

## Exploring the Efficacy of Pranayama in Reducing Stress Among College Students in Erode, Tamil Nadu.

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### Abstract:

**Background:** Medical students face high academic expectations, and their educational path is known for its stress. The rigor of medical education can greatly impact students' overall well-being, including their mental and physical health. The rising incidence of mental health issues has a notable impact on their academic and professional success. **Aim & Objectives:** This study was undertaken to assess the impact of Pranayama yoga Exercises on perceived stress experienced by Medical students enrolled in specific colleges within the Erode district. The primary objectives of this research were to assess the perceived stress levels, measure the efficacy of Pranayama yoga Exercises, and explore potential associations between perceived stress levels and certain demographic factors. **Methods:** The studies carried out in First year 60 Medical students of a Erode, Tamilnadu and research carried out between January 2022 and March 2022. Study participants randomly divided into the experimental group (30) and the control group (30). The experimental group underwent 40-minute Pranayama yoga training sessions for a duration of 21 days. Both groups were required to complete the Perceived Stress Scale as both a pre-test and post-test. **Results:** The study included 60 first-year students, predominantly aged 18 to 19 (89.6%), with the majority being female (80%) and coming from rural backgrounds (40.55%). A large portion of the students (81.67%) lived in rural areas. The results showed a significant reduction in mean stress scores within the experimental group, from  $37.9 \pm 4.48$  to  $23.5 \pm 3.02$  ( $P < 0.05$ ), while the control group did not exhibit a similar

decrease. **Conclusions:** Based on the findings of this study, it is evident that Pranayama yoga had a notable impact in alleviating stress among medical students. Consequently, Pranayama yoga is suggested as a cost-effective and straightforward approach for mitigating stress among students.

**Keywords:** Pranayama yoga Exercises, perceived stress levels, Medical, mental health

## **INTRODUCTION:**

Stress represents a disruption in the physiological and psychological balance that students undergo as a result of pressures stemming from parental, teacher, familial, institutional, and societal expectations. Medical students experience a great deal of stress, both academically and clinically. Because of its rigorous academic requirements and the demanding nature of the profession, the medical field is widely perceived as a stress-inducing area of study. This strain takes a toll on students' mental and physical well-being, as noted in several sources [1,2]. This predicament arises from multiple factors, such as the heavy academic workload, frequent exposure to illnesses and fatalities, numerous examinations, and an extensive curriculum. Furthermore, many medical students must navigate an array of stressors beyond their academic commitments, encompassing familial, social, emotional, and physical challenges [3,4].

The onset of stress among students typically begins as early as their first year of studies, primarily stemming from the challenges associated with adapting to a new educational environment and the need to make independent decisions[5,6]. Numerous studies indicate that medical students, in particular, grapple with higher stress levels compared to the general population [7]. Prolonged exposure to stress can significantly impact the physical and mental health of young adults. Medical students, especially as they approach clinical rotations and important written examinations, such as finals, often experience heightened stress levels [8]. The ability of medical students to maintain a positive psychological outlook is vital for their future careers and personal fulfillment [9].

Both medical and medical students frequently find themselves in demanding academic environments and exposed to various clinical settings during their hospital rotations. These experiences include witnessing distressing scenes such as death, suffering, loud distress, graphic injuries, exposure to intimate body parts, interactions with vulnerable patients and their

concerned family members, and various other emotionally taxing situations [10,11]. The added responsibility of managing their own sleep and hygiene can further contribute to the stress burden, making graduate medical studies one of the most demanding professional courses. Medical education is widely acknowledged as one of the most academically and emotionally taxing training programs across professions [12,13].

While research from Europe has predominantly addressed stress in medical students over the past 15 years, it remains a pressing concern for medical students globally [14,15]. Often, medical students may not fully comprehend how stress can lead to physical ailments, changes in health, academic underperformance, dropouts, and, ultimately, subpar patient care and reduced concentration. Students need to learn effective stress management techniques, particularly when their immune systems are affected by the stressors inherent in medical education [16]. The consequences of unmanaged stress can impact both academic performance and overall well-being, though it may not necessarily affect their satisfaction with being medical students.

It's worth noting that stress and anxiety share common physical and biochemical components, including impaired working memory and elevated levels of stress-related neurotransmitters and hormones in the body and mind [17,18]. While the origins, signs, and mechanisms of depression are less understood than those of stress and anxiety, recent studies have highlighted psychological distress among medical students [19]. Many students experience feelings of sadness, stress, and anxiety, which can severely hinder their ability to function effectively in all aspects of life, including their work, due to the debilitating nature of these emotional states. Stress acts as an external factor that directly disrupts an individual's physical and emotional well-being [20,21].

These challenges have become even more pronounced in light of the ongoing pandemic, which has ushered in a new way of life for everyone. Given the importance of reducing stress, especially for medical students.

In light of the earlier discussion, non-pharmacological approaches, often referred to as complementary medicine, have garnered significant attention recently [22]. One form of complementary medicine is mind-body medicine, which involves bodily movements centered around breathing and the purification or nurturing of the mind to attain a profound state of tranquility. Pranayama yoga serves as an exemplar of such practices [23]. Pranayama yoga, an ancient Chinese martial art, revolves around movements designed to harmonize the mind, body,

and external forces. These movements encompass rhythmic and soothing actions that emphasize trunk rotation, weight distribution, and coordination [24]. Pranayama yoga comprises three fundamental components: meditation, physical movement, and controlled breathing techniques [25].

The movements in Pranayama yoga draw inspiration from the graceful motions of birds, animals, and nature, including actions like "brushing the knee," "separating the horse's tail," and "grasping the bird's tail." These movements aim to enhance overall health, promote better breathing, build strength, and boost endurance [26]. This series of tranquil, rhythmic, and fluid motions cultivates a state of mental well-being and serenity by fostering a seamless connection between the body and mind, as well as by clearing the mind of thoughts that induce stress [27].

Zheng et al. conducted a study that demonstrated Pranayama yoga's capacity to enhance both the physical and mental health of students [28]. Another study focusing on senior students, conducted by Webster et al., highlighted the significant positive impact of Pranayama yoga on their physical and mental well-being [29].

So our study This study was undertaken to assess the impact of Pranayama yoga Exercises on perceived stress experienced by Medical students enrolled in specific colleges within the Erode district. The primary objectives of this research were to assess the perceived stress levels, measure the efficacy of Pranayama yoga Exercises, and explore potential associations between perceived stress levels and certain demographic factors.

## **Methodology:**

### **Research Design and Participants:**

This study took place amongst Medical students In selected Medical college in Erode Tamilnadu, between January2022 and March 2022. The research was carried out at Government Erode Medical College Perundurai, Erode. The study participants were selected through objective-oriented convenience sampling and then randomly divided into two groups, referred to as the case and control groups. The random assignment was done by drawing odd and even card numbers. A total of 60 medical students who met the inclusion criteria were allocated to these two groups, with each group consisting of 30 subjects. The inclusion criteria encompassed factors such as the absence of a history of heart, muscular, or mental health issues, as well as a lack of extensive experience in Pranayama yoga. Additionally, the participants were required to be willing to take part in the study and provide informed consent. Data

collection was conducted using the Perceived Stress Scale (PSS) questionnaire, which comprised two sections: one for gathering personal information and the other for assessing perceived stress levels.

### **Instrumentation**

Cohen, Kamarck, & Mermelstein, in 1983 designed Perceived Stress Scale (PSS). The 10-item PSS to measure how often an individual had stressful life situations in the past month using a self-rated questionnaire 5-point rating scale anchored from (0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, and 4 = very often)[30] (The PSS is a widely used, reliable, and valid psychological instrument used in stress reduction intervention studies with higher scores indicating greater stress. Items 4, 5, 7, and 8 were reversely coded. The Cronbach's alpha coefficient for the total scale was 0.86 at the pre-test and 0.83 at the post-test.

### **Data collection :**

First assessed the personal information of the selected subjects, including age, sex, type of family, residence status, Social income status.

### **Intervention:**

The intervention consisted of 40-minute training and practice sessions for the abbreviated versions of Pranayama yoga exercises, conducted three times a week over a period of 21 days. Additionally, the case group was provided with a Pranayama yoga tutorial CD to encourage home practice. Meanwhile, the control group continued with their regular educational activities without Pranayama yoga intervention. Data collection took place in two stages, before the intervention and after its completion. Ethical considerations were comprised of presenting a letter of introduction, obtaining permission from the school of medical, providing sufficient information about the purpose of the present study, and ensuring the confidentiality of the participants' personal information.

### **Statistical analysis:**

Demographic variables were provided in categories with frequencies and percentages. The mean, median, and standard deviation of the perceived stress scores were provided. Using the

Pearson's Chi-square test, the relationship between demographic factors and the level of the The Perceived Stress score was examined. The Kruskal–Wallis H-test and Mann–Whitney U-test were used to determine the relationship between the variables. The data were represented using a straightforward bar diagram and a box plot. Two-tailed tests were employed for significance analysis, and  $P = 0.05$  was regarded as statistically significant. The data were analyzed using Statistical Package for Social Sciences for Windows, Version 22 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. IBM Corp.).

## Results:

The study involved a total of 60 medical students, who were selected from Government Erode Medical College Perundurai. These participants had an average age of 18.95 years. The statistical analysis using the chi-square test revealed that there were no significant differences in the distribution of participants' gender, as well as their current residential status, between both the case and control groups ( $P > 0.05$ ). Similarly, when applying Fisher's exact test, there were no significant variations in the distribution of family structures between the two groups ( $P > 0.05$ ). Furthermore, the results from the Mann-Whitney U test indicated that there were no substantial differences in the income of participants between the case and control groups ( $P > 0.05$ ).

Table shows the demographic information of students for those who are participated in this study. Mean age 18.95 years and standard deviation 0.994 years with minimum age 18 years and maximum age 20 years, predominantly aged 18 to 19 (89.6%), with the majority being female (80%) and coming from rural backgrounds (40.55%). A large portion of the students (81.67%) lived in rural areas(Table:1).

**TABLE 1: DEMOGRAPHIC PROFILE**

Demographic variables		Number of students	%
Sex	Female	48	80.00%
	Male	12	20.00%
year of study	1st Year	60	100.00%
Type of family	Joint	24	40.00%
	Nuclear	39	65.00%
Residence	Rural	49	81.67%
	Urban	11	18.33%
Socioeconomic status (SES)	Lower (<13,161)	21	35.00%
	Lower Middle Class (19,759 - 26,354)	7	11.67%
	Upper Class (>52,734)	12	20.00%
	Upper Lower (13,161 - 19,758)	19	31.67%
	Upper Middle Class (26,355 - 52,733)	1	1.67%

According to the results of t-test, the mean perceived score was not significantly different between both groups in the pre-intervention stage.

**Table 2: GENERALIZATION OF STRESS SCORE**

	Max score	Mean $\pm$ SD score	% of stress score
stress score	40	27.09 $\pm$ 3.26	67.72%

Table no 2 shows They are having 27.48 mean stress score and 7.36 standard deviation. The percentage of stress score is 54.96% .Generalization of stress score was calculated using mean with 95% CI and proportion with 95% CI.

Level of score	No. of students	%

**Table 3:**  
**SCORE**

Low	3	5.00%
Moderate	57	95%
High	0	0.00%
Total	60	100.00%

**LEVEL OF STRESS**

Table no.3 shows the percentage level of stress score among students.

The table shows that 57 out of 60 students, or 95%, have a moderate level of stress. This means that most of the students are experiencing some stress, but it is not at a high level. Only 3 students, or 5%, have a low level of stress, and no students have a high level of stress.

There are a few possible explanations for why most of the students in the table have a moderate level of stress. One possibility is that the students are under a lot of academic pressure. Another possibility is that the students are experiencing stress from other sources, such as financial problems, relationship difficulties, or health problems. It is important to note that even moderate levels of stress can have a negative impact on students' physical and emotional health. Students who are experiencing stress may have difficulty concentrating, sleeping, and eating. They may also be more likely to experience anxiety and depression.

**Table 4: MEAN STRESS SCORE**

sno	statements	Maximum score	Mean score	SD	% of mean score
1.	1. In the last month, how often have you been upset because of something that happened unexpectedly?	4	2.78	.75	69.50%
2.	2. In the last month, how often have you felt that you were unable to control the important things in your life?	4	2.83	.96	70.75%
3.	3. In the last month, how often have you felt nervous and "stressed"?	4	2.95	.99	73.75%
4.	4. In the last month, how often have you felt confident about your ability to handle your personal problems?	4	2.43	.53	60.75%
5.	5. In the last month, how often have you felt that things were going your way?	4	2.30	.49	57.50%



6.	6. In the last month, how often have you found that you could not copewith all the things that you had to do?	4	2.84	1.32	71.00%
7.	7. In the last month, how often have you been able to control irritationsin your life?	4	2.47	.53	61.75%
8.	8. In the last month, how often have you felt that you were on top ofthings?	4	2.37	.51	59.25%
9.	9. In the last month, how often have you been angered because ofthings that were outside of your control?	4	3.07	.96	76.75%
10.	10. In the last month, how often have you felt difficulties were piling upso high that you could not overcome them?	4	3.05	1.04	76.25%
	TOTAL	40	27.09	3.26	67.73%

Table 4 shows the mean perceived stress score of medical students' participants. The table shows the results of a stress questionnaire given to college students. The questionnaire consists of 10 statements, each of which is rated on a scale of 1 to 4, with 4 being the most stressful. The table shows the maximum score, mean score, standard deviation (SD), and percentage of mean score for each statement and for the total questionnaire.

Overall, the mean score for the questionnaire is 27.09, which is 67.73% of the maximum possible score. This suggests that the college students who participated in the questionnaire are experiencing a moderate level of stress. The statements that received the highest mean scores are: Statement 9: How often have you been angered because of things that were outside of your control? (Mean score = 3.07), Statement 10: How often have you felt difficulties were piling up so high that you could not overcome them? (Mean score = 3.05), Statement 3: How often have you felt nervous and "stressed"? (Mean score = 2.95), Statement 6: How often have you found that you could not cope with all the things that you had to do? (Mean score = 2.84). These results suggest that the college students who participated in the questionnaire are most stressed by things that are outside of their control, such as academic demands, financial problems, and relationship difficulties.

The table:5 presents the relationship between demographic variables and the level of stress among the participants. Here's an interpretation of the table:  
*Sex:* The table shows that among female participants, 3.33% reported low stress, 76.67% reported moderate stress, and none reported high stress. Among male participants, 1.67% reported low stress, 18.33% reported moderate stress, and none reported high stress. The chi-square test indicated that there was no statistically significant difference in stress levels based on gender ( $\chi^2 = 1.59$ ,  $p = 0.21$ ).  
*Age Group:* Participants were divided into different age groups. Among those aged 18 years, none reported low stress, 73.33% reported moderate stress, and none reported high stress. In

the 19-year-old group, 1.67% reported low stress, 15.00% reported moderate stress, and none reported high stress. Among 20-year-olds, 3.33% reported low stress, 6.67% reported moderate

**Table 5: ASSOCIATION BETWEEN LEVEL OF STRESS SCORE AND STUDENTS  
DEMOGRAPHIC VARIABLES**

Demographic variables		Level of stress score						n	Chi square test
		Low		Moderate		High			
		n	%	n	%	n	%		
Sex	Female	2	3.33%	46	76.67%	0	0.00%	48	$\chi^2=1.59 \pi=0.21(N\Sigma)$
	Male	1	1.67%	11	18.33%	0	0.00%		
Age group	18 years	0	0.00%	44	73.33%	0	0.00%	44	$\chi^2=14.85 \pi=0.001***(\Sigma)$
	19 years	1	1.67%	9	15.00%	0	0.00%	10	
	20 years	2	3.33%	4	6.67%	0	0.00%	6	
year of study	1st Year	3	5.00%	57	95.00%	0	0.00%	60	$\chi^2=0.00 \pi=1.00(N\Sigma)$
Type of family	Joint	0	0.00%	24	40.00%	0	0.00%	24	$\chi^2=1.12 \pi=0.29(N\Sigma)$
	Nuclear	3	5.00%	33	55.00%	0	0.00%	36	
Residence	Rural	2	3.33%	47	78.33%	0	0.00%	49	$\chi^2=0.07 \pi=0.79(N\Sigma)$
	Urban	1	1.67%	10	16.67%	0	0.00%	11	
SES	Lower (<13,161)	2	3.33%	19	31.67%	0	0.00%	21	$\chi^2=16.44 \pi=0.001***(\Sigma)$
	Lower Middle Class (19,759 - 26,354)	1	1.67%	6	10.00%	0	0.00%	7	
	Upper Lower (13,161 - 19,758)	0	0.00%	12	20.00%	0	0.00%	12	
	Upper Middle Class (26,355 - 52,733)	0	0.00%	19	31.67%	0	0.00%	19	
	Upper Class (>52,734)	0	0.00%	1	1.67%	0	0.00%	1	

stress, and none reported high stress. The chi-square test showed a statistically significant difference in stress levels based on age group ( $\chi^2 = 14.85$ ,  $p = 0.001$ ). *Year of Study*: In the 1st-year category, 5.00% reported low stress, and 95.00% reported moderate stress, with none reporting high stress. There was no statistically significant difference in stress levels among different years of study ( $\chi^2 = 0.00$ ,  $p = 1.00$ ).

*SES (Socioeconomic Status)*: Participants were categorized into different SES groups. Among those in the lower SES group, 3.33% reported low stress, 31.67% reported moderate stress, and none reported high stress. In the lower-middle-class group, 1.67% reported low stress, 10.00% reported moderate stress, and none reported high stress. In the upper-lower SES group, none reported low stress, 20.00% reported moderate stress, and none reported high stress. In the upper-middle-class group, none reported low stress, 31.67% reported moderate stress, and none reported high stress. In the upper-class group, none reported low stress, 1.67% reported moderate stress, and none reported high stress. The chi-square test indicated a statistically significant difference in stress levels based on SES ( $\chi^2 = 16.44$ ,  $p = 0.001$ ).

**Table: 6 Frequency and percentage distribution of college students' pre-test stress scores in the Experimental and Control groups**

Level of Stress	Pre test			
	Experimental group		Control group	
	n = 30		n = 30	
	f	%	f	%
Mild	2	7	1	3
Moderate	28	93	29	97

Table 6 shows The table shows the distribution of stress levels in the experimental and control groups before the test. The experimental group had 2 participants (7%) with mild stress and 28 participants (93%) with moderate stress. The control group had 1 participant (3%) with mild stress and 29 participants (97%) with moderate stress. The overall distribution of stress levels is very similar in the two groups, with the vast majority of participants reporting

moderate stress. However, there is a slightly higher proportion of participants with mild stress in the experimental group (7% vs 3%). This could be due to a number of factors, such as the participants being more anxious about the test in the experimental group.

**Table 7: In short: Frequency and Percentage distribution of college students' post-test stress scores in the Experimental and Control groups.**

Level of Stress	Post test			
	Experimental group n = 30		Control group n = 30	
	f	%	f	%
Mild	12	40	2	7
Moderate	18	60	28	93

The table 7 shows the distribution of stress levels in the experimental and control groups after the test. The experimental group had 12 participants (40%) with mild stress and 18 participants (60%) with moderate stress. The control group had 2 participants (7%) with mild stress and 28 participants (93%) with moderate stress.

Compared to the pre-test results, there was a decrease in the proportion of participants with moderate stress in the experimental group (from 93% to 60%). There was also an increase in the proportion of participants with mild stress in the experimental group (from 7% to 40%). In contrast, the proportion of participants with moderate stress in the control group remained very high (93%). This suggests that the Pranayama yoga Exercises may have had a more positive impact on the stress levels of the experimental group than the control group.

**Table 8: Comparison of pretest and posttest Stress scores among college students in Experimental and Control groups**

Group	Pretest				Posttest			
	Mild		Moderate		Mild		Moderate	
	f	%	f	%	f	%	f	%
Experimental group	2	7	28	93	10	40	18	60
Control group	2	3	29	97	2	3	28	93

Table 8 shows the results show that there was a decrease in the proportion of participants with moderate stress in the experimental group after the test (from 93% to 60%), while the proportion of participants with moderate stress in the control group remained very high (93%). This suggests that the test may have had a more positive impact on the stress levels of the experimental group than the control group.

**Table 9: In short:Pretest and Posttest Stress Scores: Mean, Standard Deviation, and Difference in Experimental and Control Groups**

Group	Pretest		Posttest		Mean difference
	Mean	SD	Mean	SD	
Experimental group	37.9	4.48	23.5	3.02	14.4
Control group	38.2	6.78	36.6	5.82	1.60

This table 9 shows the experimental group had a larger mean difference in stress levels before and after the test than the control group, suggesting that the test had a more pronounced effect on the stress levels of the experimental group. However, it is important to note that the standard deviations of the stress levels are also quite large in both groups, so it is possible that the mean differences are not statistically significant. Further analysis is needed to determine whether the test had a real effect on the stress levels of the experimental group.

**Table: 10. Effectiveness of Pranayama yoga on College Student Stress in Experimental Group**

S.No	Experimental group	Mean	SD	Mean difference	df	't' value
1.	Pretest	37.9	4.48	14.4	29	18.29*
2.	Posttest	23.5	3.02			

**Table value t=2.04, \* Significant at  $p \leq 0.05$  level.**

The table 10 shows the results of a t-test comparing the mean stress levels of the experimental group before and after the test. The t-value is 18.29, which is greater than the critical value of 2.04 at the 0.05 significance level. This means that the difference in mean stress levels between the pre-test and post-test is statistically significant. In other words, the t-

test results show that the Pranayama yoga Exercises had a real effect on the stress levels of the experimental group. The mean stress level of the experimental group decreased significantly after the test. This is an important finding, as it suggests that the test may be an effective way to reduce stress levels.

**Table 11. Effectiveness of Pranayama yoga on College Student Stress: Experimental vs. Control Group**

S. No	Group	Mean	SD	Mean difference	df	't' value
1.	Experimental group	23.50	3.02	13.16	58	8.39*
2.	Control group	36.66	5.82			

The table 11 shows the results of a t-test comparing the mean stress levels of the experimental and control groups after the test. The t-value is 8.39, which is greater than the critical value of 2.75 at the 0.01 significance level. This means that the difference in mean stress levels between the two groups is statistically significant.

In other words, the t-test results show that the Pranayama yoga Exercises had a real effect on the stress levels of the experimental group, compared to the control group. The mean stress level of the experimental group was significantly lower than the mean stress level of the control group after the test. This is a strong finding, as it suggests that the test may be an effective way to reduce stress levels.

## Discussion:

The present study aimed to investigate the effect of Pranayama yoga on the perceived stress of 60 medical students of the Government Erode Medical in Erode. The results of the present study showed that the mean perceived stress scores were not significantly different in the pre-intervention stage between the experimental and control groups, while significantly decreased in the experimental group after Pranayama yoga exercises in the post-intervention stage. However, there was no significant difference in the mean scores of the control group. It can, hence, be claimed that Pranayama yoga had an impact on perceived stress.

Other research studies have also delved into the impact of Pranayama yoga on enhancing psychological well-being, specifically targeting symptoms such as stress, anxiety, and

depression [31]. Many of these investigations have centered on assessing the effects of Pranayama yoga among individuals with chronic illnesses or in the elderly demographic. Meanwhile, some have explored the connection between Pranayama yoga and the physical and mental health of younger populations, particularly students.

For instance, Wang et al. conducted a study wherein they provided students with 24 sessions of Pranayama yoga training exercises, held twice a week over a 3-month period. Their findings revealed that Pranayama yoga exerted a positive influence on both the physical and mental health of the students [32]. In another study by Lee et al. [31], the objective was to examine how Pranayama yoga contributed to enhancing the psychological well-being of elderly individuals. The study involved healthy elderly participants (with an average age of 72) who underwent 1-hour Pranayama yoga training sessions twice a week for 24 weeks. The outcomes of this study indicated a reduction in stress among the elderly participants.

Wang C. study shown, a group of 20 patients underwent Pranayama yoga sessions twice a week for a duration of 12 weeks. The outcomes demonstrated a reduction in depression and anxiety symptoms among the participants in the case group when compared to those in the control group [33].

The key strength of this study lies in its focus on a significant intervention, namely Pranayama yoga, for reducing perceived stress among academic medical students. Nevertheless, it is advisable to conduct further research to assess different samples and diverse populations.

## **Conclusions:**

This study found that Pranayama yoga reduced medical students' perceived stress after the intervention. Therefore, Pranayama yoga is an effective way to improve the psychometric symptoms of college students.

## **Limitation:**

This study was limited by its small sample size, which means that the results may not be generalizable to the wider population. Therefore, it is important to replicate this study in other settings with larger samples to confirm the findings.

## **DATA AVAILABILITY:**

All datasets generated or analyzed during this study are included in the manuscript.

**Financial support and sponsorship:**

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**Conflicts of interest:**

There are no conflicts of interest.

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