± 139.2	24.15 ± 18.81	0.266	622.4 ± 776.8	264.4 ± 226.8	0.486	559.1 ± 348.2	55.57 ± NaN	0.337	1449 ± NaN	2519 ± 3509	NaN
Ferritin (24-336 mg/L)	1654 ± 2141	830.6 ± 650.2	0.219	1440 ± 1345	1050 ± 809.5	0.403	1263 ± 984	1110 ± 876.6	0.626	1051 ± 808.1	1623 ± 1767	0.742
Procalcitonin (≤0.1 ng/mL)	0.55 ± 1.34	3.16 ± 11.61	0.207	0.78 ± 1.44	0.37 ± 0.55	0.728	1.29 ± 2.66	0.46 ± 0.51	0.798	1.87 ± 3.17	0.26 ± 0.30	0.517
LDH (140-280 U/L)	423.4 ± 149.5	572.2 ± 248.9	0.033	446.1 ± 161.1	674.7 ± 194	< 0.001	487.3 ± 171.6	826 ± 318.1	0.003	280.3 ± 167.8	969.9 ± 269.2	< 0.001
D-Dimer (≤0.5 mg/L)	621 ± 663.2	2464 ± 3295	0.098	1280 ± 1528	5928 ± 13039	0.027	1688 ± 1983	4453 ± 4662	0.029	1077 ± 1431	5603 ± 5192	< 0.001

Red Highlighted: *Significant difference between lab values of discharged and expired patients (P < 0.05).* ***Abbreviations:*** *WCC = White Blood Cell, Neutro = percentage of Neutrophils, Lymph = percentage of Lymphocytes, NLR = Neutrophil to Lymphocyte ratio, INR = International Normalised Ratio, ALT = Alanine Aminotransferase, AST = Aspartate Aminotransferase, CK-MB = Creatine Kinase-MB, Pro-BNP = Pro Brain Natriuretic Peptide, CRP = C-Reactive Protein, IL-6 = Interleukin 6, LDH = Lactate Dehydrogenase.*

The expired group had a significantly lower platelet count which is a trend seen across various studies; a meta-analysis by Lippi *et al*. (2020) shows that patients with lower platelet counts are seen in severe COVID-19 compared to those with a milder form of the disease. Several other types of research such as Guclu *et al*. found that surviving patients expressed a significantly higher platelet count compared to the expired patients. Data from Wuhan shows that patients with thrombocytopenia have a higher mortality rate than those with normal thrombocyte count and for every 50 x 10⁹ /L increase in platelet there is a 40% reduction in mortality risk [34].

We also found bacterial co-infections and raised AST to be associated with higher mortality. The use of TCZ is known to be associated with, and may have contributed to, both [35, 36]. In our study co-infection was observed

in a total of 12 patients, 10 of whom expired and 2 were discharged. This meant in our study patients who expired were 8.21 times more likely to have suffered a co-infection, specifically bacterial. According to a study by Peng *et al.*, there is a significantly increased risk of fungal co-infection in COVID-19 pneumonia patients receiving tocilizumab [37]. Unfortunately, our study patients were not tested for any fungal co-infection, however, precautionary steps should be taken to prevent all co-infections and in case they do occur, early diagnosis and treatment should be the goal when treating with tocilizumab. Aseptic measures should also be followed within hospitals, applicable to all patient areas, with zero tolerance for ICUs and HDUs. This is even more important for developing countries, such as ours, that suffer from extremely high infection rates in the ICUs [38] as compared to developed countries, such as the USA [39].

Few studies have been conducted locally in Pakistan on tocilizumab use in COVID-19 patients. In a small study from Peshawar a fall of ≥50% in CRP was reported as one of the predictors of a positive response to tocilizumab [40], however in our study, despite a fall in CRP post tocilizumab infusion, there was no significant difference in patient's outcome. Another study from Pakistan showed the benefit of tocilizumab in patients with moderate to severe disease not requiring mechanical ventilation [41]. The same was the case in our setting in which invasive ventilation was associated with poor outcomes.

 We realise the limitations of the present study. First, the clinical characteristics of the included cases may have had gaps in documentation due to the resource limitations of the COVID-19 pandemic. The small sample size, lack of random sampling, non-parametric nature of part of the data, as well as the retrospective and single-center nature of the study make it less than ideal. However, valuable information has been collected which we deem useful in looking at all variables impacting COVID outcomes in a Pakistani hospital setting, including but not exclusive to, the administration of tocilizumab.

CONCLUSION

This study found a marked difference in D-Dimers and LDH between the two groups, being consistently elevated in the expired group, supporting a hypothesis that micro thrombosis may be the cause of death in these patients. Interestingly, D-Dimer's significant difference coincided with TCZ infusion and raises the question of whether these may be used as indicators for early anticoagulation in those given TCZ, but larger studies are needed before a definitive conclusion.

In line with other studies of COVID pneumonia treated with intravenous tocilizumab, our study also showed a significantly higher rate of co-infection in the expired group, therefore we need strict application of aseptic measures and guidelines for minimising the risk of infection in those currently considered for treatment with intravenous tocilizumab in an ICU/HDU setting.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Review Committee of National Hospital and Medical Center, Lahore Cantt (REF letter No. NHMC/ l0H07, dated: 20-07-2011). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR'S CONTRIBUTION

Sumaira Farman: Conceptualization, Data curation, Methodology, Supervision, Writing - review & editing, Writing - original draft.

Madeeha Kamil Habib Raja: Data curation, Formal analysis, Writing - original draft, Writing - review & editing.

Muhammad Kamil Hussain Raja: Data curation, Formal analysis, Writing - original draft, Writing - review & editing.

Syed Daniyal Amjad: Data curation, Formal analysis, Writing - original draft.

Muhammad Ahmed Saeed: Writing - review & editing.

Nadia Majeed: Data Curation.

Nighat Mir Ahmad: Concept of Study, Critical Input, Review.

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ORIGINAL ARTICLE

Changing Trends of Suicide in Punjab from the Year 2016 to 2020: A Comparative Study

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Abstract

Background: Each year, around 800,000 people die by suicide. The world is facing multiple issues related to economic recession and disastrous health conditions. In turn, people must face a high rise in poverty, unemployment, financial crises, and domestic and family issues which are ultimately linked with serious mental health problems.

Objective: The study aimed to get a deeper insight into the prevalence and changing trends of suicide in Pakistan from the year 2016 to 2020.

Methods: This study followed a descriptive approach. The data was collected considering two regionally published newspaper archives. The suicide cases reported from January 2016 to December 2020 were considered only. The data based on age, gender, locality, year, marital status, methods adopted, and reasons to commit suicide were extracted.

Results: A total of 2411 suicide cases were reported in the newspaper based on medico-legal police reports, during those five years. Most of the suicide victims were male with 1434 (59.5%) cases, while 977 (40.5%) were females. The age range was from 10 to 80 years (mean=28.12, SD=10.96). The young adults (19 to 39 years) cases were reported highest, 932 (38.7%), and 238 (9.9%) suicide victims were adolescents (18 years and below). About 47.9% (1153) of suicide victims were married. The most adopted methods for committing suicide were chemical poisoning, strangulation, gunshot, and drowning. Family discord/disputes, failed love affairs, domestic violence, and financial crises including poverty and unemployment were reported as contributing factors to suicide. Further, year-wise differences were also discussed.

Conclusion: The study demonstrates the rise in suicide cases in Pakistan, highlighting the contributing factors that facilitate such a rise. So, with the help of this study, intervention strategies could be devised to deal with the risk factors to control suicide cases in Pakistan.

Keywords: *Suicide, completed suicide, Pakistan, periodical, archives.*

INTRODUCTION

Suicide is one of the leading causes of death around the world and it is estimated that every year about 800,000 people die from suicide referring to one death every 40 seconds. Globally, suicide is the second leading cause of death in youth [1]. Suicide occurs across all regions in the world, however, over three-quarters of global suicides (79%) occur in low- and middle-income countries. Reported rates of suicide in several Asian countries appear to be higher than the average global rates with only two countries China and India [2], while a lower rate was reported in Sri Lanka, Bangladesh, Afghanistan, and Pakistan of the same region. It is estimated that every year, at least 60 million people are affected by suicide or attempt suicide in Asia [3].

The global age-standardized suicide rate was higher in males (12.6 per 100,000) than in females (5.4 per 100,000). For females, the highest rates in countries were above 10 per 100,000, for males they were above 45 per 100,000 [4]. The economic instability of any country can have adverse effects related to job loss, poverty, and unemployment leading to mental health sufferings

like depression, anxiety, stress, *etc.*, mediating suicide attempts and suicides [5, 6].

Pakistan is a low- and middle-income country with an estimated population of 200 million, making it the 6th most populous country in the world [7]. Presently, Pakistan is facing many challenges including poverty, unemployment, Inflation, economic and political instability, and various other unceasing natural and manmade disasters, *etc.* This condition is quite disappointing [8]. Furthermore, there is a rapid increase in suicide cases in Pakistan and the data highlights that about 24% of the total population lives below the national poverty line and 38.8% are poor based on multidimensional poverty, which may result in uncertain disappointing circumstances which sometimes results in suicide [9]. Since Pakistan has no vital registrations for suicidal death and hence lacks accurate figures for death by suicide.

In Islam, suicide is considered a sin, and Pakistani law is solely based on Islamic values, so suicidal behavior and attempts are socially and religiously condemned and considered criminal offenses that are punishable by law, with fines and/or imprisonment, that's a reason it is underreported offense [10, 11]. Furthermore, International Association for Suicide Prevention (2020) issued its policy recommending that attempted suicide

be decriminalized, and preventive measures be taken [12]. This is the reason suicidal behavior remains an under-researched and under-studied subject in many countries including Pakistan.

Considering the above scenario, the present study focuses on 1) the trend of suicides during the last five years *i.e.*, 2016 to 2020, also 2) compares the rate, gender distribution, marital status, age group, and methods adopted in committing suicides as well as reasons for committing suicide. This study is a retrospective psychological autopsy, based on the newspaper reporting on suicide from 2016 to 2020 (five years), which can serve as a foundation for comprehensive suicide prevention efforts in Pakistan. This study can be important for stakeholders to take proactive and coordinated steps to address the contributing factors and save lives.

METHODOLOGY
Study Design and Detailed Procedure
It was a cross-sectional study determining the change in trends of suicide for the last five years from 2016 to 2020. Ethical approval was obtained from the institutional review board of King Edward Medical University, which is affiliated with Mayo Hospital, Lahore before the commencement of the study. For the present study, data was collected through secondary sources *i.e.*, newspaper archives. To investigate the trends of suicide in Punjab, the authors conducted a manual search of two regionally published newspapers (Jang and The News). The newspapers were available in the forensic section of a manual archive at the respective newspaper head office. The articles reporting suicide, based on medico-legal police reports, in the province of Punjab from January 2016 to December 2020 were reviewed only. A total of 2411 deaths were reported due to suicide. The authors opted for a manual search of data as digital records back 5 years were not accurately maintained. To reduce data entry errors, omissions, and duplication in reporting, the authors searched for suicide reports one by one. This process took over 3 months. Two researchers independently reviewed and compared the data several times to ensure accuracy, avoid duplication, and hence record all the data by agreement.

A questionnaire was developed using Google Forms which served as the medium of data entry. The news article was searched for the following 1) the exact date of the act, 2) the name of the reporting newspaper, 3) the area where the suicide was reported, 4) the Age of the deceased 5) Gender, 6) Marital status, 7) Reason for committing suicide as mentioned by the newspaper, 8) Method adopted to commit the act, 9) Psychiatric history, 10) Substance use history, 11) Any other information

reported about the act. Articles with deaths resulting due to suicide were only included in the study. News items reporting suicidal attempts, deliberate self-harm, and homicide were excluded from the research.

Data Analysis
Data was analyzed using software version 22. Descriptive statistics (percentages, mean, SD) were used to describe the data. All the variables were coded as per the relevance of the themes. A Chi-Square test for goodness of fit was applied to see the comparison between the year of committing suicide and other qualitative variables. The significance level was set at $\alpha=0.05$.

RESULTS
Socio-Demographic Characteristics of the Sample
Age and Gender
The current study included 2411 suicidal deaths during five years of the collected data, from January 2016 to the end of December 2020. The age of suicidal victims ranged between 10 to 80 years (mean=28.12, SD=10.96). Out of 1397 reported suicide cases in different age groups, young adult (19 to 39 years) suicide victims reported the highest number of suicides with 932 (38.7%) cases, however 238 (9.9%) suicide victims were adolescents (18 years and below), 193 (8%) suicide victims were middle adults between 40 to 59 years age and 29 (1.2%) cases were of elders with age 60 and above. Most of the suicide victims were male with 1434 cases (59.5%), while 977 cases (40.5%) were females.

Marital Status
From the reported cases, 47.9% of suicide victims were married with 1153 cases and 42.7% were unmarried with 1032 suicide victims, while 25 (1.0%) suicide victims were divorced and 3 (0.1%) were widowed.

Further data showed that almost all the cases were from Punjab Province with a high rate of suicide cases in Districts Lahore and Faisalabad. However, Kasur, Gujranwala, Okara, and Sheikhupura Districts also highlighted high cases of suicide. Further, it was also revealed that in 2018, the highest cases of suicide 533 (22.1%) were reported, with the least difference in cases reported during 2017 and 2020.

Comparison between Year of Committing Suicide and Other Qualitative Variables
The detailed results of the Chi-Square are discussed below in Table **1**.

The results showed significant gender differences over the said period, X^2 (4) = 31.66, p < 0.001, indicating higher suicide cases of males from the year 2017 to 2020. The results of a year-wise comparison of all 1434 male suicide reported cases showed that the highest number

Table 1: Distribution of suicide cases in term of gender and year of committing suicide.

Variable (Gender)	Total (N=2411)	Year					Chi-Square	p-value
		2016 (n=438)	2017 (n=506)	2018 (n=533)	2019 (n=419)	2020 (n=515)		
Male	1434 (59.5)	214 (14.9)	298 (20.8)	349 (24.3)	267 (18.6)	306 (21.3)	31.66	0.000***
Female	977 (40.5)	224 (22.9)	208 (21.3)	184 (18.8)	152 (15.6)	209 (21.4)		

Data is expressed as n(%) df = 4, *** p < 0.001.

Table 2: Year wise distribution of suicide cases in terms of marital status of the suicide victims.

Variable (Marital Status)	Total (N=2411)	Year					Chi-Square	p-value
		2016 (n=438)	2017 (n=506)	2018 (n=533)	2019 (n=419)	2020 (n=515)		
Unmarried	1032 (46.6)	164 (15.9)	203 (19.7)	256 (24.8)	215 (20.8)	194 (18.8)	29.01	0.004
Married	1153 (52.1)	264 (22.9)	228 (19.8)	245 (21.2)	194 (16.8)	222 (19.3)		
Divorced	25 (1.1)	9 (36)	6 (24)	4 (16)	4 (16)	2 (8)		
Widow	3 (0.1)	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	1 (33.3)		

Data is expressed as n(%) df = 12, ** p < 0.01.

Table 3: Year wise distribution of suicide cases in term of age group.

Variable (Age Group)	Total (N=2411)	Year					Chi-Square	p-value
		2016 (n=438)	2017 (n=506)	2018 (n=533)	2019 (n=419)	2020 (n=515)		
Adolescents (18 and below)	238 (17.1)	30 (12.6)	49 (20.6)	70 (29.4)	44 (18.5)	45 (18.9)	46.65	0.000***
Young Adults (19 to 39)	932 (67)	269 (28.9)	202 (21.7)	180 (19.3)	142 (15.2)	139 (14.9)		
Middle Adults (40-59)	193 (13.9)	52 (26.9)	33 (17.1)	42 (21.8)	30 (15.5)	36 (18.7)		
Elders (60 and above)	29 (2.1)	1 (3.4)	6 (20.7)	5 (17.2)	9 (31)	8 (27.6)		

Data is expressed as n(%) df = 12, *** p < 0.001.

of male suicide cases were reported (n=349, 24.3%) in 2018 while minimal, 14.9% cases (n=214) were reported in the year 2016. Further year-wise comparison of all the 977 reported female suicide cases indicated that the highest number of female suicide cases (n=224) with 22.9% were reported in 2016, while the least number of female suicide cases (n=152) with 15.6% were reported 2019.

The results showed year-wise differences in terms of the marital status of the suicide victims, X^2 (12)=29.01, p < 0.001, indicating the highest cases of married suicide victims during these years (**Table 2**). About 1153 reported suicide cases from year 2016 to 2020 were married with the highest deaths 22.8% (n= 264), reported in year 2016, and the least cases about 16.8% (n=194) were reported in 2019, while during 2018, 21.2% (n= 246) of all the reported cases were married, 19.2% (n=222) during 2020, and 19.6% (n=230) of all the reported married cases were reported in 2019. Further results revealed during the years 2016 to 2020 as per reported cases, 1032 unmarried individuals committed suicide, highest 20.8% of the cases (n=256) were reported in 2018 while the least cases 15.9% (n=164) were reported in 2016. Further results revealed that from 2016 to 2020, 25 divorced individuals committed suicide with the highest cases of 36% of divorced suicide victims (n=9) in 2016,

6 cases (24%) in 2017, 4(16%) in 2018, and 2019 each, and 2 cases with least number (8%) were reported in 2020. Further during the said years 3 widowed suicide cases were reported with one case each in 2017, 2018, and 2020.

The results also showed year-wise differences in terms of the age group of the suicide victims, X^2 (12)=29.01, p<0.001, indicating the highest cases of the young adult group during these years (**Table 3**). The results highlighted that during the years 2016 to 2020, 932 young adults committed suicide. Out of these 932 reported cases of young adults, the highest cases (n=269) with 28.9% reported in 2016 and with the lowest rate in 2020, 139 cases (14.9%) were reported. The results also revealed that from 2016 to 2020, about 238 adolescents committed suicide which was the second-highest suicide number among all age groups with the highest cases (n=70) at 29.4% in 2018, 30 cases (12.6%) in 2016, 49 cases (20.6%) in 2017, 44 cases (18.5%) in 2019 and 45 cases (18.9%) in 2020 as per newspaper reported cases of all the adolescents. Further, middle adults were in the third highest number with 193 total cases from 2016 to 2020. The yearly distribution revealed that in 2016, the highest 52 suicide cases (26.9%) of middle adults were reported. Further, 33 cases (17.1%) in 2017, 42 cases (15.5%) in 2018, 30 cases (15.5%) in 2019, and 36 cases

Table 4: Year wise distribution of suicide cases in term of methods adopted for committing suicide.

Variable (Methods Adopted for Committing Suicide)	Total (N=2411)	Year					Chi-Square	p-value
		2016 (n=438)	2017 (n=506)	2018 (n=533)	2019 (n=419)	2020 (n=515)		
Acid/ corrosive intake	39 (1.6)	11 (28.2)	7 (17.9)	8 (20.5)	6 (15.4)	7 (17.9)		
Drowning	126 (5.2)	35 (27.8)	25 (19.8)	25 (19.8)	16 (12.7)	25 (19.8)		
Gunshot	324 (13.4)	76 (23.5)	56 (17.3)	64 (19.8)	64 (19.8)	64 (19.8)		
Hanging	28 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	9 (32.1)	19 (67.9)		
Jumped	92 (3.8)	25 (27.2)	16 (17.4)	18 (19.6)	16 (18.5)	16 (17.4)		
Chemical Poisoning	1228 (50.9)	197 (16)	296 (24.1)	286 (23.3)	202 (16.4)	247 (20.1)	105.51	0.000***
Self-immolation	60 (2.5)	12 (20)	15 (25)	14 (23.3)	6 (10)	13 (21.7)		
Self-inflicted cut/ Injury	22 (0.9)	5 (22.7)	2 (9.1)	6 (27.3)	3 (13.6)	6 (27.3)		
Strangulation	488 (20.2)	76 (15.6)	89 (18.3)	111 (22.8)	96 (19.8)	114 (23.5)		
Not Mentioned	6 (0.2)	1 (16.7)	0 (0)	1 (16.7)	0 (0)	4 (66.7)		

*Data is expressed as n(%) df = 36, *** p < 0.001.*

Table 5: Distribution of suicide cases in terms of reasons and year of committing suicide.

Variable (Reasons for Committing Suicide)	Total (N=2411)	Year					Chi-Square	p-value
		2016 (n=438)	2017 (n=506)	2018 (n=533)	2019 (n=419)	2020 (n=515)		
Chronic Health issues	41 (1.7)	14 (34.1)	10 (24.4)	10 (24.4)	5 (12.2)	2 (4.9)		
Domestic Violence	215 (8.9)	25 (11.6)	53 (24.7)	46 (21.4)	29 (13.5)	62 (28.8)		
Failed Love Affair	170 (7.1)	56 (32.9)	35 (20.6)	30 (17.6)	34 (20)	15 (8.8)		
Divorced	78 (3.2)	26 (33.3)	13 (16.7)	12 (15.4)	19 (24.4)	8 (10.3)		
Family Discord/ Disputes	1155 (47.9)	187 (16.2)	263 (22.8)	279 (24.2)	192 (16.6)	234 (20.3)		
Lack of Tolerance	14 (0.6)	0 (0)	5 (35.7)	2 (14.3)	4 (28.6)	3 (21.4)	177.00	0.000***
Marital Discord	21 (0.9)	0 (0)	3 (14.3)	2 (9.5)	5 (23.8)	11 (52.4)		
Poverty	205 (8.5)	47 (22.9)	36 (17.6)	38 (18.5)	34 (16.6)	50 (24.4)		
Mental illness	56 (2.3)	2 (3.6)	10 (17.9)	26 (46.4)	9 (16.1)	9 (16.1)		
Unemployment	102 (4.2)	35 (34.3)	16 (15.7)	15 (14.7)	20 (19.6)	16 (15.7)		
Not mentioned	354 (14.7)	46 (13)	62 (17.5)	73 (20.6)	68 (19.2)	105 (29.7)		

*Data is expressed as n(%) df = 40, *** p < 0.001.*

(18.7%) in 2020 were reported as per reported suicide cases of all the middle adults. The results revealed that from 2016 to 2020, about 29 older adults committed suicide with the highest death rate of 9 cases (31%) in 2019, 8 cases (27.6%) in 2020, 6 cases (20.7%) in 2017, 5 cases (17.2%) in 2018 and 1 case (3.4%) in 2016 as per suicide reported cases of older adults.

The results also showed year-wise differences in terms of methods adopted to commit suicide, X^2 (36)=105.51, p<0.001, indicating the highest cases of chemical poisoning and strangulation during these years (**Table 4**). The year-wise distribution of suicide for the method adopted to commit suicide indicated that 1228 cases of chemical poisoning were reported from 2016 to 2020. Out of all the suicides using chemical poisoning, 197 cases (16%) in 2016, 296 cases (24.1%) in 2017, 286 cases (23.3%) in 2018, 202 cases (16.4%) in 2019, and 247 cases (20.1%) in 2020 were reported in the newspaper. Strangulation was the second most used method for committing suicide with 488 cases from 2016 to 2020. As per reported cases, in 2020 highest (23.5%) cases of suicide (n=114) were reported using the strangulation

method, 111 cases (22.8%) in 2018, 96 cases (19.8%) in 2019, 89 cases (18.3%) in 2017, and 76 cases (15.6%) in 2016 were reported in the newspaper. The results showed that gunshots were the third most adopted method for committing suicide with 324 cases from 2016 to 2020. Out of all the 324 suicide cases, 76 cases with the highest number (23.5%) were reported in 2016, 56 cases (17.3) in 2017, and 64 cases with 19.8% were reported in 2018, 2019, and 2020. Drowning was another most adopted method to commit suicide with 126 reported cases from 2016 to 2020. The year-wise comparison revealed that 35 cases (27.8%) in 2016 with the highest number, 25 cases (19.8%) in 2017, 2018, and 2020, and 16 cases (12.7%) in 2019 with the lowest number were reported suicide cases using drowning. Jumping in front of a train/ from a bridge was the other method adopted to commit suicide with 92 reported cases. Out of all these 92 suicide cases using the jumping method, 25 cases (27.2%) in 2016, 18 cases (19.6%) in 2018, and 25 cases (17.4%) each in 2017, 2019, and 2020 were reported in newspapers. Further self-immolation was the other method of suicide with 60 reported cases from 2016 to 2020. Out of these

60 suicide cases using self-immolation, 15 cases (25%) in 2017, 14 cases (23.3%) in 2018, 13 cases (21.7%) in 2020, 12 cases (20%) in 217, and 6 cases (10%) in 2019 were reported in newspapers. Further acid/corrosive intake, hanging, and self-inflicted injury were also the methods that were used to commit suicide, but the number of suicide deaths was relatively lower than other mentioned methods during these years.

The results also showed year-wise differences in terms of reasons to commit suicide, X2 (40) = 177.00, p<0.001, indicating high suicide cases due to family discord/ disputes, poverty, and domestic violence from 2016 to 2020 (**Table 5**). The results indicated that about 1155 individuals committed suicide just because of family discord/ disputes from 2016 to 2020. Out of these 1155 suicide cases, 279 cases (24.2%) in 2018, 263 (22.8%) in 2017, 234 cases (20.3%) in 2020, 192 cases (16.6%) and 187 cases (16.2%) in 2016 were reported as per newspaper suicide cases with reason of family discord/ disputes. Domestic violence was the second highest reason for committing suicide with 215 reported cases. The year-wise distribution of suicides due to domestic violence reasons indicated that 62 cases (28.8%) in 2020, 53 cases (24.7%) in 2017, 46 cases (21.4%) in 2018, 29 cases (13.5%) in 2019 and 25 cases (11.6%) in 2016 were reported. Poverty was the third highest reason for suicide with 205 reported cases from 2016 to 2020. The year-wise distribution of suicides due to poverty reasons indicated that 50 cases (24.4%) in 2020, 47 cases (22.9%) in 2016, 38 cases (18.5%) in 2018, 36 cases (17.6%) in 2017 and 34 cases (16.6%) in 2018 were reported. Further, results revealed that a failed love affair was also a reason for committing suicide with 205 reported cases. Year-wise distribution of suicide cases due to reason of failed love affair highlighted 56 cases (32.9%) in 2016, 35 cases (20.6%) in 2017, 34 cases (20%) in 2019, 30 cases (17.6%) in 2018 and 15 cases (8.8%) in 2020 were reported. Unemployment was also a reason for committing suicide with 102 reported cases. The results indicated that the highest, 35 individuals committed suicide (34.3%) in 2016 while 20 cases (19.6%) in 2020, 16 cases (15.7%) in 2017 and 2020, and 15 cases (14.7%) in 2018 with the least number were reported due to unemployment. Further data indicated that divorce was also a reason for committing suicide with 78 cases. The distribution of these 78 cases over these years indicated that 26 suicides (33.3%) in 2016, 19 suicides (24.4%) in 2019, 13 suicides (16.7%), 12 suicides (15.4%) in 2018, and 8 suicides (10.3%) in 2020 with the least number were reported in the newspaper. Furthermore suicides due to health conditions such as chronic health issues (n=41) and Mental illness (n=56)

were also the reasons for committing suicide with the highest cases during 2016 and 2018 respectively. Further, Marital discord (n=21) and lack of tolerance (n=14) were also reported as the reason for suicide with the highest cases in 2020 and 2017 respectively.

DISCUSSION

In Pakistan, social problems such as poverty, deprivation, unemployment, lack of law & order, injustice, *etc.* are factors that lead to stress and other mental health problems. Out of this some people become clinically depressed & get on the suicidal pathway [10]. Punjab is the second largest province of Pakistan, with a population of about 110,000,000 as of 2021 [13]. Understanding the trends of suicide in a diverse province such as Punjab and with the available data was quite a challenge. This study was the first attempt to gather and analyze province-wide data on suicide through medicolegal police records which made it to the regional newspapers. The greatest number of total reported suicides was in the year 2018 (n=533) and the least total number was reported in the year 2019 (n=419). The authors believed that these numbers are not representative of any factual findings as the exact number of actual suicide cases in Punjab is far less than the reported ones in police records which ultimately make it to the printed News. A few factors which contribute to underreporting are 1) criminal penalty associated with suicidal attempts and suicide 2) associated stigmatization with suicidal death as Islam denounces suicide and calls it the forbidden 'sin' 3) National suicide statistics are not compiled on a formal level nor officially reported to the World Health Organization by Pakistan, and 4) national newspaper archives are not digitalized [14].

Overall, the findings highlighted that a greater number of men (59.5%) died by suicide as compared to females during the years 2016 to 2020. This trend is like the USA or European countries where male suicides far outnumber female suicides (3:1 or 4:1) [15]. This finding concludes that either 1) men used more lethal ways of dying by suicide or 2) men have more risk factors (psychiatric illness, unemployment, and substance use) that led to suicide. Men's deaths by suicide were reported high during the said duration, which could correlate to the economic instability and inflation in the country due to COVID-19 pandemic. It is also worth mentioning that poverty, unemployment, domestic violence, and family discord were listed as major causes of suicide. In the present study, the age group in which the maximum number of deaths by suicide was reported in the news was young adults (19 to 39 years). It could be the fact that the youth face adversities like poverty,

academic failures, rejection in love, pressures to be social in the social media age, emotional/ sexual abuse, and unemployment. The United Nations Development Programme report (2020) states that four million youngsters enter the working-age population and only 39 percent get employed every year [9]. This age group also coincides with the traditional age for marriage in the Pakistani population and more than half of the suicide cases in our data were of married individuals (52.1%). Therefore, marriage cannot be counted as a protective factor for our study population as compared to the Western data. Cultural attitudes like arranged marriages, dowry-related demands, social pressure to stay married despite being in an abusive relationship, and stigma related to divorce can be common factors leading to suicide in the married population [16]. South-Asian families have traditionally lived in joint or extended family systems where a symbiotic relationship exists; however, since the last decade, social transformation and globalization have changed the role of the family and the relationships between the individual and the family. Interpersonal conflicts, particularly those with family members, are usually reported in regional literature [17]. It is hence understandable why news articles listed family discord/ disputes as the most common cause of suicide (47.9%). The results are also confirmed by previous literature highlighting that the causes of suicide in Pakistan are generally, relationship problems, domestic disputes, and financial problems [18- 20].

Furthermore, chemical poisoning (50.9%) especially with organophosphate pesticides followed by strangulation due to hanging (20.2%) was the most common method of suicide reported in the news from 2016 to 2020. Gunshots and jumping in front of a train were also common methods. Vijayakumar *et al.* (2013) succeeded in testing the feasibility of a centralized pesticide storage facility [21]. Recent publications show the use of *Kala Pathar* (Paraphenylenediamine, PDD) as a substitute for pesticides which are rather difficult to purchase after multiple reports of misuse [8]. Another study by Safdar *et al.* (2021) reported that organophosphate poisoning was reported from all the provinces of Pakistan. However, 60% of cases of organophosphate poisoning were reported from North Punjab and interior Sindh, while aluminum phosphide (wheat pill) poisoning was reported mainly from North Punjab and North KPK, whereas paraphenylenediamine (*kala pathar*) was primarily used in suicide from South Punjab, with some reports from South KPK and interior Sindh. Their findings also reported that in rural populations pesticides and paraphenylenediamine were most common, while the urban population chose

more varied agents for overdose, including household chemicals (bleach, corrosives), medicines (sedatives, tranquilizers, NSAIDs, antidepressants), rat poison pills and other toxic substances [22, 23]. It is to conclude that the utmost urgent efforts are required by National policymakers to restrict access to other highly lethal means (Acids, wheat pills, rat pills, benzodiazepines firearms, *etc.*) to prevent suicides. A few news articles (0.2%) did not comment on the method used for suicide and kept most of the information general, which is in line with the international publication guidelines for reporting suicide cases. However, these news reports did not follow other important recommendations which included using appropriate terms, providing resources to readers, identifying risk factors like mental health issues or substance use, and asking for expert opinion from mental health professionals. In more than half the news articles analyzed for this research, past psychiatric history and substance use were not mentioned. It was also observed that the police medico-legal reports and newspapers use a reductionist approach in reporting risk factors *i.e.*, mentioning proximal factors and ignoring distal factors.

There are certain limitations in the present study. It relies on newspapers' reporting of suicide, therefore suicide rates deduced cannot be a true representation of actual population statistics, for future studies data from hospitals and police stations should also be considered. In the present study, the data were collected using two regionally published newspapers, which is why it is solely representative of only one province's data, for future studies to get the overall data on suicide in Pakistan, the representative newspapers of other provinces should also be considered. Further, a region-wise comparative study should also be done.

CONCLUSION
The current study shows that men had highest the rate of suicide than women in Punjab. It was found that suicidal deaths were associated with family discord, domestic violence, financial instability, and relational issues. The findings concluded that most adopted methods of committing suicide included chemical poisoning, strangulation, and gunshot. It was also found that suicidal deaths were most prevalent in young adults and adolescents. It is therefore extremely important to pursue further research studies on suicide deaths as well as to devise strategies to control this public health issue.

IMPLICATIONS OF STUDY
Our study points out disparities in available data, yet it identifies various correctable issues which are: National statistics on suicide mortality should be gathered in the

upcoming census of 2022. Further, decriminalization of suicide; The World Health Organization's Comprehensive Mental Health Action Plan (2021-2030) has decriminalizing suicide as an important target, seeking to end criminalization, however the bill to remove legal penalty from suicide was recently deferred in December 2021 by the Senate in Pakistan seeking advice from the Islamic ideological council in this matter. Further, it is recommended that the teaching and training of journalists according to internationally accepted guidelines on the reporting of suicide should be prioritized as media can create a significant difference in the mindset of masses through sensitive reporting. These findings could help raise public awareness about prevention strategies and the importance of seeking professional help using mass and social media. These findings emphasize the urgent need to define methods to screen at-risk individuals and implement local and national initiatives to curb their potential detrimental effects. Furthermore, suicide prevention strategies should broaden their narrative to include relational, community, and social interventions as anti-suicide measures. In summary, this study serves as an important source of information for policymakers, healthcare providers, and mental health advocates in Pakistan. It underscores the need for comprehensive approaches to address the rising rates of suicide by targeting the contributing factors and implementing effective prevention and support measures.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Review Board of King Edward Medical University, Lahore (REF letter No. 2/89/RC/KEMU Dated: 16/12/2019). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

The data was collected from published newspaper archives, so consent for publication was not required.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

CONFLICT OF INTEREST

The author(s) declare no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

ACKNOWLEDGEMENTS

AUTHOR'S CONTRIBUTION

Prof. Dr. Aftab Asif: Conception, Design, Supervision and Review.

Ms. Sumaira Ayub: Design, Statistical Analyses, and interpretation, Write-up.

Dr. Irum Aamer: Data Collection, Write-up, Review.

Dr, Usama Ali. Cheema: Data Collection, Write up.

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ORIGINAL ARTICLE

Associated Risk Factors with Tooth Wear in Patients Attending Private Dental Hospital in Karachi: A Cross-Sectional Study

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Abstract

Background: Tooth wear is non-carious enamel and dentinal destruction with multi-factorial etiology affecting oral health-related quality of life. Identification of risk factors and their prevention are crucial in the management of such cases.

Objective: To determine risk factors associated with tooth wear in patients attending private dental hospital.

Methods: A cross-sectional study was conducted from February to July 2023. Non-probability consecutive sampling was done. Patients with tooth wear were identified according to Smith and Knight Criteria of tooth wear. Patients with tooth wear were interviewed on a modified questionnaire to identify further associated risk factors. Data was entered and analyzed in SPSS version 22. Descriptive statistics were used for categorical variables. Univariate and multivariate logistic regression were used to determine predictive factors associated with tooth wear. Crude and adjusted Odds ratios with 95% confidence intervals were used to measure association. P-values < 0.05 were considered statistically significant.

Results: Overall, 755 patients were examined and participated in the study accounting for a 98% response rate. 62.6% were males and 37.4% were females with an age range of 18-65 years. Tooth Wear was present in 75.6% of participants with 58.8% erosion, 31.5% attrition, and 6.1% abrasion cases. 3.5% of patients demonstrated more than one type of TW. Carbonated drinks showed a higher risk of tooth wear, followed by bruxism, gastric problems, and aggressive tooth brushing.

Conclusion: Associated risk factors of tooth wear should be given due consideration to implementing patient education and preventive strategies to preserve dental health.

Keywords: *Tooth wear, tooth surface loss, risk factors, bruxism.*

INTRODUCTION

Tooth wear (TW) or tooth surface loss (TSL) is a subtle, multifactorial condition that involves non-carious enamel and dentinal destruction which can threaten tooth survival and also affect oral health-related quality of life [1]. TW seems to impact different age groups and both genders [2, 3]. It is often intricate to find out if TW is pathological or age-dependent *i.e*., physiological. The cause of pathological TW involves physical and thermo-physical processes which are attrition, erosion, abrasion, and abfraction. Some evidence suggests that tooth wear is age-dependent [4]. However, in literature TW seems to be increasingly common amongst younger age groups and, as these people will retain their teeth into old age, it is imperative that wear is identified quickly and managed appropriately [1-6].

TW may yield various patterns that commonly occur simultaneously, complicating analysis and management even further. Severe TW may lead to hypersensitivity, reversible and irreversible pulpitis, gingivitis, and periodontitis which can negatively impact esthetics and function [5]. Continued TW may generate or propagate cracks or fractures of the tooth which can lead to subsequent tooth loss [6]. Esthetically, the loss of enamel due to TW may also increase the visibility of the underlying dentine, producing discoloration [7]. In extreme cases, pulpal exposure can occur, further complicating management [8]. Conservation of loss of tooth tissue is often substantial and the need to restore remaining tooth structure is vital [8].

TW prevalence is increasing globally as a result of changes in diet, modified lifestyles, and lack of awareness [9, 10]. In literature, the prevalence of tooth wear in the United Kingdom is reported as 29% [11], Germany as 23.4% [12], Brazil as 38.2% [13], Indonesia as 23% [14], and Jordan as 51% [15].

TW is reported to have a multifactorial etiology where identification of risk factors and implementation of related preventive strategies are keystones in management [1-6]. Although studies have been conducted on the Pakistani population highlighting the prevalence of TW the causative factors associated with TW have not been explored much specifically in the population of Karachi [16-18]. Diversity in demographics, lifestyle, dietary habits, parafunctional habits, and oral health behaviors in the local context as compared to the global population

warrants the need for further investigation. Thus this study is aimed to determine the associated risk factors with TW in our population. Regular assessment of risk factors can help in designing accurate dental health programs which will raise public awareness related to prevention according to the needs of specific populations thus promoting oral health. This can also help dental clinicians identify patients early and design an accurate management plan for TW.

MATERIAL AND METHODS

A cross-sectional study design was adopted to achieve the study objective. The duration of the study was six months conducted from 1st February to 31st July 2023. The study was carried out in a private institute Hamdard Dental Hospital, Karachi. The study proposal was reviewed by the Scientific Review Committee of Hamdard University Dental Hospital, under Hamdard University which provided institutional approvals. (IRB Approval letter number: 1025-01-23).

A sample size of 770 was selected using a non-probability consecutive sampling technique. The online "calculator. net" for sample size calculation was used to compute a minimal number of participants to meet the desired statistical constraints. To calculate sample size the frequency of carbonated drink consumption identified as an associated factor with TW in a previous study reported as 78% was considered [19]. Confidence level of 95% was taken and with absolute precision of ±3%, the sample size calculated was 732. To account for non-respondents and potential missing data, we have increased the sample size by 5%. Therefore, the estimated sample size for the study was set at n=770.

The study team included the principal investigator and four house officers in the Operative and Endodontic Department at Hamdard University Dental Hospital. Data collectors received thorough training from the principal investigator. To maintain data quality and reliability, the principal investigator performed both field editing and office editing daily, carefully reviewing the collected information for any missing or incorrect entries.

In the initial step before the data collection procedure, examiners explained to the patients the aims and details of the study and assured them that their relevant information would be kept confidential. Patients between the ages of 18 and 65 years who presented with complaints of dental pain and sensitivity were included in the study (assessed on the Visual Analogue Scale with a score of 3 or greater) [7] whereas patients with dental developmental defects, history of trauma or grossly carious dentition were excluded from the study. Patients' written consent was obtained before being recruited into the study.

History and clinical presentation were used to determine TW. The methodology described by Smith and Knight [20, 21] was followed for clinical assessment to identify patients with TW (**Table 1**). Clinical examination was carried out using intra-oral examination instruments under the dental operating light. Patients identified with TW were then interviewed a modified comprehensive questionnaire adopted from previous studies [21, 22]. The questionnaire was designed to target the evaluation of risk factors of all types of tooth wear. It included questions related to demographic data such as (Name, Gender, Age, and Education) and dental history (Past dental history, Brushing, frequency of brushing, nighttime grinding *i.e.*, bruxism, nail biting, pen biting). It also included the patient's relevant medical history such as gastrointestinal problems and smoking.

Data was entered and analyzed using SPSS version 22 software. To maintain the confidentiality of the data, a hard copy was securely stored in a locked location, while the SPSS files were saved on a password-protected personal computer that only the principal investigator could access. Unique identifiers were given to each patient's form to maintain privacy. As dependent and independent variables were categorical, descriptive statistics *i.e.*, frequency and percentage were used for describing the study variables like gender, educational status, presenting complaint, past dental history, tooth wear, tooth wear type, and factors responsible for TW. Further, univariate and multivariate logistic regression were used to determine the predictive factors associated with tooth wear. In the first step, an association of each independent variable with the dependent variable was assessed. In the second step, variables significant at a p-value of less than or equal to 0.20 in the univariate analysis were included in multivariable logistic regression. Crude and adjusted Odds ratios with 95% confidence intervals were used to measure association. P-values of less than 0.05 were considered statistically significant. The final model was constructed using backward elimination; variables were retained if the p-value was less than 0.05. The calculated final model represented statistically significant risk factors that are associated with the dependent variable.

Table 1. Smith and Knight Tooth Wear Index.

Surface	Criteria	Score
Buccal/Lingual/Occlusal/Incisal	No loss of enamel surface characteristics	**0**
Contour	No loss of contour.	
Buccal/Lingual/Occlusal/Incisal	Loss of enamel surface characteristics.	**1**
Contour	Minimal loss of contour.	
Buccal/Lingual/Occlusal	Loss of enamel exposing dentine for less than one-third of the surface.	**2**
Incisal	Loss of enamel just exposing dentine. Defect less than 1 mm deep.	
Contour	Defects less than 1 mm deep	
Buccal/Lingual/Occlusal	Loss of enamel exposing dentine for more than one-third of the surface.	**3**
Incisal	Loss of enamel and substantial loss of dentine.	
Contour	Defects less than 1-2 mm deep	
Buccal/Lingual/Occlusal	Complete enamel loss - pulp exposure - secondary dentin exposure.	4
Incisal	Pulp exposure or exposure to secondary dentine.	
Contour	Defect more than 2mm deep - pulp exposure - secondary dentine exposure	

RESULTS

A total of 755 patients were examined and participated in the study accounting for a 98% response rate. The variables categorized as the demographics (gender, age, and education), dental characteristics (presenting complaint, duration of presenting complaint, past dental history, and the study outcome variable tooth wear and type of tooth wear), oral health behavior (brushing, frequency of tooth brushing, pan/gutka, carbonated drink, smoking), parafunctional habits (bruxism, nail biting, pen biting) and systemic condition (gastric problem).

Demographic Characteristics of Study Participants

The male and female distribution of our study is presented in Table **2**. The age range of participants in our study was 18 to 65 years. Further categorization of different age groups is also presented in Table **2**. Most participants had more than 10 years of education 613 (81.1%).

Dental Characteristics of Study Participants

Among the participants, 474 (62.8%) were presented with complaints of pain and 281 (37.2%) with sensitivity, and the maximum duration of their presenting complaint was 1 or more than one month 539 (71.4 %). The majority had a past dental history of previous dental treatment 488 (64.7%) (**Table 2**).

Table 2: Independent Variables – Demographic and Dental characteristics.

Demographic Characteristics	n	%
Gender		
Male	473	62.6
Female	282	37.4
Age (years)		
18-25	61	8.1
26-35	195	25.8
>36	499	66.1
Education		
1-10	142	18.5
>10 years	613	81.5
Dental Characteristics		
Presenting Complain		
Pain Complain	474	62.8
Sensitivity Complain	281	37.2
Duration of Complain		
2 weeks	34	4.5
4 weeks	182	24.1
>1 month	539	71.4
Past Dental History		
Yes	490	64.9
No	265	35.1

Dependent Variable- Tooth Wear

The outcome variable *i.e.*, TW was present in 571 (75.6%) participants. Among them, 336 (58.8%) showed erosive type of TW, 180 (31.5%) patients demonstrated attrition, and 35 (6.1%) showed abrasive type. However, 20 (3.5%) patients demonstrated more than one type of TW. Table **3** presents the frequency and percentages of dependent variables for tooth wear. **Fig. (1)** presents a case of tooth wear (primary attrition and secondary erosion) recorded in our study.

Table 3: Dependent Variable – Tooth Wear.

Variable	n	%
Tooth Wear		
No	184	24.4
Yes	571	75.6
Type of Tooth Wear		
Erosion	336	58.8
Attrition	180	31.5
Abrasion	35	6.1
More than one type	20	3.6

Fig. (1): Case of tooth wear.

Oral Health Behavior and Dental Habits

Table **4** shows the independent variables of our study *i.e.*, oral health behavior and dental habits. The most common parafunctional habit was bruxism (38%) followed by biting objects (nail; 11.9%, pen: 4.5%).

Univariate Logistics Regression

Table **5** shows the unadjusted odd ratio (UOR), 95% CI, and p-values of univariate analysis of each independent variable associated with tooth wear. Age group 26-35 had an odds ratio indicating lower odds of tooth wear compared to 18–25-year category. Similarly, individuals above the age of 36 had an odds ratio suggesting reduced odds of tooth wear compared to the 18-25 years reference category. There was no statistically significant association observed between education levels and tooth wear. The odds suggest that there was no meaningful difference in

Table 4: Independent Variables - Oral Health Behavior and Habits.

Variable	n	%
Frequency of Brushing		
No brushing	222	29.5
Less than once daily	50	6.6
Once or Twice daily	390	51.7
Thrice or more daily	93	12.2
Aggressive Brushing		
No	222	29.4
Yes	533	70.6
ByPan Eating		
Yes	256	33.9
No	499	66.1
Carbonated Drink		
Yes	562	74.4
No	193	25.6
Smoking		
Yes	137	18.2
No	618	81.8
Bruxism		
Yes	355	47.1
No	400	52.9
Nail Biting		
Yes	90	11.9
No	665	88.1
Pen Biting		
Yes	34	4.5
No	721	95.5
Systemic Condition- Gastric Problem		
Yes	453	60
No	302	40

the odds of tooth wear between individuals with 1-10 years of education compared to participants having more than 10 years of education. The odds of tooth wear were not associated with pain and sensitivity complaints. There was a statistically significant association observed between the duration of complaint of more than 1 month and the tooth wear. Participants who had past dental treatment history were two times more likely to have tooth wear compared to those who didn't visit any dentist. The results of the frequency of brushing, pan, and smoking were not significant. The odds ratios and their corresponding confidence intervals suggest that there is no meaningful difference in the odds of tooth wear in these categories.

Participants who had parafunctional habits showed higher odds of tooth wear than those who did not have these habits. Carbonated drinks showed an 8 times higher risk of tooth wear followed by bruxism, gastric problems, and aggressive tooth brushing.

Table 5: Univariate and Multiple Logistic Regression risk factors associated with tooth wear.

Variable	Univariate Logistics Regression[¥]			Multiple Logistics Regression[€]		
	95%C.I	OR	*P-Value*	95%C.I	aOR[a]	*P-Value*
Aggressive Brushing						
No	-	Ref	-	-	Ref	-
Yes	(5.896-14.237)	8.207	<0.001*	(17.44-52.32)	35.46	<0.001*
Carbonated Drinks						
No	-	Ref	-	-	Ref	-
Yes	(4.237-15.896)	8.207	<0.001*	(16.34-40.12)	35.46	<0.001*
Bruxism						
No	-	Ref	-	-	Ref	-
Yes	(8.489-31.66)	16.394	<0.001*	(27.37-61.21)	55.15	<0.001*
Gastric Problem						
No	-	Ref	-	-	Ref	-
Yes	(1.311-21.68)	4.602	0.021*	(11.50-62.84)	21.10	<0.001*

[¥]*p value ≤ 0.20 statistically significant in the univariate analysis,* [€]*p value <0.05 statistically significant in the multivariate OR=Odds ratio, Ref=Reference category,* [a]*Adjusted for gender and age, *statistically significant.*

Multivariate Logistics Regression

When adjusted in the multivariate model at p values less than 0.05, variables such as carbonated drink, bruxism, gastric problems, and aggressive tooth brushing were found to have a statistically significant association with tooth wear. However, variables such as past dental history and duration of presenting complaint were not statistically significant with tooth wear.

DISCUSSION

The present study aimed to identify the risk factors associated with TW in patients attending a private dental hospital in Karachi, Pakistan. Overall, the occurrence of TW was high in the study setting. The univariate logistic regression analysis provided initial insights into the relationship between various independent variables and tooth wear. The subsequent multivariate logistic regression analysis adjusted for confounding factors and identified the significant predictors of TW. In our investigated sample, the use of carbonated drinks, bruxism, gastric diseases, and aggressive tooth brushing were found to have a significant association with TW.

The frequency of presentation of TW in our study was found to be 75.6%. Sahab [16] investigated a sample of 250 participants and reported a high prevalence rate of TW at 92.4% among patients attending a dental hospital in Karachi. Contrary to this, Toufique et al. [22] reported 10% of cases presenting with TW in their study conducted in Karachi in a sample of 400 participants.

In literature, the most reported risk factors that contribute to TW are parafunctional activities, gastrointestinal problems, oral health behavior, dietary habits, medicaments, and acid regurgitation [1, 18-20, 23]. Carbonated drinks, a dietary factor, were found to be significantly associated with TW in our study. Participants who consumed carbonated drinks had a substantially higher risk of TW compared to those who did not. A study found that acidic drinks were the most common factor associated with TW [19]. In our study also patients The erosive properties of carbonated drinks, attributed to their high acidity and sugar content, can contribute to enamel erosion and tooth wear over time [24]. Dental practitioners should educate patients about the potential harm of excessive carbonated drink consumption and encourage moderation to preserve dental health.

In our study, parafunctional habits, including bruxism were found to be strongly associated with increased odds of TW. Bruxism, characterized by grinding or clenching of teeth, was found to increase the odds of TW by a substantial magnitude. Patients with a history of bruxism were associated with increased pathological wear [24]. These findings highlight the detrimental effects of parafunctional habits on tooth structure and emphasize the need for interventions to manage and mitigate these behaviors.

Gastric problems were also statistically significant in our study. It is worth noting that they are a potential risk factor for tooth wear. Gastric issues, such as acid reflux or gastroesophageal reflux disease (GERD), can result in acid regurgitation into the oral cavity, leading to enamel erosion and tooth wear. Patients with GERD show an increase in tooth wear scores due to the regurgitation of gastric acidic contents into the oral cavity [17, 25]. In our study, 60% of patients gave a history of gastric problems including GERD. Yanushevich [26] in their

meta-analysis reported that dental erosion in patients having GERD is observed commonly and is often seen in about half of the cases of GERD. In the literature the reported prevalence of patients with GERD having dental erosion wear ranges between 24%-51.52% [26, 27]. In Pakistan prevalence of dental erosion in GERD patients is reported as 35.3% by Warsi [28] and 44.16% by Iqbal [29]. Further research with a larger sample size is needed to ascertain the association between different gastric problems and tooth wear more accurately.

Our finding also highlights the importance of oral hygiene practices such as aggressive tooth brushing in influencing tooth wear. 70.2% of patients in our study reported practicing aggressive tooth brushing which was then confirmed with the presence of clinical signs of non-carious cervical lesions on examination. Penoni reported that 39.5% of patients in their study were practicing harmful aggressive toothbrushing [30]. Alam [31] in their study conducted at a tertiary care hospital setting in Pakistan noted hard bristles and variable tooth brushing movements to be significantly associated with non-carious cervical lesions [27]. Also in our study, past dental treatment of restorative work emerged as a significant predictor, with participants who had a history of dental visits being more likely to have tooth wear. This finding indicates that individuals who sought dental care in the past may have pre-existing dental conditions or behaviors that contribute to tooth wear. Dentists often use 'aesthetic' indirect restorations such as porcelain or ceramics irrespective of whether the restoration is visible. These materials have the potential to accelerate tooth surface loss, particularly if used on occluding surfaces in parafunctional patients [32, 33]. The specific factors within dental history that may contribute to tooth wear, such as previous dental treatments or oral habits, were not examined in this study and warrant further exploration.

Exploration of risk factors related to tooth wear in our study provides evidence to propose recommendations for future experimental and large-scale research. Dentists in their practice also should emphasize counseling patients presenting with the associated factors of tooth wear. Appropriate prevention, early detection, and targeted treatment approaches can lead to successful management of tooth wear cases. Public awareness programs that will raise awareness regarding tooth wear and its' causative factors can also help in declining the incidence.

LIMITATION OF STUDY

The factors that were not included in this study were the amount of pressure applied for brushing, the pH of the oral environment, any developmental disturbances of teeth, medication, and biological factors such as saliva, tooth composition, and structure. Further investigations and continuous follow-up may allow the mapping of the relationship of biological factors with the occurrence of tooth wear. It was a cross-sectional study design which limits the establishment of causal relationships between the identified risk factors and tooth wear. Longitudinal or case-control studies should be done in the future for better elucidation of the risk factors of tooth wear.

CONCLUSION

Risk factors associated with tooth wear should be considered during clinical assessments, patient education, and implementation of preventive strategies to preserve dental health. Carbonated drink consumption, bruxism, aggressive brushing, and gastric diseases are found to be associated with the development of tooth wear.

ETHICAL APPROVAL

Ethical approval was obtained from the Scientific Review Committee of Hamdard University Dental Hospital, under Hamdard University, Karachi (REF letter No. 1025-01-23). All procedures performed in studies involving human participants were by the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR'S CONTRIBUTION

Dr. Hina Nafees: Conceptualization of study design and Write-up, Dr. Wardah Ahmed: Write-up, Data Analysis& interpretation, Dr. Fariha Irfan: Write-up, Data Analysis & interpretation, Dr. Hina Hammad Khan: Write up, Data Collection & interpretation, Dr. Zohaib Younus: Data Collection, Dr. Sheikh Haroon Shah: Proofreading, Dr. Syed Abrar Ali: Critical review of Manuscript

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REVIEW ARTICLE

The Current Monkeypox Outbreak: Highlighting Gaps in Approach to Disease in Endemic *vs.* Non-Endemic Countries

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Abstract

The appearance of monkeypox cases in non-endemic regions of the world has sparked concern in the global community, raising questions about prior undetected spread as well as suspicion of changing epidemiology. However, Africa has contained this burden for decades without much attention on global forums. Contributing factors in Africa include socioeconomic and political turmoil which have led to disturbance of habitats of various host species, with larger populations at risk of transmission, whereas the current outbreak in other countries has shown human-to-human transmission, mostly *via* sexual contact with infected individuals. While it is important to deal effectively with the situation at hand, prompt and equitable efforts are needed to control the spread of disease in endemic areas in the long term. Only then is it possible to prevent such multi-country outbreaks in the future.

Keywords: *Monkeypox, endemic disease, infectious diseases, endemic, human to human transmission, public health crisis.*

INTRODUCTION

Monkeypox is a zoonotic viral infection transmitted through contact with the blood, bodily fluids, or injuries of infected animals; human contaminations have been recorded through exposure to monkeys, Gambian giant rats, and squirrels with rodents being the most likely reservoir of infection. The clinical presentation includes fever, headache, swelling of the lymph nodes, back pain, muscle aches, and fatigue. There may be skin rashes at the beginning of the infection on the face spread to other parts of the body and gradually evolve into pustules and crusts. Rarely and more recently, have neurological manifestations such as panencephalitis been noted in severe cases. There are currently no specific medicines or vaccines for monkeypox virus disease, but prior vaccinia inoculation may decrease the impact of the disease [1, 2].

Monkeypox was first detailed in 1958 when two outbreaks of a pox-like infection happened in colonies of monkeys kept for investigation, thus the title 'monkeypox.' The primary human case of monkeypox was recorded in 1970 within the Law-based Republic of the Congo (DRC) amid a period of intensified effort to eliminate smallpox [3, 4]. Since that point, monkeypox has been detailed in individuals in a few other central and western African countries: Benin, Cameroon, Central African Republic, Cote d'Ivoire, the Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Republic of the Congo, South Sudan, and Sierra Leone, with the average case fatality ratio (CFR) ranging from 0-11% [4]. The larger part of these infections is in the Democratic Republic of the Congo with 760 confirmed cases reported between November 2005 to 2007 and since 2016, more than 1000 cases of monkeypox per year have been confirmed in DRC [5, 6]. Some of the recent outbreaks in Africa are in Cameroon, from 30 April to 30 May 2018 and this outbreak was declared to be ceased with one confirmed and 15 suspected cases and no deaths. Nigeria had an outbreak from 4th September lasting till 9th December 2017. This outbreak was declared over with 172 suspected and 61 confirmed cases and no deaths were reported. In the Central Africa Republic, the outbreak began on 4th September and lasted till 7 October 2016. There were 26 suspected and three confirmed cases with one death reported [1].

Monkeypox had been neglected in Africa for years until cases began to rise in non-endemic countries. Transmission of monkeypox virus happens through large respiratory droplets, close or direct contact with skin injuries, and possibly through contaminated fomites. Young children and immunocompromised people, including people with human immunodeficiency virus (HIV) disease, have been reported to be at increased risk for severe outcomes. The solid probability of sexual transmission was supported by the discoveries of primary genital, anal, and oral mucosal lesions, which may represent the inoculation location [7]. Investigations of the epidemiology of the disease are progressing and most reported cases so far have been transmitted through sexual health or other health services in primary or secondary healthcare facilities and have included primarily, but not solely men who have sex with men (MSM) [8, 9]. Monkeypox virus DNA was detectable by PCR in seminal liquid in 29 of the 32

cases in which seminal liquid was tested further supports this hypothesis. However, whether semen is capable of transmitting disease remains to be investigated, since it is obscure whether the viral DNA recognized in these specimens was replication-competent [7]. Although the virus cannot be regarded as a sexually transmitted disease, a higher number of detected cases have been linked to sexual activities especially among the MSM population through mucosal contact. This phenomenon can be attributed to both behavioral and biological factors. Additionally, this puts HIV- gay-related immunodeficiency higher up on the list of risk factors given its association with the group in question. A lack of proper research in this regard resulting in insubstantial proof means the effectiveness of preventive measures and overall motivation in people to implement them may be insufficient [10]. Additionally, seasonal and environmental variations, epigenetics, and the ability to evade host T-cell attacks have also been shown to play a role in viral replication and spread [11, 12].

From 13 May 2022 to 8 June 2022, 1285 laboratories confirmed cases of monkeypox have been reported to or identified by WHO from 28 non-endemic Member States over four WHO regions including Portugal, Spain, and the United Kingdom having the highest burden of monkeypox cases. Since the beginning of the year, there have been 1536 suspected cases of monkeypox with 72 deaths reported across 8 African countries [13]. The sudden and unforeseen emergence of monkeypox simultaneously in several non-endemic countries suggests that there might have been undetected transmission for an unknown duration of time leading to recently amplified events making the exact epidemiology of such outbreaks unclear. As a result a lack of information on why and how transmission occurred could hinder the development and implementation of preventive measures, detection of possible mutations in the virus, and subsequent complications in disease [7].

On August 4th, 2022, the United States declared monkeypox to be a public health emergency, and the U.S. Department of Health and Human Services has allocated over 1.1 million vaccines throughout the country to combat the spread of the infection [14]. More recently, the International Health Regulations Committee met in February of 2023, and concluded that monkeypox was still a public health emergency of "International Concern" [15].

CHALLENGES

Non-Endemic Regions
The recent surge of monkeypox cases was the first large-scale multi-country outbreak in non-endemic regions across the globe, such as Canada, France, and the United Kingdom [16]. The expanding monkeypox episode is posing colossal communication challenges for public well-being specialists keen to keep this virus from becoming entrenched as a human pathogen Transmission between sexual partners, due to intimate contact amid sex with infectious skin lesions appears as the mode of transmission among men who have sex with men (MSM) [9]. Given the unusually tall recurrence of human-to-human transmission watched on this occasion and the likely community transmission without a history of traveling to endemic regions, the probability of further spread of the infection through near contact, for cases amid sexual activities, is high. The link between sexual transmission and disease prevalence in non-endemic areas could potentially help in prevention by encouraging at-risk groups, especially MSM, to implement precautionary measures such as the use of condoms [7].

Stress and misinformation can be a concern if healthcare workers do not communicate with exceptional clarity to the public on the characteristics of the disease and the poignance of vaccination campaigns. As this outbreak of monkeypox expands, the infection has an exceptional opportunity to set up itself in non-African species, which might infect people and give a more prominent opportunity for more perilous variations to evolve [17]. Monkeypox causes a rash that is similar to those in other diseases, like herpes, syphilis, and chickenpox. It will be crucial to distinguish monkeypox from these diseases which can all cause rashes similar in appearance to monkeypox, bearing in mind the possibility of variation in symptoms between individuals, to avoid misdiagnosis [18]. The most common methods of testing include PCR and ELISA on collected samples. However, the effectiveness of serological testing may be limited in suspected individuals with low immune responses. The process also requires highly specific primers for accurate detection which may be unavailable in non-endemic countries. The situation also calls into question the availability of highly skilled lab technicians due to their time-consuming and labor-intensive nature. Recently, biosensors have emerged as better options due to their high sensitivity, specificity, automation, and portable nature as seen by their use in the detection of various viruses. However, it would require training and monetary capital [19].

Unpreparedness among the healthcare community in non-endemic countries owing to a lack of exposure to this disease, as well as the public poses a risk for such situations.

Endemic Regions

In comparison, monkeypox has had a regular incidence in various African countries for decades, especially in locations with or near large semi-deciduous forest cover, which makes optimum breeding and housing conditions for rope squirrels, a notable reservoir for the monkeypox virus [20]. In African countries endemic to monkeypox, recent spikes in reported cases may be due to deforestation, which enables closer contact of humans with infected animal species.5 In addition, the migration of people due to political instability may have led to increased contact with infected wild animals [21]. The resultant poverty from the mass displacement of people and reduced outlets of nutritional intake, also further exacerbated during COVID-19, may have also resulted in more people coming into contact with wild infected animals, to use as an alternate protein source [22].

In addition to the impact of abundant host species of the virus, a lack of effective surveillance particularly in areas afflicted by war and rural areas has resulted in an understatement of case counts [23]. The COVID-19 pandemic also greatly affected surveillance, coupling this factor with the socioeconomic and health-related implications of COVID-19 [24].

The burden of prevalent diseases such as HIV, tuberculosis, and other infectious diseases on the poor healthcare system in most countries of Africa which are endemic for monkeypox makes the situation more complicated due to inadequate medical resources to deal with the impacts of such co-morbidities on overall health, [25] especially in individuals suffering from monkeypox.

MONKEYPOX: AFRICA *VS*. THE WORLD

The current outbreak of monkeypox in non-endemic countries has highlighted an important aspect of disease management: the disparity in approach between endemic and non-endemic countries. While the surge in cases raised eyes, and rightly so, it is important to note that countries such as the Democratic Republic of Congo, Nigeria, and many others were suffering for years with high case counts and subsequent deaths without active eradication plans or external aid from other, more stable parts of the world. Shockingly, it was only until the recent multi-country outbreak that many first became aware of the threat of monkeypox [26, 27].

Ever since the first case was reported in the UK on May 7, 2022, WHO has taken an active part in helping countries effectively manage the spread. On May 20th, 2022, a meeting of the Strategic & Technical Advisory Group on Infectious Hazards with Pandemic and Epidemic Potential [STAG-IH]) was held to discuss strategies to tackle the outbreak [28]. While it was stated that mass vaccination is not a requirement now, countries are looking into using stockpiled smallpox vaccines for exposed populations, as well as ordering new stock for future use, owing to its 85% effectiveness against monkeypox as well [3]. Ever since the outbreak, Britain has successfully vaccinated more than 1,000 at-risk individuals and ordered 20,000 more doses, while the US has released 700 doses in affected states.26 However, the 31 million doses pledged by WHO members for African countries were never used [29]. Another advantage in first-world countries facing the monkeypox epidemic is effective surveillance which is important in containing the spread, as well as research facilities that can help identify specific strains and their vulnerabilities to certain drugs.

A contrasting picture is seen in third-world African countries. After the eradication of smallpox in 1977 and the consequent discontinuation of smallpox vaccination, large populations were left at risk of infection due to waning cross-protection [4]. Given the poor economic conditions, vaccine availability was scarce, unlike the situation in first-world countries facing the monkeypox threat today. Subsequently, in 2016, only 10.1% of the population was vaccinated against smallpox [30]. Additionally, the US and UK are employing an FDA-approved vaccine produced by Bavarian Nordic which is unavailable in endemic countries today [27].

Inequity is also heavily reflected through the lack of effective drugs for monkeypox management in Africa [20] whereas the Strategic National Stockpile in the US currently has antiviral drugs such as Tecovirimat (TPOXX), Brincidofovir (CMX001), and cidofovir (Vistide) which may be useful in managing cases [31]. To bridge this gap, SIGA in collaboration with Oxford University had pledged to provide 500 tecovirimat doses free of cost for the treatment of monkeypox in the Central African Republic in 2021 [32].

Without significant intervention by the global community during situations of humanitarian crises that sped up the transmission, frequent outbreaks in endemic countries were inevitable. WHO has been working in various affected countries to improve surveillance, diagnosis, treatment methods, community-level awareness, and professional training to curtail monkeypox spread and associated mortality [33]. However, endemic countries are still showing case counts significantly higher than other parts of the world, highlighting the need for more rigorous efforts.

RECOMMENDATIONS

Considering the socioeconomic, political, and geographical differences between endemic African countries and non-endemic countries such as the US

and various European nations, appropriate infection control to mitigate this outbreak will require separate and equitable strategies. A key factor in prevention is case surveillance and contact tracing. International health authorities recommend the use of vaccinations in close contact with infected individuals and those with occupational exposure [34]. Adequate use of vaccinations can curb outbreaks in endemic and non-endemic countries and provide vast immunity. Since vaccinations against smallpox have proven to also provide immunity against monkeypox, the continuation of mass smallpox vaccinations could prove as an important infectious control measure [35]. Equipping dermatologists and general physicians through robust training to correctly diagnose monkeypox from other poxvirus infections and to provide adequate referral can reduce transmission and complications [36]. Exposed individuals can then be provided with the smallpox vaccine for cross-protection against monkeypox, prioritizing high-risk individuals such as exposed individuals, children under the age of 10, and those with co-morbidities such as immunodeficiency or other systemic disorders [37]. In addition, the WHO mentions the use of a new vaccine that has been approved against monkeypox and an antiviral agent that was initially licensed for smallpox but can now be used for treating monkeypox [35].

Although COVID-19 and monkeypox are different in terms of pathogenesis and manifestation, the various protocols advised during the COVID-19 pandemic such as reduced gatherings, regular handwashing as well as the blueprint of effective testing and subsequent hot-spot identification can prove extremely useful [38].

Non-Endemic Regions

Multiple reports of recent monkeypox infections in non-endemic countries reveal that infected individuals had a history of sexually transmitted infections and had recent unprotected sexual encounters [39]. Therefore, a simple recommendation to reduce transmission of monkeypox in the short term is for individuals to reduce the amount of high-risk, unprotected sexual encounters, especially in non-endemic countries. Almost all individuals affected by monkeypox in non-endemic countries were MSMs, and the WHO has published a detailed pamphlet to provide accurate information for gay, bisexual, and other MSMs about their public health regarding monkeypox [40, 41].

The WHO reveals that the most significant risk factor in the transmission of monkeypox during human outbreaks is close contact with body fluids, contaminated materials, and lesions [41]. Therefore, proper isolation of infected individuals is key to preventing transmission

to close contacts and healthcare workers [40]. Since most monkeypox cases do not require hospitalization, the public must be adequately enlightened about proper self-isolation techniques. For example, the public should be aware that individuals with monkeypox are infectious until all lesions have crusted and new skin has appeared to replace fallen scabs [40]. Monkeypox can also be transmitted through respiratory droplets, with transmission requiring prolonged face-to-face contact, putting family members and healthcare workers at risk [42]. Therefore, HCWs managing a patient infected with monkeypox must exercise proper infection control measures including the use of PPEs, FFP2 or N95 respirators, and hand hygiene. Hospitalized patients should be isolated in a single room with a separate bathroom, and adequate ventilation, and HCWs using protective measures to reduce transmission [40].

Endemic Regions

Vaccine availability will not be an issue for first-world countries, that are already ordering stocks or making stockpiled doses available to the public. However, African countries will require collaborations to effectively acquire, distribute, and administer vaccines within their populations, which has been a struggle in previous monkeypox surges in these countries.

Control of host species breeding and containment can prove to be useful in endemic countries with high populations of such animals through the re-establishment of lost habitats whilst limiting contact with humans. Education of the public in these areas to limit hunting and subsequent use of contaminated meats is also equally important, [5, 43] alongside the extension of foreign aid to boost nutrition in poor countries to prevent the need to turn towards these alternative protein sources. Facilitating the development of the agriculture sector and food animal breeding to meet food requirements can also prove to be beneficial in this regard [43].

It is also essential to direct attention towards at-home prevention strategies such as isolation and avoidance of shared utensils and clothing in case of suspected but undiagnosed infections, since this may help curb transmission at the grassroots level [38]. Lab confirmation of the virus can be made possible *via* improved research and testing facilities. With collaborative efforts, additional research focusing on the Congo Basin strain, responsible for most monkeypox-related deaths in DRC owing to its increased transmission and mortality rates compared to West African clade, [44]. can be useful in formulating better strategies. Introduction and maintenance of such facilities in countries lacking them can help track cases effectively as shown by joint efforts by the Ministry of

Health, INRB, and the US centers of CDC in DRC since 2010 [45].

Endemic countries also require attention towards disease management given the fact that monkeypox has led to many deaths, unlike the current epidemic. The provision of antiviral drugs such as brincidofovir and a prophylactic regimen can help improve the prognosis of monkeypox infection. Improved surveillance of prevalent immunocompromising diseases such as HIV and tuberculosis can also help assess risk levels for monkeypox-affected areas considering the impact of these comorbidities on prognosis.

CONCLUSION
The monkeypox situation in Africa has deteriorated over the years due to a lack of surveillance, treatment options, and various socioeconomic reasons. Efforts must be made by the global superpowers in collaboration with WHO and other organizations to bring African countries at par with the rest of the world regarding research, medical facilities, and infrastructure to enable them to tackle diseases such as monkeypox effectively.

CONSENT FOR PUBLICATION
Written informed consent was taken from the participants.

CONFLICT OF INTERESTS
The authors declare no conflict of interest.

AUTHORS CONTRIBUTION
Conceptualization: Sameer Saleem Tebha, Writing original draft: Hira Anas Khan, Parvathy Mohanan, Zainab Syyeda Rahmat, Una Kanor, Review and editing: Una Kanor and Sameer Saleem Tebha.

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COMMENTARY

Bridging the Gap between the Students and Faculty Members

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Abstract

The "student-teacher gap" is the term used to describe the disconnect or differences between learners and their educators in many facets of a learning environment. It's critical to remember that this disparity does not necessarily signal a problem; rather, it draws attention to the unique roles, backgrounds, and perspectives that students and teachers bring to the classroom. A happier and more cooperative intellectual community enhanced educational outcomes, and increased student involvement can all result from enhanced interaction and comprehension between the two sectors.

Nowadays, it is observed that the gap between students and teachers is minimized. People think the credit goes to information technology which has invented different strategies for teaching and learning. According to the people's opinion, there should be no gap between students and teachers so that they can communicate with each other easily without any hesitation or fear. As students close the distance between their present abilities and the anticipated level of competency, positive feedback is essential. Good communication and collaboration is also necessary to bridge this gap.

Keywords: *Student-teacher gap, technology, communication, and collaboration, intellectual community, beauty in diversity.*

INTRODUCTION

The term "student-teacher gap" is employed to describe the disconnect or differences between learners and their educators in various facets of a learning environment. It encompasses disparities in communication, knowledge, goals, mindsets, and viewpoints. However, it's important to note that this gap isn't necessarily a problem but rather an opportunity to recognize the unique backgrounds and experiences that both students and teachers bring to the classroom.

Reducing this gap can lead to a more cooperative intellectual community, improved educational outcomes, and increased student engagement. The advent of information technology and innovative teaching strategies has played a significant role in minimizing this gap in recent times. In an ideal learning environment, there should be no significant division between students and teachers, allowing for open and fear-free communication.

In recognition of the remarkable versatility of human interaction, instructors can impart extremely theoretical and innovative knowledge to their learners [1]. It may also take many different forms. It's critical to remember that this disparity does not necessarily signal a problem; rather, it draws attention to the unique roles, backgrounds, and perspectives that students and teachers bring to the classroom.

Building a strong and stimulating learning atmosphere depends on reducing the gap between learners and educators. A happier and more cooperative intellectual community, enhanced educational outcomes, and increased student involvement can all result from enhanced interaction and comprehension between the two sectors.

PERSONAL EXPERIENCE

In terms of personal experience, it has traditionally been observed that a gap exists between teachers and students. However, contemporary trends indicate that this gap is gradually narrowing over time, thanks to factors like information technology and advancements in teaching strategies. A particular experience involves the supervision of fourth-year Bachelor of Science in nursing students during their clinical practice at Aga Khan University Hospital in Karachi. In this capacity, the supervisor played a crucial role in guiding students through clinical objectives, ensuring that they could communicate their issues and opinions without hesitation, fostering a conducive learning environment.

In the role of a student supervisor, the individual exhibited a high level of enthusiasm for the task. Simultaneously, they derived immense happiness and satisfaction from their supervisory responsibilities. In addition to guiding the students, they also acknowledged personal learning experiences from this role. They highlighted the universal aspect of human experiences and the potential for personal growth by listening to and learning from others' stories. The value of diversity was underscored, emphasizing its inherent beauty and the motivation it instilled in the individual to acquire new knowledge and skills from a variety of sources.

Regarding the current educational landscape, the observer noted a narrowing of the gap between students and teachers. They attributed this positive development to the influence of information technology, which has

46 ISSN: 2960-2963 (Online) *Journal of Liaquat National Hospital 2024; 2(1): 46-48*

introduced diverse teaching and learning strategies. The observer firmly held the belief that there should be minimal separation between students and teachers, advocating for open and uninhibited communication. They stressed the importance of fostering an inclusive culture that promotes equality, where all individuals have the opportunity to share their ideas and thoughts. The observer also underscored the continuous need for educators to update their knowledge and skills, staying attuned to modern techniques and approaches. Literature also says that a good teacher should stay current on the most recent developments and maintain good lines of communication with students and their families. All genuine connections must have this at their core [2]. According to the literature, Instructors need a method of preparedness that is by the needs and complexities of learning if tutoring is to turn into a recognized profession, and schools play a critical role in this. As teachers develop from novice to expert along the career advancement spectrum, they are in the perfect position to mentor formative assessment and practicing instructors [3]. From an external perspective, it is believed that the implementation of projects and pilot programs is instrumental in reducing the divide between students and teachers. Additionally, the practice of gathering students' evaluations and feedback about their instructors plays a pivotal role in comprehending the students' perspectives and their level of understanding. These initiatives are seen as valuable steps in enhancing the educational experience and bridging the gap between learners and educators.

CONCLUSION

In conclusion, there should be a conclusive culture and environment in which every student can share and express their thoughts and ideas efficiently and coherently without any fear or hesitation. Without an inclusive environment, students become reluctant and their intellectual growth becomes stagnant. Here are some strategies to help bridge the gap:

1. Develop regular lines for interaction with educators. Make sure these channels are obvious and simple for students to use. This could involve using email, internet chat rooms, message services, or even a specific website to conduct educational debates.

2. Teachers should exhibit an open and friendly demeanour to make learners experience at ease while raising queries, getting assistance, and exchanging ideas.

3. Develop engaging lessons that invite involvement, inquiries, and conversations from the students. Students who are actively involved are more likely to have a good rapport with their lecturers.

4. Personalized Recommendations: Offer prompt and helpful suggestions for improving tasks and assessments. This demonstrates to pupils the significance of their work and enables them to identify their areas of strength and growth.

5. Educational institutions must train instructors to accommodate the different requirements of today's students.

6. Mentorship Programs: Create mentoring programs so that professors may assist students in pursuing their educational and professional objectives. These connections can continue outside of school and increase students' sense of community.

7. Initiatives involving student-faculty collaboration: Promote joint initiatives between students and academic staff. This could include activities that promote an awareness of society including volunteering or artistic projects.

8. Teachers' Participation in Student Programs: Instructors may take part in or promote associations, operations, and additional activities for students. This demonstrates their concern for the total growth of the learners.

9. Town Hall Gatherings or Public Platforms: Set up recurring community conversations or discussions wherein learners can freely voice their opinions. This encourages openness and diversity.

10. Using innovation to enhance exchanges, such as through online forums, seminars, and groups on social networks, can increase engagement chances.

11. Recognize and value the efforts made by faculty members to develop connections with students. More professors may interact with learners more actively if they receive encouragement. There should be chances for students to take on teaching responsibilities. Ideas for curriculum topics, instructional strategies, and evaluation techniques should also be recommended [4].

12. Feedback Mechanisms: Establish an exchange of information so that students may offer opinions on the way instructors present the material and how the class as a whole is going.

As students close the distance between their present abilities and the anticipated level of competency, positive feedback is essential. Giving insightful critique is a quality that may be developed through practice. The goal is to investigate techniques in healthcare settings and evaluate how well they may be used for

various healthcare feedback experiences [5]. Using a context-specific teaching method, such as the situated theory of learning, in formal educational programs can help to bridge this gap and successfully prepare graduate teachers for the classroom [6]. It's important to keep in mind that creating links between learners and educators is a continuous process that calls for dedication and work on both sides. Collaboration and good communication between students and faculty members improve the learning process as a whole and foster a more peaceful academic environment. By recognizing and appreciating these differences as well as trying to establish a welcoming and encouraging learning environment where effective communication, empathy, and mutual respect may flourish, we can close the student-teacher communication gap. A study was done that raised the potential that focused training might help close the distance between student evaluation and professor evaluation [7]. This gap can be closed and good relationships between students and teachers can be fostered *via* open communication, attentive listening, and a readiness to modify teaching and learning strategies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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