Title: "Stress Levels and Coping Strategies in Medical Students and its Association with Salivary IL-6 Levels"

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Authors Contribution Statement:

	Monica	Anahita	Chandralekha	Cleeta
Conceptualization	+	+		
Data curation	+	+	+	+
Formal analysis	+	+		
Funding acquisition	+	+		
Investigation	+	+	+	+
Methodology	+	+	+	+
Project administration		+	+	
Resources	+	+	+	+
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Validation				
Visualization	+	+	+	+
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ABSTRACT

Background: Medical students experience stress throughout their training period, to which they have built their own coping mechanisms. Stress alters various physiological processes, including serum and salivary markers. IL-6 a pro-inflammatory marker, is altered in stress and depression. The present study was conducted to study the stress levels and coping strategies in medical students and its association with salivary IL-6 levels.

Methods: This descriptive study was conducted after obtaining institutional ethical clearance. 76 undergraduate medical students who gave their consent, answered the Cohen's perceived stress scale and BriefCOPE questionnaire. Unstimulated saliva was collected to assess salivary IL-6 levels.

Results: Out of the 76 participants 77.6% were females and 22.4% were males. 9 students perceived mild, 53 moderate and 14 severe stress. Based on Kurskal Wallis p test, in all grades of stress, approach method of coping had a higher score. Most commonly used coping strategies in students with mild and medium stress was acceptance, positive-refrain and planning. Students with severe stress, planning, self-distraction and self-blame were adopted. In spite of the perceived stress, there was no significant difference in the salivary IL-6 levels among the three categories.

Conclusion: The common coping strategies employed by students to handle stress was approach, which has been shown to be associated with better outcomes. In spite of this, a vast number of students have reported to experience stress. Therefore, more effective coping strategies are needed to handle stress and demands of the profession.

Key Words : stress, coping strategies, medical students, IL6 levels

INTRODUCTION.

Stress in today's world has become every man's concern. Stress is defined as a state of psychological and physiological imbalance resulting from disparity between situational demand and the individual's ability and motivation to meet those needs. It is the mental and physical response and adaptation by our bodies to real or perceived changes and challenges in our life. A stressor is any real or perceived physical, social and psychological event or stimulus that causes our bodies to react and respond.[1]

The students of medical college experience stress from the time they enter the curriculum. Ranging from the very game changer entrance exam, the postings, to the university exams. A medico faces different domains of stress namely, academic related stress, interpersonal and intrapersonal stress, teaching and learning related stress, social stress, drive and desire related stress and group activity stress.[1] Acute stress results in decreased cognitive function, impaired attention, problem solving abilities and performance. Chronic effects of stress on the students are predisposition to cardiovascular diseases, type 2 diabetes mellitus, metabolic syndrome, depression and also suicide. Hence, addressing stress related psychological problems is the necessity of the hour.[2]

Different students have built their own coping strategies. Coping with stress can be defined as the process of managing external or internal demands that are perceived as taxing on personal capacities and resources. Many coping strategies like effective time management, social support, positive reappraisals have been broadly grouped as approach and avoidant strategies.[3]

With advent of COVID 19 pandemic, there has been an add-on stress on the medical students. Being a total newbie to management and etiquette during a pandemic situation, concerns regarding safety of family, friends and oneself. Effectively adapting to the new way of virtual teaching in contrast to the age-old classroom and bedside learning. All these factors were new stressors that had to be efficiently faced. This led to the students looking out for new coping strategies that can effectively combat and also develop the skill to face any such situation arising suddenly in future.[2, 3]

Stress also has considerable corollary on the biochemical aspects of the body. IL-6 is a pro-inflammatory marker known to be altered in many diseases with studies suggesting a markable rise in the level of IL6 in context with psychological stress and depression. [4] Salivary IL - 6 is considerable easy marker in terms of sample collection and analysis. Saliva collection is a non – invasive method and an alternative for stressful serum sample collection.[5]

There has been limited number of studies that look into IL-6 levels and stress, especially in medical students. Therefore, the aim of the study is to find the association of salivary IL-6 with stress in medical students and coping strategies used by them.

METHODS.

An institution based descriptive study was conducted from 2021-2022 in department of Physiology, Father Muller Medical College, Mangalore- India, after obtaining institutional ethical clearance. The ethical clearance was issued by Father Muller Institutional ethics committee reference no – FMIEC/CCM/113/2021. Written informed consent of all the students participating was taken with confidentiality assured to the students. Medical students from second year to interns were chosen as the study population. First year students were excluded due to ethical considerations. Students who smoke and consume alcohol, who take drugs, have any acute or chronic infections and are taking any medications were excluded. A sample size of 75 was obtained with 95% confidence interval. Participants were enlisted by snowball sampling technique.

Participants and Study technique:

76 undergraduate medical students who gave their consent to the study underwent clinical examination by the clinician to rule out any systemic illness which was then followed by answering the Cohen's perceived stress scale and BriefCOPE questionnaire on coping strategies. Unstimulated saliva was collected to assess the levels of IL6.

Questionnaire

Cohen's Perceived Stress Scale (PSS), having 10 questions was used to assess the perceived stress in students which evaluates the feelings and thoughts in the previous month. The students were categorised to mild (score 0-13), moderate (score 14-26) and severe perceived stress (score 27-40). BriefCOPE was used to assess the coping strategies of the students to handle stress which is a 28 item questionnaire. The coping strategies were broadly categorized into avoidant and approach, where, self-distraction, self-blame, denial, substance abuse, venting and behaviour were included in avoidant and active, emotional, refrain, acceptance, planning and information were included in approach with each sub-category having 2 questions (score 2-8). The approach and avoidant categories were scored in the range of 12-48. Both the questionnaires were graded using 5 pointing Likert's Scale scaling from 0-4.

Salivary IL-6

10 ml of unstimulated salivary was collected without spitting, minimum 1hr after breakfast. The sample was centrifuged at 3400rpm for 7 mins to get pure saliva in the supernatant. 100microl of supernatant along with control and diluent standard and 50microl diluted biotinylated antibody was added into the ELISA wells then incubated for 1 hr at room temperature. Diaclone human IL 6 ELISA kit was used for the analysis. The sample was washed 3 times before addition of 100microl of diluted streptavidin-HRP which was again incubated at room temperature for 30mins. 100microl of TMB substrate and 100microl of stop reagent was added after 3 times wash. Absorbance was read at 450nm using Biorad reader.

Statistical Analysis

Data collected was entered in Microsoft Excel sheet and analysed using SPSS software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, New York, IBM Corp) for statistics.

Descriptive statistics:

Data was presented as appropriate tables and figures. Mean ± SD for data following normal distribution and median/ interquartile range was used for skewed values.

Inferential statistics:

Both of the questionnaires were graded using 5 pointing Likert's Scale scaling from 0-4. Mean and standard deviation for each question was calculated. For PSS, the students were categorized to mild (score 0-13), moderate (score 14-26) and severe perceived stress (score 27-40). For BriefCOPE, mean score <4 was considered was used least, 4-6 moderately used and >6 the coping strategy was actively used. Kruskal Wallis test was used to explore statistical significance of the questionnaire and demographic details. 'p'-value <0.05 was considered statistically significant.

RESULTS.

Total of 76 medical undergraduate students from phase II to interns participated in the study. Table 1 shows the demographic details of the participating students. Majority of the participants were females (77.6%) with 22.4% students being males. Most of the students were aware of benefits of yoga (89.5%) but only a few practiced in reality (17.1%).

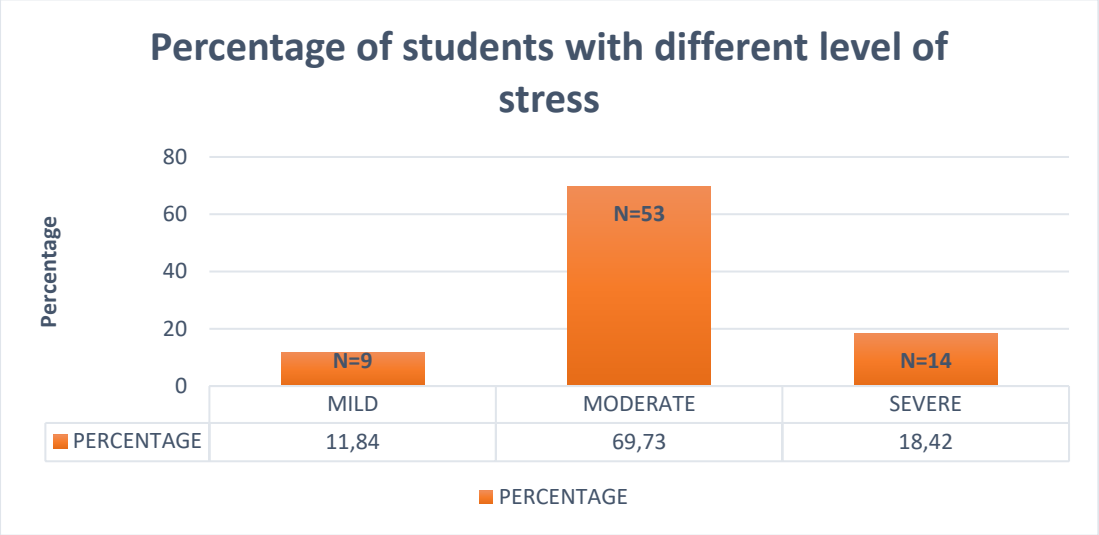
Table 1: Demographic characteristics with lifestyle data of the participating students

		Count	**Column N %**	**Kruskal wallis test p value**
Gender	Female	59	77.6%	0.268
	Male	17	22.4%	
Age	18 - 20 years	25	32.9%	0.000
	21 - 23 years	51	67.1%	
Currently Studying In	Phase II	8	10.5%	0.001
	Phase III Part I	15	19.7%	
	Phase III Part II	40	52.6%	
	Interns	13	17.1%	
Sleep	1. Disturbed	7	9.2%	0.000
	2 Undisturbed	69	90.8%	
Bowel Bladder Habits	Regular	69	90.8%	0.017
	Irregular	7	9.2%	
Lifestyle	Sedentary	37	48.7%	0.433
	Active	39	51.3%	
Exercise	Regular	24	31.6%	0.082
	Irregular	52	68.4%	
Are You Aware Of The Benefits Of Yoga And Breathing Exercises?	Yes	68	89.5%	0.906
	No	2	2.6%	
	Maybe	6	7.9%	
Do You Practice Yoga Or Breathing Exercises?	Yes	13	17.1%	0.264
	No	47	61.8%	
	Maybe	16	21.1%	

p value< 0.05 significant

Based on the response to Cohen Perceived Stress Scale, students were categorized into mild, moderate and severe stress as depicted in Figure 1. 9 students perceived mild stress, 53 moderate and 14 perceived severe stress.

Figure 1: Percentage of students with different level of stress



The response to the BRIEFCOPE questionnaire is presented in Table 2. The data has been compared against mild, moderate and severe stress. Kruskal wallis test reveals avoidant coping strategies to be highly significant with majority of students using it in all the categories of perceived stress. Inspite of perceived stress, there was no significant difference seen in the salivary IL-6 levels of the students among the three categories.

Table 2: Responses to BRIEF COPE questionnaire

	Mild stress(n=9) mean± SD	**Moderate stress(n=53) Mean± SD**	**Severe stress(n=14) Mean± SD**	**Kruskal wallis test p value**
Avoidant	**21.11±5.09**	**23.98±4.57**	**30.50±4.67**	**o.ooo**
Denial	4.11±1.05	4.04±0.88	4.79±0.89	0.026
Substance abuse	2.67±1.32	2.45±0.91	2.64±1.45	0.759
Venting	3.00±1.12	4.26±1.42	5.57±1.50	0.000
Behavior disengagement	3.00±1.41	3.53±1.35	4.86±1.70	0.004
Self-distraction	4.89 ± 2.15	5.21±1.41	6.36±1.50	0.029
Self-blame	3.44±1.67	4.49±1.59	6.29±2.20	0.000
Approach	**30.22±5.36**	**30.30±6.01**	**34.93±5.85**	**o.o35**
Positive refrain	5.67±1.12	5.70±1.64	5.86±2.03	0.945
Planning	5.56±1.51	5.51±1.55	6.50±1.51	0.104
Acceptance	6.11±1.54	5.51±1.65	6.21±1.67	0.272
Emotional support	4.44±1.01	4.81±1.73	5.07±1.94	0.693
Use of instrumental support	4.33±1.50	4.49±1.44	6.07±1.49	0.002
Active	4.11±1.36	4.28±1.28	5.21±0.80	0.032
Humor	4.11±1.90	4.51±1.93	6.21±1.76	0.008
Religion	5.11±1.27	4.89±1.87	5.36±2.10	0.689

P value< 0.05 significant

The median salivary IL-6 in mild category (n=9) was 4.1(3-17.7), in moderate category (n=53) was 4.4(2.9-6.8) and in severe category (n=9) was 4.7(3.1-7.7) which was not statistically significant (p value=0.823).

DISCUSSION.

This study aimed to investigate the stress levels and coping strategies in undergraduate medical students and its association with salivary IL6. A total of 76 students participated in our study of which 22.4% were males and 77.6% were females.

Based on Cohen's Perceived Stress Scale we found that majority of the students (69.7%) were moderately stressed, 18.4% were severely stressed and 11.8% were found to be mildly stress. The least score obtained was 5 and the maximum score obtained was 36. This indicates that all students were experiencing some degrees of stress. In a study by Saravanan C et al 73% of the medical students enrolled in their study were found to be stressed.[6] Another study, reported the stress levels to be 51.7% among medical students.[7]

We did not find a significant difference between gender and stress levels. A study by Amr et al also showed similar results, where level of perceived stress and number of stressors were similar between males and females.[8] A study conducted by Das *et al* had concluded that gender influenced the level of depression rather than the level of stress.[9]

In our study, second phase students reported a higher degree of stress as compared to other phases. A previous study showed stress was substantially greater in Second and Third phase students than in First phase students ($p < 0.05$).[6] This shift in stress category could indicate effective coping strategies with adaptation to the stress of medical education as the students pass out each year evincing their preparedness for the future. Contradictory results were found in the studies by Supe, Sherin and Shaikh et al which have reported a higher level of perceived stress among third and fourth phase students.[10-12]

Mental and physical adverse effects have been well documented side effects of stress.[13] Cognitive decline and learning difficulties are associated with high levels of stress.[14] It is hypothesized that stress activates hypothalamo-pituitary axis which causes changes in neurotransmitters serotonin, dopamine, and nor-epinephrine, that can have serious mental effects like anxiety and depression.[2] Thus, there is a need in finding ways to manage stress effectively.

The median weight of the students in mild category (n=9) was 69(58-82), moderate category (n=53) was 60(53.5-70) and severe category (n=14) was 54.5(46.5-64.3) which was statistically highly significant (p value-0.005). This can be attributed to unhealthy eating habits that was used as a stress busters, a coping strategy adapted, leading to the students perceiving mild stress but at the same time gaining more weight than their peers. [15]

Although 89.5% of participants were aware of the benefits of yoga, only 10 students in moderate category were actually practicing it. This result is in acceptance with the study done by Kathapillai where 89.26% of medical students knew the benefits of yoga but only 30.87% were practically doing it.[16]

Using the Brief Cope questionnaire, we studied the coping methods of the students. We found that in all grades of stress, approach method of coping had a higher score indicating that it was a commonly used coping strategy. The most commonly used coping strategies in students with mild stress was found to be acceptance, positive refrain and planning. Students with medium stress adopted positive refrain more commonly. Whereas in students with severe stress planning, self-distraction and self-blame were adopted.[3] Coping strategies such as use of alcohol, tobacco and drugs were commonly used in medical students in the United Kingdom. In our study, these were reported to be least commonly used. However, under reporting cannot be definitively ruled out.[17-21]

Among the avoidant coping mechanisms, self-distraction, self-blame and venting had higher scores and there was also a statistically significance between the groups in its usage. The use of avoidant coping mechanisms like denial and behavioral disengagement were also statistically different between the three groups, with the students in the high stress group having a higher score. “Denial” is an attempt to reject the reality of a stressful event. “Behavioral disengagement” means giving up or withdrawing efforts to attain a goal. These Coping strategies help in tackling stress but on the other side, they are more likely to worsen the stress inclining them to psychological morbidity. Similar results of anger, distraction and avoidance being the coping strategies of choice for highly stressed students was reported in other studies. [22 - 24]

Humor as a coping mechanism was also reported to be used commonly, especially by the high stress group in our study. Humor is considered to be one of the mature defense mechanisms which contributes to one’s resilience and wellbeing. [25]

Among approach strategies, active coping (5.21+0.8) and use of instrumental support (6.07+1.49) were significantly used by high stressed students with overall approach strategy predominantly used by high stressed students. “Active coping” means taking action or exerting efforts to remove or circumvent the stressor.[24, 26] Students have cognitively refashioned stress as a daily challenge. They accepted the fact and are coming up with ways to positively and effectively handle the stress experienced during medical school to achieve socially and a financially stable life in the future.[27] Thus, it can be assumed that the students use the coping strategy based on the situation they are in and how effectively the stress can be avoided.

In the present study, there was no significant association between stress levels and salivary IL-6 levels which is consistent with study done by Edan.[28] But in a study done by Vernaza assessing the relationship between perceived stress and serum IL-6 levels, there was significant association present between the two, with increase in stress levels, there was statistically significant rise in serum IL-6 levels. [29] This could be due to various factors like genetics and others that affect salivary IL-6 levels more than serum IL-6 levels.[28, 29] In a study done by Izawa et al, they found significant rise in salivary IL-6 levels following an acute psychological stress that was created among the young participants following an arithmetic task, which was attributed to sympathetic activity with cortisol secretion stimulated by the acute stress event.[30]

The common coping strategy employed by the students to handle stress was approach, which has shown to be associated with better outcomes and more stable emotional response. In spite of using the

approach strategy a vast number of students have reported to experience stress. Thus, there exists a need to teach more effective coping strategies to efficiently handle the stress and demands of their profession without comprising their service and health.

Limitations of the study – The study involved self-reporting of stress, thus under reporting or over reporting cannot be ruled out. Majority of the participants were females. Equal distribution of genders would have enabled better comparison between the groups.

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SUMMARY - ACCELERATING TRANSLATION

"Stress levels and coping strategies in medical students and its association with salivary IL-6 levels"

The medical students experience stress from the time they enter the medical course. Stress alters various physiological processes, including serum and salivary markers and is also linked to the development of various diseases like hypertension, diabetes mellitus, depression etc. Students have developed their own coping mechanism to handle this stress.

Aim: The present study was conducted to correlate the stress levels and coping strategies in medical students and the effect of stress on salivary IL-6 levels among medical students.

Methods: This descriptive study was conducted in Father Muller Medical College after obtaining institutional ethical clearance. A total of 76 undergraduate medical students participated in the study. After ruling out Systemic illness clinically Cohen's perceived stress scale and BriefCOPE questionnaire were distributed and collected . Unstimulated saliva was collected to assess salivary IL 6 levels. The data was entered into Excel sheet and analyzed.

Results: Out of the 76 participants 77.6% were females and 22.4% were males. Based on the Cohen's perceived stress scale score, students were categorized into having mild stress (9 students), 53 participants with moderate stress and 14 severe stress. We found that in all grades of stress, approach method of coping had a higher score indicating this was the method most employed by the students to handle stress. Under approach method of coping, the most commonly used coping strategies in students with mild stress was found to be acceptance, positive-refrain and planning. Students with medium stress adopted positive-refrain. Whereas students with severe stress, planning, self-distraction and self-blame were adopted. In spite of the perceived stress, there was no significant difference seen in the salivary IL 6 levels of students among the three categories.

Conclusion: The common coping strategies employed by the students to handle stress was approach, which has shown to be associated with better outcomes and more stable emotional response. In spite of this, a vast number of students have reported to experience stress. Therefore, a need to teach more effective coping strategies to handle stress and demands of their profession without comprising their service and health.

FIGURES AND TABLES.

Figure 1. Percentage of Students with Different Level of Stress

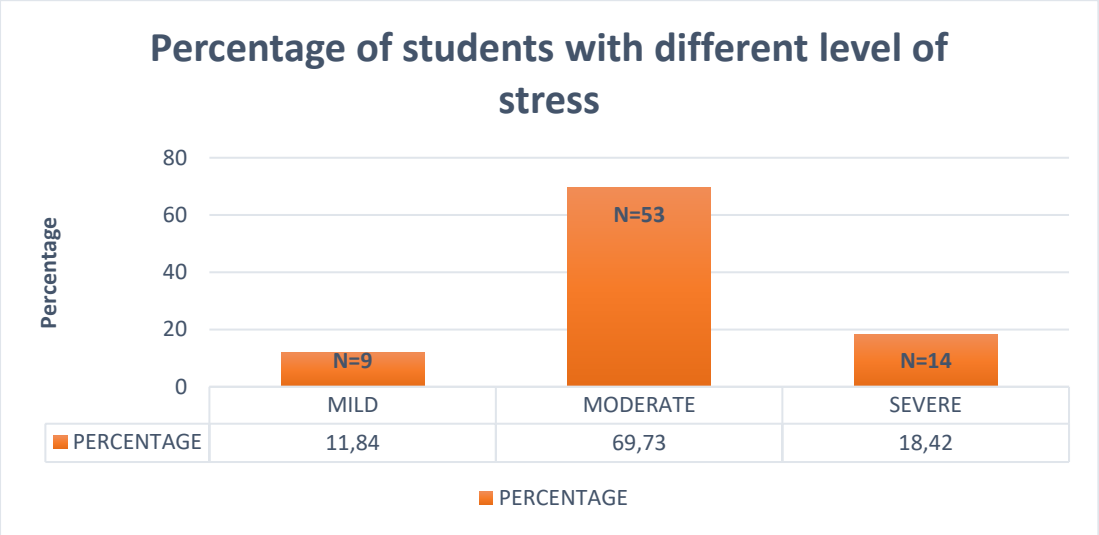

Table 1: Demographic Characteristics with Lifestyle Data of the Participating Students

		Count	Column N %	Kruskal wallis test p value
Gender	Female	59	77.6%	0.268
	Male	17	22.4%	
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	Active	39	51.3%	
Exercise	Regular	24	31.6%	0.082
	Irregular	52	68.4%	
Are You Aware Of The Benefits Of Yoga And Breathing Exercises?	Yes	68	89.5%	0.906
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Do You Practice Yoga Or Breathing Exercises?	Yes	13	17.1%	0.264
	No	47	61.8%	
	Maybe	16	21.1%	

1 **Table 2:** Responses to BRIEF COPE Questionnaire

	Mild stress(n=9) mean± SD	**Moderate stress(n=53) Mean± SD**	**Severe stress(n=14) Mean± SD**	**Kruskal wallis test p value**
Avoidant	**21.11±5.09**	**23.98±4.57**	**30.50±4.67**	**o.ooo**
Denial	4.11±1.05	4.04±0.88	4.79±0.89	0.026
Substance abuse	2.67±1.32	2.45±0.91	2.64±1.45	0.759
Venting	3.00±1.12	4.26±1.42	5.57±1.50	0.000
Behavior disengagement	3.00±1.41	3.53±1.35	4.86±1.70	0.004
Self-distraction	4.89 ± 2.15	5.21±1.41	6.36±1.50	0.029
Self-blame	3.44±1.67	4.49±1.59	6.29±2.20	0.000
Approach	**30.22±5.36**	**30.30±6.01**	**34.93±5.85**	**o.o35**
Positive refrain	5.67±1.12	5.70±1.64	5.86±2.03	0.945
Planning	5.56±1.51	5.51±1.55	6.50±1.51	0.104
Acceptance	6.11±1.54	5.51±1.65	6.21±1.67	0.272
Emotional support	4.44±1.01	4.81±1.73	5.07±1.94	0.693
Use of instrumental support	4.33±1.50	4.49±1.44	6.07±1.49	0.002
Active	4.11±1.36	4.28±1.28	5.21±0.80	0.032
Humor	4.11±1.90	4.51±1.93	6.21±1.76	0.008
Religion	5.11±1.27	4.89±1.87	5.36±2.10	0.689

2