



## **Stress and Oral Health among Medical Students. A Cross Sectional Clinical Study**

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### **Author's contribution**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Aim:** To evaluate the perceived stress and its effect on gingival inflammation among medical students'.

**Methodology:** A Perceived Stress Scale questionnaire by Cohen and an self-administered potential stress factor questionnaire and was given to a convenient sample of 85 study subjects in an private medical college and hospital to assess perceived stress and possible potential factors. To assess the gingival inflammation, indices like Modified Quigley Hein plaque Index, Loe and Silness Gingival index, sulcus bleeding index was used.

**Results:** Around 85% of them were stressed according to Perceived stress score by Cohen, and among possible potential factors; 51.8% of study subjects who were not staying in hostel previously were stressed and 75.3% study subjects who were having nuclear family were stressed.

**Conclusion:** Majority of the first year Medical students experience perceived stress, and factors

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like students having experience of hostel stay and nuclear type of family showed more stress, whereas the perceived stress dint had any effect on gingival inflammation. Future longitudinal studies are emphasized to know its effect on oral health

**Keywords:** Oral health; medical students; dentistry.

## 1. INTRODUCTION

Stress is defined as a pressure or worry caused by personal or social problems in an individual's life' [1], whereas it also attributes to external demands (physical or mental) of an individual's physical and psychological wellbeing. The perception of stress, varies frequently by one's own personal system of beliefs and attitudes. Various perception of thoughts, beliefs & self-cognitions of an individual leads to stress and consequent behavior in turn affects the academic performance of a student [1,2].

Hypothalamus-pituitary-adrenal cortex (HPA) axis, gets activated by series of stress reactions which leads to the release of corticotrophin-releasing hormone from the hypothalamus, and glucocorticoids, including cortisol from the adrenal cortex [3]. In the HPA system, adrenocorticotrophic hormone regulates cortisol secretion through pituitary gland. Salivary cortisol levels are closely correlated to blood cortisol levels and, therefore, reliably reflect HPA activity [4].

Among various educational systems, Medical education forms a distinctive educational procedure and is being perceived as stressful, which may have a negative effect on cognitive functioning and learning of students in a medical school [5]. It involves the attainment of various academic, clinical and interpersonal skills within educational programs which is challenging task for students as they have never experienced such learning programs before, irrespective of their pre-professional background [2].

Academic stress appears to affect gingival inflammation, shown by more plaque accumulation and in turn effecting periodontal health [5-10].

Many stress related studies has been done & their have been well established on medical students health status because of various stress conditions. There is a paucity about the stress related studies on the medical students in the present region and its effects, especially on oral health .Thus the present study aimed

to evaluate the perceived stress and its effect on gingival inflammation among medical students'

## 2. METHODOLOGY

### 2.1 Source and Method of Collection of Data

The study has been conducted after taking the approval from the institutional review board and being conducted with the ethical principles of the World Medical Association Declaration of Helsinki.

Medical students involved in the study were from a private medical college and hospital.

Aim & importance of the study & procedures involved were explained to the students.

The enrollment of students for the study has been done purely on voluntary basis & the students who agreed to give consent for the participation. A Perceived Stress Scale self-administered questionnaire by Cohen and a self-administered potential stress factor questionnaire was given to a convenient sample of 85 study subjects to assess perceived stress and possible potential factors.

To assess the gingival inflammation of oral health, the indices like Modified Quigley Hein plaque Index, Loe and Silness Gingival index, sulcus bleeding index was used.

## 3. RESULTS

Among 85 medical study subjects, who were in age group of 17-19 years, majority were females 61.2% (n=52); among 52 students 51 (60%) study subjects were not staying in hostel previously, 68.2% (n=58) study subjects were having an single parent; whereas the majority were staying in nuclear family 87% (n=74) (Table 1).

Perceived stress scale self-administered questionnaire by Cohen, showed that majority of the participants were stressed (score>13) 85.9% (n=73). Among this 54.1%( n=46); were females, 60% of study subjects were not staying in hostel previously, among which, majority (n=44) of the

study subjects were stressed, 68.2% of study subjects were having single parent as working, among which, majority (n=49) study subjects were stressed, followed by 31.8% study subjects having with both parents working, 24 study subjects were stressed; 87.1% of study subjects were having a nuclear family among which majority of study subjects (n=73) were stressed, followed by 12.9% study subjects having joint family a total of 9 subjects were stressed (Table 2).

Correlation (Pearson) between Various Perceived stress scale scores and clinical parameters showed non-significant correlation; Whereas Spearman Correlation test between potential stress scores like interpersonal stress scale scores, Clinical skill stress scale scores and clinical parameters showed Non significant correlation (Table 3)

Multiple linear regression analysis of clinical parameters with perceived stress scores showed that, Significant inverse relation was found between miscellaneous stress scores only with Gingival index (-0.0089,  $p < 0.005$ ), whereas non-significant correlation between clinical

parameters and perceived stress scores (Table 4).

Whereas t test between Hostellers and Non-hostellers showed Significant difference between students staying at hostels and day boarders with their Cohen stress scores ( $t = 3.0453$ ,  $p < 0.05$ ). Significant difference was also observed between students staying at hostels and day boarders with their pIPQue scores ( $t = -2.2618$ ,  $p < 0.05$ ) at 5% level of confidence (Table 5)

#### 4. DISCUSSION

While it's been usually believed that stress has an effect on health, which has long been recognized as a cause for concern in both developed and developing countries. It has been described as an unavoidable experience for undergraduate medical trainees. Students who have been suffering from the stress especially during the undergraduate medical training period, if not addressed early, may have dire consequences on them as professionals, to their patients and the society as a whole. The present study tried to overcome and give a clear cut and differentiated picture of the perceived stress and its effect on gingival health.

**Table 1. Gender, parent working status, family and stay wise distribution of study subjects**

	Frequency (Out of 85)	Percent (%)
Females	52	61.2
Males	33	38.8
Both Parent Working	27	31.8
Single Parent Working	58	68.2
Subject from Joint Family	11	12.9
Subject from Nuclear Family	74	87.1
Not Staying at Hostel	51	60.0
Staying at Hostel	34	40.0

**Table 2. Stress scale scores (Cohen) among various factors**

Gender	< 13(Not stressed)	>=13(Stressed)
Female Count	6(7.1%)	46(54.1%)
Male Count	6(7.1%)	27(31.8%)
Total Count	12(14.1%)	73(85.9%)
<b>Type of parents working status</b>		
Both	3(3.5%)	24(28.2%)
Single	9(10.6%)	49(57.6%)
Total Count	12(14.1%)	73(85.9%)
<b>Type of family</b>		
Joint	2(2.4%)	9(10.6%)
Nuclear	10(11.8%)	64(75.3%)
Total Count	12(14.1%)	73(85.9%)
<b>Type of previous stay</b>		
Staying at Hostel	7(8.2%)	44(51.8%)
Not Staying at Hostel	5(5.9)	29(34.1%)
Total Count	12(14.1%)	73(85.9%)

**Table 3. Correlation between various perceived stress scale scores and clinical parameters**

Parameters	Pearson correlation between cohen stress scores with		
	r-value	t-value	p-value
Plaque Index	-0.1415	-1.2465	0.2164
Gingival Index	-0.1443	-1.2717	0.2074
Bleeding on probing	-0.1647	-1.4554	0.1497
Parameters	Pearson correlation between potential factor stress scale scores with		
	r-value	t-value	p-value
Plaque Index	-0.0829	-0.0829	-0.0829
Gingival Index	-0.1525	-0.1525	-0.1525
Bleeding on probing	-0.0788	-0.0788	-0.0788
Parameters	Pearson correlation between academics stress scores with		
	r-value	t-value	p-value
Plaque Index	-0.0585	-0.0585	-0.0585
Gingival Index	-0.1036	-0.1036	-0.1036
Bleeding on probing	-0.0659	-0.0659	-0.0659
Parameters	Spearman correlation between Inter personal relations stress scores with		
	r-value	t-value	p-value
Plaque Index	0.0359	0.0359	0.0359
Gingival Index	0.0190	0.0190	0.0190
Bleeding on probing	0.0861	0.0861	0.0861
Parameters	Spearman correlation between clinical skill stress scores with		
	r-value	t-value	p-value
Plaque Index	0.0059	0.0512	0.9593
Gingival Index	-0.0298	-0.2599	0.7957
Bleeding on probing	0.0378	0.3298	0.7424

As the study comprised of perceived stress component, the perceived stress was estimated with the help of PSS, which showed that majority of the participants were stressed (i.e. having score more than 13) 85% (n=73) followed by 14.1% (n=12) not stressed. Among this, majority were females 54.1% (n=46) followed by males 31.8% (n=27). The results of the present study are in accordance & results were comparable with most of the other studies [19,28,31,32], among health professionals. One possible reason could be due to the fact that most of the students are not adequately prepared for what to be done during the medical training and may fail to cope effectively when they face various pressures and expectations of being a medical student, thereby they perceive it as stress during their academic course.

Around 60% of study subjects were not staying in hostel previously, among which , majority (n=44) study subjects were stressed, followed by 40% study subjects stayed in hostels, 29 study

subjects were stressed which is seen in a similar study [37]. Stress among subjects staying in hostel previously might be due to their constant pressure of being staying outside since their college days before professional course, and it has continued after joining medical course [41]. And for the study subjects not staying in hostel previously also felt stressed, which might be due to coming out of family for first time.

Around 68.2% of study subjects were having single parent as working, among which, majority (n=49) study subjects were stressed, followed by 31.8% study subjects having their both parents working, 29 study subjects were stressed . As in the modern era with rising cost of living, probably single parent working status may be found difficult to match the rising cost for day to day life, which makes the things stressful for the participants.

Around 87.1% of study subjects were having a nuclear family among which majority of study

**Table 4. Multiple linear regression analysis of clinical parameters with perceived stress scores**

Dependent variables	Independent variables	Estimates	SE	t-value	p-level
P.I	Intercept	0.3444	0.0542	6.3514	0.0001
	Cohen stress scores	-0.0043	0.0039	-1.1092	0.2710
	Academics stress	0.0042	0.0058	0.7241	0.4713
	Inter personal relations stress	0.0102	0.0118	0.8685	0.3880
	Miscellaneous stress	-0.0071	0.0055	-1.2841	0.2032
	Clinical skills stress	0.0033	0.0069	0.4829	0.6306
	R= .24136348 R <sup>2</sup> = .05825633				
	F(5,72)=.89079 p<.49195 Std.Error of estimate: .14308				
G.I	Intercept	0.1896	0.0348	5.4494	0.0000
	Cohen stress scores	-0.0008	0.0025	-0.3173	0.7519
	Academics stress	0.0011	0.0037	0.2854	0.7762
	Inter personal relations stress	0.0106	0.0076	1.4023	0.1651
	Miscellaneous stress	-0.0089	0.0035	-2.5192	<b>0.0140*</b>
	Clinical skills stress	0.0022	0.0044	0.4992	0.6192
	R= .33049083 R <sup>2</sup> = .10922419				
	F(5,72)=1.7657 p<.13084 Std.Error of estimate: .09178				
B.O.P	Intercept	0.2661	0.0554	4.8045	0.0001
	Cohen stress scores	-0.0048	0.0040	-1.2077	0.2311
	Academics stress	0.0032	0.0060	0.5301	0.5977
	Inter personal relations stress	0.0192	0.0120	1.5958	0.1149
	Miscellaneous stress	-0.0103	0.0056	-1.8365	0.0704
	Clinical skills stress	0.0055	0.0070	0.7808	0.4375
	R= .32552175 R <sup>2</sup> = .10596441				
	F(5,72)=1.7067 p<.14402 Std.Error of estimate: .14610				

**Table 5. Hostellers and non-hostellers comparison with various variables by t test**

Variables	Hostellers		Non-hostellers (Day boarders)		t-value	p-value
	Mean	Std. dev.	Mean	Std. dev.		
Cohen stress scores	21.84	6.43	17.68	5.53	3.0453	<b>0.0032*</b>
Total stress	22.94	12.43	18.51	9.91	1.7431	0.0854
Academics stress	8.45	4.72	6.89	3.86	1.5941	0.1151
Inter personal relations stress	1.81	1.89	2.00	1.84	-0.4498	0.6541
Miscellaneous stress	8.97	4.75	6.45	3.79	2.5961	0.0113
Clinical skills stress	3.68	3.39	3.23	2.77	0.6327	0.5288
P.I	0.23	0.09	0.30	0.16	-2.2618	<b>0.0266*</b>
G.I	0.13	0.10	0.15	0.09	-1.1617	0.2490
B.O.P	0.14	0.15	0.20	0.15	-1.6914	0.0948

subjects (n-73) were stressed, followed by 12.9% study subjects having joint family a total of 9 subjects were stressed. This might be due to the poorer interactions with the family members because of which they can't easily share and discuss their problems and relieved by the stress to an extent, which is also reported in other studies [33] whereas gender wise distribution showed no differences in stress among male and female which is in according to a similar study conducted [20].

Whereas significant difference was observed in perceived stress in students having hostel stay experience, which is reported in other similar

studies [32]. This could be due to staying away from home after schooling, separated from family, lack of adjustment of hostel facilities like food and accommodation.

As observed from the results, perceived stress scores were high in students staying in hostels which are in accordance to many studies [37] and also significant difference was observed between students staying at hostels and day boarders with their Plaque scores, which means that PI scores are significantly lesser in hostilities as compared to day boarders. This could be due to their medical profession and also staying with the same peer group might have played a role in

keeping their oral health in better manner. Over all the results suggest that the majority of subjects were having perceived stress which shows that there is also need to bring about changes in the quality of evaluation system.

The second part of the study was to know that whether the perceived stress has any effect on gingival health. But it didn't show any significant association towards the same. In the present study, probably the reason of being not effecting gingival health would be; they might have perceived life as stressed, wherein perceived stress as such might not have affected their health aspect.

One of the limitations of the present study as mentioned previously would be because of the cross sectional study which precludes evaluation of temporal associations and information was collected on self-administered questionnaires; there remains the possibility of information bias. Future this cohort can be longitudinally followed to know the effect of perceived stress on cortisol, interleukin 1 beta and gingival health. Prospective studies are necessary to study the associations between occurrence of stressors and incidence of stress.

## 5. CONCLUSION

Most of the first year medical students showed perceived stress, among which the students having experience of hostel stay showed more stress, whereas the perceived stress didn't had effect on gingival health.

There is need to address these stressors by student advisors, peer education, and planning academic schedule and curriculum of professional health sciences and further to develop scientific evidence based modules to effectively manage stress in academic environment. The students should be taught different stress management techniques to improve their ability to cope with a demanding professional course.

## CONSENT

The enrollment of students for the study has been done purely on voluntary basis & the students who agreed to give consent for the participation.

## ETHICAL APPROVAL

The study has been conducted after taking the approval from the institutional review board and

being conducted with the ethical principles of the World Medical Association Declaration of Helsinki.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Westerman GH, Grandy TG, Ocanto RA, Erskine CG. Perceived sources of stress in the dental school environment. *J Dent Educ.* 1993;57:225-31.
2. Divaris K, et al. The academic environment: The students' perspective. *Eur J Dent Educ.* 2008;12(Suppl1):120-130.
3. Chrousos GP. The hypothalamic-pituitary-adrenal axis and immune-mediated inflammation. *N Engl J Med.* 1995;332(20):1351-62.
4. Kirschbaum C, Hellhammer DH. Salivary cortisol in psychoneuroendocrine research: Recent developments and applications, *Psychoneuroendocrinology.* 1994;19:313-33.
5. Shah M. The potential negative effects of emotional distress on medical students include impairment of functioning in classroom performance and clinical practice, stress-induced disorders and deteriorating performance, *BMC Medical Education* 2010;10:2-8.
6. Deinzer R, Forster P, Fuck L, Herforth A, Stiller-Winkler R, Idel H. Increase of crevicular interleukin 1beta under academic stress at experimental gingivitis sites and at sites of perfect oral hygiene. *J Clin Periodontol* 1999;26:1-8.
7. Deinzer R, Hilpert D, Bach K, Schawacht M, Herforth A. Effects of academic stress on oral hygiene – a potential link between stress and plaque-associated disease? *J of Clin Periodontol.* 2001;28:459-64.
8. Deinzer R, Rattermann S, Mobes O, Herforth A. Increase in gingival inflammation under academic stress. *J Clin Periodontol.* 1998;25:431-33.
9. Johannsen A, Bjurshammar N, Gustafsson A. The influence of academic stress on gingival inflammation. *Int J Dent Hyg.* 2010;8:22-27.
10. Deinzer R, Kottman W, Forster P, Herforth A, Stiller-Winkler R, Idel H. After-effects of stress on crevicular interleukin-1beta. *J Clin Periodontol.* 2000;27(1):74-77.

11. Murphy RJ, Gray SA, Sterling G, Reeves K, DuCette J. A comparative study of professional student stress. *J Dent Educ.* 2009;73(3):328–37.
12. Aboalshamat K, Hou XY, Strodl E. Psychological health of medical and dental students in Saudi Arabia. *A Longitudinal Study Public Health Research* 2014;4(5): 179-184.
13. Masry EL R, Ghreiz SM, Helal RM, Audeh AM, Shams T. Perceived stress and burnout among medical students during the clinical period of their education. *Ibnosina J Med BS.* 2013;5(4):179-188.
14. Polychronopoulou A, Divaris K. Dental students' perceived sources of stress: A multi-country study. *J Dent Educ.* 2009; 73(5):631–39.
15. Garbee WH Jr, Zucker SB, Selby GR. Perceived sources of stress among dental students. *J Am Dent Assoc.* 1980;100(6): 853–57.
16. Acharya S. Factors affecting stress among Indian dental students. *J Dent Educ.* 2003; 67(10):1140–48.
17. Ng V, Koh D, Mok BY, Chia SE, Lim LP. Salivary biomarkers associated with academic assessment stress among dental undergraduates. *J Dent Educ.* 2003; 67(10):1091–94.
18. Available:[http://www.who.int/rpc/research\\_ethics/InformedConsent-clinicalstudies](http://www.who.int/rpc/research_ethics/InformedConsent-clinicalstudies). 22/4/15
19. Iqbal S, Gupta S, Venkatarao E. Stress, anxiety & depression among medical undergraduate students & their socio-demographic correlates. *Indian J Med Res.* 2015;141(3):354-357.
20. Waqas A, Khan S, Sharif W, Khalid U, Ali A. Association of academic stress with sleeping difficulties in medical students of a Pakistani medical school: a cross sectional survey. *Peer J.* 2015;12(3):840-51.
21. Oku AO, Owoaje ET, Oku OO, Ikpeme BM. Prevalence of stress, stressors and coping strategies among medical students in a Nigerian medical school. *Afr J Med Health Sci.* 2015;14:29-34.
22. Ravi Shankar TL, Ain TS, Gowar O. Effect of academic stress on plaque and gingival health among dental students of Moradabad. *India J In Acad Periodontol.* 2014;16(4):115-20.
23. Mercz CJ, Wolf OT. Examination of cortisol and state anxiety at an academic setting with and without oral presentation Stress. 2015;18(1):138-42.
24. Kötter T, Pohontsch NJ, Voltmer E. Stressors and starting points for health-promoting interventions in medical school from the students' perspective: A qualitative study. *Perspect Med Educ.* 2015;4: 128–135.
25. Borjalil S, Mohammadi A, Mojtahedzadeh R. Sources and severity of perceived stress among Iranian medical students. *Iran Red Crescent Med J.* 2015;17(10): e17767.
26. Oamar K, Khan NS, Kiani MRB. Factors associated with stress among medical students. *J Pak Med Assoc.* 2015;65:753.
27. Slavish DC, Graham-Engeland JE, Smyth JM, Engeland CG. Salivary markers of inflammation in response to acute stress. *Brain Behav Immun. Review.* 2015;44:253-69.
28. Eva EO, Islam MZ, Mosaddek AS, Rahman MF, Rozario RJ, Iftekhhar AF, Ahmed TS, Jahan I, Abubakar AR, Dali WP, Razzaque MS, Habib RB, Haque M. Prevalence of stress among medical students: A comparative study between public and private medical schools in Bangladesh. *BMC Res Notes.* 2015;8:327.
29. Liu M, Gu K, Wong TKS, Luo MZ, Chan MY. Perceived stress among Macao nursing students in the clinical learning environment. *International Journal of Nursing Sciences.* 2015;2:128-133.
30. Gupta S, Choudhury S, Das M, Mondol A, Pradhan R. Factors causing stress among students of a medical college in Kolkata, India. *Educ Health (Abingdon).* 2015;28(1): 92-5
31. Crego A, Carrillo-Diaz M, Armfield JM, Romero M. Stress and academic performance in dental students: The role of coping strategies and examination-related self-efficacy. *J Dent Educ.* 2016;80(2):165-172.
32. Malviya A, Tiwari S, Meena V, Simhal B, Singh D. Stress among post graduate medical students in central India: A cross section study using perceived stress scale. *Global Journal for Research Analysis.* 2016;5(3):368-370.
33. Ghazanfar H, Haq I, Bhatti JRA, Hameed S, Shafi MS, Hussain A, Javaid A, Naseem S. Severity of stress in Pakistani medical students. *Rawal Medical Journal.* 2016; 41(1):116-120.

34. Seraphim AP, Chiba FY, Pereira RF, Mattera MS, Moimaz SA, Sumida DH. Relationship among periodontal disease, insulin resistance, salivary cortisol, and stress levels during pregnancy. *Brazilian Dental Journal*. 2016;27(2):123-7.
35. Abu-Ghazaleh SB, Sonbol HN, Rajab LD. A longitudinal study of psychological stress among undergraduate dental students at the university of Jordon, *BMC Medical Education*. 2016;16(1):1-6.
36. Gordon NA, Rayner CA, Wilson VJ, Crombie K, Shaikh AB, Yasin-Harnekar S. Perceived stressors of oral hygiene students in the dental environment. *African Journal of Health Professions Education*. 2016;8(1):20-4.
37. George LS, Balasubramanian A, Paul N, Leelamoni K. A study on perceived stress and coping mechanisms among students of a medical school in south India. *J. Evid. Based Med. Healthc*. 2016;3(38):1889-1895.
38. McGregor BA, Murphy KM, Albano DL, Ceballos RM, Stress, cortisol, and B-lymphocytes: A novel approach to understanding academic stress and immune function. *Stress*. 2016;19(2):185-191.
39. Northover C, Thapar A, Langley K, Fairchild G, Van Goozen S. Cortisol levels at baseline and under stress in adolescent males with attention-deficit hyperactivity disorder, with or without comorbid conduct disorder. *Psychiatry Res*. 2016;242:130-136.
40. Suzuki N, Nakanishi K, Yoneda M, Hirofuji T, Hanioka T. Relationship between salivary stress biomarker levels and cigarette smoking in healthy young adults: an exploratory analysis, *Tobacco Induced Diseases*. 2016;14(1):1-7.
41. Shodan M, Srinath Thakur, Jaykumar HL, Priya G, Javali SB, Preetha J. Shetty. Academic stress and its effect on salivary biomarker and oral hygiene among medical students. *European Journal of Pharmaceutical and Medical Research*, 2019;6(3):404-409.

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