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Correlation and prevalence of recurrent aphthous stomatitis with stress among undergraduates in private dental institutions of Lahore, Pakistan

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ABSTRACT

BACKGROUND & OBJECTIVE: Oral ulcers, commonly associated with stress, serve as significant indicators of psychosomatic interactions impacting oral health. Stress is known to compromise the immune system, making individuals susceptible to various health challenges. This study aimed to explore the intricate connection between recurrent oral ulcers and stress among dental students in Lahore, Pakistan.

METHODOLOGY: This descriptive cross-sectional study was conducted in multiple private dental colleges in Lahore. Non-probability consecutive sampling was employed, and the calculated sample size was 598. Data collection utilized a pre-validated questionnaire with two sets of closed-ended questions rated on a 5-point Likert scale. Statistical analysis was performed using SPSS version 25, and the Chi-square and Fisher exact tests were applied to assess the association between ulcers and stress.

RESULTS: Out of 598 participants, 51.3% reported a history of oral ulcers, with 7.82% of participants reporting current oral ulcers. Notably, 47.23% had oral ulcers within the past six months, and the majority (66.45%) experienced 2-6 ulcers per episode. The duration of ulcers predominantly ranged from 1-2 days (38.20%). Family history was significant (51.47%), and stress was identified as a major cause, especially during examinations (68.4%). Perceived stress scores were high among the previous history of oral ulcers group ($p=0.001$).

CONCLUSION: This research reveals a compelling association between stress and recurrent oral ulcers, underscoring stress as a crucial factor. The results of this study will help to improve the quality of life of dental students, either by addressing their stress levels or by recommending appropriate remedies.

KEYWORDS: Oral Ulcers, Psychological Stress, Dental Students.

INTRODUCTION

One of the most prevalent painful mucosal disorders of the mouth is recurrent aphthous stomatitis (RAS) or recurrent oral ulcers (ROUs)^[1]. RAS is a prevalent oral condition affecting approximately 20% of individuals without underlying health issues, typically manifesting during the early stages of puberty and requiring several days for complete resolution^[2]. RAS frequently appears on non-keratinized surfaces such as lips, the ventral side of the tongue, buccal mucosa, the floor of the mouth, and the soft palate. They are typically circular to oval, painful, superficial ulcers with an erythematous foundation^[3].

Stanley identified three forms of RAS: minor, major, and herpetiform ulcers. The majority (80%) of RAS are mild or minor. These are tiny, 8–10 mm ulcers that affect nonkeratinized mucosa and can occur in one to five different places. They heal completely in 10–14 days with no significant pain. Major aphthous ulcers are larger than minor ones (>1 cm) and affect 10–15% of the population, which affects the keratinized oral mucosa, including the fauces and hard palate. They frequently leave a scar and can take up to six weeks to heal. Herpetiform ulceration appears as clusters of small ulcers, up to 100 in number and 1-3 mm in diameter, that heal without leaving scars and remain for 10–14 days known as herpetiform ulceration^[4].

How to cite this: Anwar MA, Rehman IU, Tayyab TF, Shoaib M, Awais S, Baig MA. Correlation and prevalence of recurrent aphthous stomatitis with stress among undergraduates in private dental institutions of Lahore, Pakistan. *Journal of University Medical & Dental College*. 2025; 16(1):992-999.



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Recurrent aphthous stomatitis (RAS) manifestations, which include pain when speaking, eating, and swallowing, as well as general discomfort and obstructions in food and liquid consumption, have a significant negative impact on the oral health-related quality of life that affected individuals experience [5].

RAS does not have a clear, known etiology. Predisposing factors that may contribute to its development include stress, physical or chemical trauma, infection, allergies, hormones, genetic susceptibility, hypersensitivity, use of drugs or tobacco, dietary deficiencies, as well as autoimmune diseases such as systemic lupus erythematosus (SLE) [6,7]. Many contributing factors are known to cause RAS; one of the main risk factors for their emergence in young people is mental stress. Stress is assumed to be the root cause of RAS, but it also has a significant negative influence on the physical health of the individual and can result in several systemic issues, including neurological and cardiovascular ailments. Stress can pose a serious risk to students and have a detrimental effect on their physical and mental well-being, which will lower their performance in the classroom and the standard of their education [8].

Various studies have found a positive correlation between stress and RAS [1,9]. Several studies indicate that individuals, particularly students and those with higher educational levels, exhibit a higher prevalence of RAS. This outcome indicates the involvement of stress and anxiety, particularly during the examination period, in the development of RAS in educated individuals [10].

Stress can pose a serious risk to dental students and have a detrimental effect on their physical and emotional well-being, which will lower their quality of life and academic performance. Therefore, educators need to become more knowledgeable about preventing RAS to assist their students in managing these difficulties [11]. Although most people are aware of the concept of stress, a significant proportion of people might not be aware that stress is associated with oral ulcers. The purpose of this study was to investigate the relationship between oral ulcers and stress in dental students in Lahore and, if needed, support regular psychological treatment for these individuals as a means of reducing stress.

METHODOLOGY

This was a descriptive cross-sectional study conducted among 598 dental students from various dental colleges in Lahore, Pakistan. Non-probability consecutive sampling was done among the participating six private dental colleges between 24th November 2023 to 15th April 2024. Ethical clearance was obtained with ethics certificate number UCD/ERCA/763 from the Ethical Review Committee at University College of Dentistry, The University of Lahore. Informed consent was obtained from the students who agreed to take part in the research. Dental students from all academic years were included in the study. House officers, post-graduate residents, general dentists or specialists, and those who did not consent to participate, and incomplete forms were excluded.

Surveys and questionnaires were distributed through online Google Forms (Google, Inc., Mountain View, CA, USA) among the students who provided their consent. The study utilized a pre-validated modified Perceived Stress Scale (PSS) questionnaire by Cohen et al. published in 1983 [12]. Self-reported data from these instruments were collected and analyzed to assess the participants' perceived stress levels.

It consists of two sets of closed-ended questions. In addition to the established questions, new inquiries related to gender and academic year (ranging from year 1 to year 4) were included to investigate their potential association with stress and the occurrence of oral ulcers. The first set of questions, totaling 11 questions, focused on clinically relevant details concerning recurrent aphthous ulcers. The subsequent set, comprising 10 questions, specifically addresses symptoms related to stress by the Perceived Stress Scale [12].

Participants were required to respond using a 5-point Likert scale ranging from 0 to 4, where: 0 indicated "never", 1 indicated "nearly never", 2 indicated "occasionally", 3 indicated "very often", and 4 indicated "very frequently". The overall stress score is calculated by adding the responses of four affirmatively stated items (items 4, 5, 7, and 8) whose values are inverted (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1, and 4 = 0) to the responses of the remaining items. The stress levels of individuals with and without aphthous ulcers were contrasted. According to Cohen et al, perceived Stress Scale scores 0-13 were considered low stress, whereas 14-26 and 27-30 were considered moderate and high stress [12].

The Statistical Package for the Social Sciences (SPSS) version 25 (IBM SPSS Statistics, Armonk, NY, USA) and Microsoft Office Excel (Microsoft Corp., Redmond, WA, USA) were used for the statistical analysis. Quantitative variables were presented with means and standard deviations. Qualitative variables were presented with frequency and percentage. Appropriate statistical (Chi-square, Fisher exact, and regression analysis) tests were applied to study the association of oral ulcers with stress. Statistical significance was determined with a p-value equal to or less than 0.05.

RESULTS

The demographic distribution of participants categorized based on the presence or absence of a previous history of oral ulcers is demonstrated in Table- I.

Table I: Frequency distribution of individuals with and without previous history of oral ulcers by gender and year of study.

Demographics		Previous History of Oral Ulcers	
		Yes (n=307)	No (n=291)
		n(%)	n(%)
Gender	Male	129(42.02)	79(27.15)
	Female	178(57.98)	212(72.85)
Year of Study	1st year	57(18.57)	78(26.80)
	2nd year	105(34.20)	71(24.40)
	3rd year	77(25.08)	75(25.77)
	Final year	68(22.15)	67(23.02)

Table-II: Characteristics of participants with a previous history of oral ulcers.

Questions	Options	n(%)	P-value
Family history of recurrent oral ulcers	Yes	158(51.47)	<0.001*
	No	149(48.53)	
Time of the last ulcer	> 6 months ago	105(34.2)	<0.001*
	One month ago	62(20.2)	
	3 months ago	61(19.87)	
	6 months ago	55(17.92)	
	Experiencing now	24(7.82)	
Frequency of ulcers	Once in 6 Months	145(47.23)	<0.001*
	Once in 3 Months	128(41.69)	
	Once in a Month	34(11.07)	
Duration of ulcer	0-2 days	72(23.45)	<0.001*
	3-6 days	220(71.66)	
	7-10 days	15(4.89)	
Is the ulcer painful	Yes	126(41.04)	<0.001**
	No	181(58.96)	
Number of ulcers noticed in each episode	1	93(30.29)	<0.001*
	2-6	204(66.45)	
	>6	10(3.26)	
Area of occurrence	Multiple areas	155(50.49)	<0.001*
	Cheeks	67(21.82)	
	Lips	30(9.77)	
	Gums	29(9.45)	
	Tongue	26(8.4)	
Treatment received	Self-healing	198(64.5)	0.396*
	Topical gels	61(19.87)	
	Doctors' consultation	30(9.77)	
Associated with any condition	Stress	210(68.4)	<0.001*
	Gastric problems	50(16.29)	
	Hormonal change	21(6.84)	
	Skin problems	14(4.56)	
	Fever	8(2.61)	
	Trauma	4(1.3)	
Possible cause of stress	Examination	165(53.75)	<0.001*
	Multiple reasons	130(42.3)	
	Change in food	12(3.91)	

Note: (*): Chi-Square test, **(**)**: Fisher Exact test

In a closer examination of the group with a history of oral ulcers (n=307), a significant portion, specifically 66.45% (n=204), reported having 2–6 oral ulcers during each episode. Among this cohort, a significant proportion, precisely 71.66% (n=220), reported having ulcers that persisted for 3-6 days. However, 58.96% (n=181) of the participants had painless oral ulcers (Table- II).

Examining the distribution of oral ulcers across different sites, more than half of the participants, accounting for 50.49% (n=155), reported the occurrence of oral ulcers at multiple sites. Within the subset of 307 students, oral ulcer frequency varied, with 47.23% (n=145) once every six months, 41.69% (n=128) experiencing ulcers once every three months,

10.1% (n=31) once a month, and a minimal 0.98% (n=3) once a week. A significant proportion, specifically 41.04% (n=126), reported experiencing painful oral ulcers, while 58.96% (n=181) did not report pain associated with these ulcers. Concerning the medication used for these ulcers, the majority, constituting 64.5% (n=198) did not use any prescription drugs. (Table- II).

In our study, a substantial 51.47% (n=158) of participants reported a positive family history of oral ulcers, and this association was found to be statistically significant (p=0.001). Among the 307 contributors, a majority (68.4%, n=210) attributed their oral ulcers to stress with examination being the major cause of the stress (53.75%, n=165) (Table-II).

Gender and academic year were considered variables as the study examined the correlation between Perceived Stress Scale (PSS) scores and prior oral ulcer experience. The findings showed a statistically significant correlation ($p < 0.001$) between the PSS scores and the history of oral ulcers in general as well as in particular gender and academic year groups. Higher PSS scores were linked to a higher prevalence

of oral ulcer history in females, and similar tendencies were seen in males. Furthermore, during academic years, higher stress levels were linked to a larger chance of having oral ulcers in the past. These results indicate the possible association between stress and mouth ulcer occurrence, with differences in this link between gender and academic year. (Table- III)

Table-III: Perceived Stress Scale (PSS) scores and their association with previous history of oral ulcers by gender and year of study.

Variables	Categories	PSS Score	Previous History of Oral Ulcers		P-value
			Yes (n=307)	No (n=291)	
			n(%)	n(%)	
Gender	Male	Low	2(0.3)	18(3.0)	<0.001*
		Moderate	67(11.2)	171(28.6)	
		High	109(18.2)	23(3.8)	
	Female	Low	3(0.5)	11(1.8)	<0.001*
		Moderate	55(9.2)	59(9.9)	
		High	71(11.9)	9(1.5)	
Year of study	1st year	Low	1(0.2)	8(1.3)	<0.001*
		Moderate	28(4.7)	60(10.0)	
		High	28(4.7)	10(1.7)	
	2nd year	Low	0(0.0)	7(1.2)	<0.001**
		Moderate	32(5.4)	54(9.0)	
		High	73(12.2)	10(1.7)	
	3rd year	Low	2(0.3)	9(1.5)	<0.001*
		Moderate	26(4.3)	61(10.2)	
		High	49(8.2)	5(0.8)	
	Finale year	Low	2(0.3)	5(0.8)	<0.001**
		Moderate	36(6.0)	55(9.2)	
		High	30(5.0)	7(1.2)	

Note: (*): Chi-Square test, **(**)**: Fisher Exact test

When PSS scores were compared between the two groups based on the history of oral ulcers, the p-value was calculated to be statistically significant ($p=0.001$) which showed that the perceived stress scores were high among the dental students with a positive history of oral ulcers (Table -IV).

Table-IV: Relation between aphthous ulcer and stress according to Perceived Stress Scale (PSS) score.

Perceived Stress Score PSS	Previous History of Oral Ulcers		Total n=598	P-value
	Yes (n=307)	No (n=291)		
	n(%)	n(%)		
Low	5 (1.6)	29 (10)	34	<0.001*
Moderate	122 (39.7)	230 (79)	352	
High	180 (58.6)	32 (11)	212	
Mean \pm SD	26.20 \pm 4.96	20.21 \pm 5.33	598	

Note: (*): Chi-Square test

Among the 307 dental students with a positive history of oral ulcers, there were no gender-related variations in the incidence or duration of oral ulcers. On the other hand, a statistically significant p-value for ulcer duration was noted. When compared to females, men were more likely to experience ulcers that lasted three to six days. However, no significant differences were seen in the frequency or size of ulcers between the genders. These findings emphasize the

complex nature of RAUs and the need to consider a wide range of factors when examining their incidence among dental students (Table- V).

Among 210 students who reported stress as the cause of oral ulcers, 69.05% ($n=145$) reported examination as the form of stress followed by 29.5% ($n=62$) with multiple reasons which were statistically significant ($p<0.001$). When examining the correlation between gender and year of education within the same group, no statistically significant difference was observed. However, when the Fisher exact test was applied to compare possible causes of stress among the students who had ulcers, it was found to be significant ($p < 0.001$). (Table -VI)

Regression analysis was performed to assess the relationship between stress levels and predictors such as a history of oral ulcers and a family history of recurrent oral ulcers. Among the predictors analyzed, only the history of oral ulcers and family history of recurrent oral ulcers showed significant associations with stress levels. For moderate stress, these predictors exhibited higher odds ratios (2.510 and 2.279, respectively) but were not statistically significant ($p > 0.05$). Conversely, for high-stress levels, both predictors were statistically significant. A history of oral ulcers was associated with a markedly increased odds ratio of 18.612, while a family history of recurrent oral ulcers had an odds ratio of 5.712. These associations were significant with p-values of 0.000 and 0.026, respectively.

Table-V: Association of gender and previous history of oral ulcers with oral ulcer characteristics.

Questions	Options	Previous History of Oral Ulcers (n=307)		P-value
		Male (n=129) n(%)	Female (n=178) n(%)	
Time of the last ulcer	3 months ago	23(17.8)	38(21.3)	0.835*
	6 months ago	23(17.8)	32(18.0)	
	Experiencing presently	11(8.5)	13(7.3)	
	>6 months ago	48(37.2)	57(32.0)	
	One month ago	24(18.6)	38(21.3)	
Frequency of ulcers	Once in 3 Months	50(38.8)	78(43.8)	0.342*
	Once in 6 Months	67(51.9)	78(43.8)	
	Once in a Month	12(9.3)	22(12.3)	
Duration of ulcer	0-2 days	23(17.8)	49(27.5)	0.018*
	3-6 days	103(79.8)	117(65.7)	
	7-10 days	3(2.3)	12(6.7)	
Number of ulcers noticed in each episode	1	2(1.6)	8(4.5)	0.347**
	2-6	38(29.5)	55(30.9)	
	>6	89(69.0)	115(64.6)	
Area of occurrence	Cheeks	33(25.6)	34(19.1)	0.455*
	Gums	14(10.9)	15(8.4)	
	Lips	14(10.9)	16(9.0)	
	Multiple areas	58(45.0)	97(54.5)	
	Tongue	10(7.8)	16(9.0)	

Note: (*): Chi-Square test, (**): Fisher Exact test

Table-VI: Association of gender and year of study and possible cause of stress with previous history of oral ulcers and stress.

Variables	Categories	Previous History of Oral Ulcers (n=307)		P-Value
		Stress Yes (n=210)	Stress No(n=307)	
		n(%)	n(%)	
Gender	Male	89(42.3)	40(41.24)	0.850*
	Female	121(57.62)	57(58.76)	
Year of study	1st year	39(18.57)	18(18.56)	0.148*
	2nd year	75(35.71)	30(30.93)	
	3rd year	45(21.43)	32(32.99)	
	Finale year	51(24.29)	17(17.53)	
Possible cause of stress	Examination	145(69.05)	20(20.62)	<0.001**
	Multiple reasons	63(30)	67(69.07)	
	Change in food	2(0.95)	10(10.31)	

Note: (*): Chi-Square test, (**): Fisher Exact test

DISCUSSION

The exact cause and pathophysiology of RAU remain unknown. Research suggests that psychological stress may be a trigger for RAUs, which are frequently seen during stressful events such as final exams, dental work, or major life transitions. Stress has been associated with alterations in the number, distribution, and functionality of immune system cells, including lymphocytes and natural killer T cells, although their exact roles remain unclear. In addition, the release of antibodies and cytokines has been connected to stress. RAUs and immune system alterations

have been linked, supporting the theory that stress plays a role in their emergence^[13]. Additional factors that may contribute to mouth ulcers include an increase in salivary cortisol levels or reactive oxygen species. For those who are vulnerable, para-functional oral activities like lip and cheek biting that are linked to anxiety associated with stress can cause physical harm that starts the ulcerative process^[14]. Studies have shown that 30% to 59% of undergraduate healthcare students report stress-induced lip biting and other oral parafunctional habits, which is directly correlated with anxiety^[15,16].

The current investigation found an incidence of recurrent aphthous stomatitis at 51.3%, which is relatively on the higher side compared to other studies. For example, research from India shows differing results: George et al. reported a prevalence of 62.3%, while Handa et al. found it to be 26%^[17,18]. In contrast, other studies revealed lower incidence rates, with Verma et al. reporting 32.7% and Naito et al. finding 31% in Japan^[1,19]. Overall, the literature indicates a broad range in the prevalence of recurrent aphthous ulcers, from 5% to 60%, depending on the population studied^[20].

Our findings suggested females were more prone to RAUs, with 57.98% having a history of oral ulcers compared to males (42.02%). The majority (34.2%) of them had at least one episode in the last six months. In a large-scale investigation on RAU involving 10,000 young adults from twenty-one countries, researchers found that 49.7% of female patients and 38.7% of male patients had experienced RAU at some point in their lives. Additionally, nearly 25% of the participants had an episode in the past 12 months^[21].

In our study, participants displayed a prevalent occurrence of oral ulcers across various areas in the mouth, such as the cheeks, lips, and gums, averaging 2–6 ulcers during each episode. This differs from the findings in the existing literature, where the lips and cheeks were identified as the most common sites, often associated with a single oral ulcer per episode. Nevertheless, the duration of each episode of oral ulcers in our study was consistent for less than a week, aligning with similar durations reported in the literature^[1,17]. A direct association between stress and ulcers was observed in 68.4% (n = 210) of the 307 participants in this study who had a prior history of oral ulcers. However, in a study by George et al., 46.2% of students were found stressed out with a history of oral ulcers, whereas Verma et al. found this to be lower (37.2%)^[17]. The variance in these findings may be attributed to our survey's completion after a block examination of modular sections, a period when students likely faced increased pressure to complete prescribed work and heightened nervousness about impending evaluations. Additionally, individuals with higher educational attainment consistently showed a greater prevalence of RAS, aligning with the notion that stress and anxiety, especially during test periods, play a significant role in the development of RAS in educated individuals^[17].

When it came to the need for medical measures, the results were in line with previous research showing that most participants believed the oral ulcers would heal on their own^[1,17]. A statistically significant relationship was observed between family history and ulcers ($p = 0.001$). Individuals with a positive familial history of recurrent aphthous stomatitis (RAS) may experience more severe symptoms and develop ulcers at an earlier age compared to those without such a familial history^[22,23]. These results suggest that familial predisposition plays a crucial role in the manifestation of oral ulcers. The consistent pattern observed across studies emphasizes the need for increased awareness and targeted management strategies for individuals with a family history of RAS.

In our study, 46.2% (n=212) of the participants revealed significantly higher stress levels, as seen by their high PSS scores. Out of these students, 84.9% (n=180) had previously experienced oral ulcers. The increased occurrence of RAS among dental students in this study is due to the elevated stress levels associated with the demanding dental curriculum. Multiple investigations, like those conducted by Huling et al., and Huda et al., indicate a connection between anxiety, depression, and psychological stress with RAS^[24,25]. Dental graduates, who experience significant stress, frequently employ maladaptive coping strategies, such as biting their lips and cheeks. These behaviors can cause damage to the oral mucosa and contribute to the formation of mouth ulcers^[25]. On the other hand, Pederson A's research did not find any correlation between stress and RAS^[26].

Symptom relief and the prolongation of periods without ulcers should be the primary objectives of treatment strategies for recurrent aphthous ulcers that can be achieved if stress can be managed among students. Furthermore, it is advised that proactive steps be taken to lessen stress among dental students to both ease their suffering and improve their academic achievement. Study groups should be formed, and counseling sessions should be conducted to help students manage their stress. Collaborative learning environments and access to psychological support can help students manage stress and support each other^[27].

The study's findings demonstrate a link between psychological variables and RAS and provide insightful information on the psychological stress and mental health of dental students. By addressing stress levels and identifying relevant therapies, this research helps to improve the well-being of the individuals under consideration.

CONCLUSION

Our study reveals a significant association between stress and RAUs among dental students. Stress emerged as a major factor, with 68.40% of participants identifying it as the primary cause of their oral ulcers. Additionally, 51.47% reported a positive family history of oral ulcers, while 69.09% attributed examinations as the cause of their stress. Notably, 46.2% of participants exhibited significantly elevated stress levels, as reflected in their high Perceived Stress Scale (PSS) scores, and within this subgroup, 84.9% had a history of oral ulcers. The prevalence of heightened stress underscores the urgent need for targeted interventions to alleviate stress within this demographic, crucial for both student well-being and effective management of recurrent oral ulcers in dental education.

ACKNOWLEDGEMENT: We would like to express our sincere appreciation to Mr. Kashif Siddique for his invaluable assistance with biostatistics throughout this research project.

CONFLICT OF INTEREST: None.

GRANT SUPPORT AND FINANCIAL DISCLOSURE: None.

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Submitted for publication: 12-03-2024
Accepted after revision: 8-11-2024

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