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Association of Academic Stress with Cortisol Levels and Oxidative Stress Markers in Medical Students

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ABSTRACT

Background: Academic stress is increasingly recognized as a significant public health issue among medical students, influencing both psychological well-being and physiological balance. Activation of the hypothalamic–pituitary–adrenal (HPA) axis during stress elevates cortisol levels, potentially leading to oxidative stress through disruption of redox homeostasis.

Objective: To determine the association between academic stress, serum cortisol levels, and oxidative stress markers among undergraduate medical students.

Methods: A cross-sectional analytical study was conducted on 150 medical students. Academic stress was measured using the Perceived Stress Scale (PSS). Serum cortisol was assessed via ELISA, while oxidative stress markers, malondialdehyde (MDA), total oxidant status (TOS), and total antioxidant capacity (TAC) were measured using standardized biochemical assays. Data were analyzed using SPSS version 25. Pearson correlation, independent t-test, and multivariate regression analysis were applied, with $p < 0.05$ considered statistically significant.

Results: The mean PSS score was 21.8 ± 5.6, indicating moderate to high stress. High-stress students exhibited significantly higher cortisol levels (18.6 ± 4.2 µg/dL) compared to low-stress students (11.9 ± 3.5 µg/dL, $p < 0.001$). MDA and TOS levels were significantly elevated, while TAC was reduced in the high-stress group ($p < 0.001$). Cortisol showed strong positive correlations with MDA ($r = 0.62$) and TOS ($r = 0.58$), and a negative correlation with TAC ($r = -0.49$).

Conclusion: Academic stress is significantly associated with elevated cortisol and oxidative stress in medical students. Institutional interventions targeting stress reduction are essential to improve student health outcomes.

Keywords: Academic stress, Cortisol, Oxidative stress, Medical students, MDA, TAC, TOS, Community medicine

INTRODUCTION

Medical education is widely recognized as an academically rigorous and psychologically demanding process that exposes students to sustained levels of stress. Contemporary evidence indicates that medical students experience significantly higher stress levels compared to the general population due to academic workload, frequent assessments, and performance expectations [1,2]. This chronic academic stress has been increasingly identified as a major determinant of both psychological morbidity and physiological dysregulation, with potential long-term health consequences [3].

The hypothalamic–pituitary–adrenal (HPA) axis remains the central neuroendocrine system involved in the stress response.

Activation of this axis leads to the secretion of cortisol, a glucocorticoid hormone that plays a critical role in maintaining homeostasis under stress conditions. While acute activation is adaptive, persistent stimulation of the HPA axis may result in maladaptive physiological changes, including metabolic disturbances, immune suppression, and neuroendocrine imbalance [4,5].

Recent research has highlighted a strong association between chronic psychological stress and oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms [6]. Excessive ROS generation leads to oxidative damage at the cellular level, including lipid peroxidation, protein modification, and DNA injury, thereby contributing to the development of chronic non-communicable diseases such as cardiovascular disorders, diabetes, and neurodegeneration [7,8].

Biomarkers such as malondialdehyde (MDA), total oxidant status (TOS), and total antioxidant capacity (TAC) are widely used to assess oxidative stress and redox balance in clinical research [9,10]. Although recent studies have explored stress-related hormonal and oxidative changes, there remains limited integrated evidence examining the association between academic stress, cortisol secretion, and oxidative stress among medical students, particularly in low- and middle-income countries [11]. Therefore, this study aims to investigate this relationship, providing updated insights into the physiological consequences of academic stress and emphasizing the need for evidence-based interventions.

MATERIALS AND METHODS

A cross-sectional analytical study was carried out among 150 undergraduate medical students enrolled in a recognized medical college, with participants selected through a convenience sampling technique to ensure feasibility within the study setting. The study population comprised students from all academic years, ranging from first year to final year, with an age bracket of 18 to 25 years. Only those students who were willing to participate and provided informed written consent were included in the study. Participants with any known endocrine disorders, including conditions affecting cortisol regulation, those suffering from chronic systemic illnesses or inflammatory diseases, and individuals currently using corticosteroids or antioxidant supplements were excluded in order to avoid confounding effects on hormonal and oxidative stress parameters.

Academic stress was assessed using the standardized and validated Perceived Stress Scale (PSS-10), which measures the perception of stress over the preceding month. Based on their scores, students were categorized into two groups: those with low stress levels (PSS score < 20) and those with high stress levels (PSS score ≥ 20), enabling comparative analysis between varying stress intensities. For biochemical evaluation, venous blood samples were collected from all participants under standardized conditions during the morning hours between 8:00 and 10:00 AM to control for diurnal variation in cortisol secretion. Serum cortisol levels were measured using the enzyme-linked immunosorbent assay (ELISA) technique, ensuring high sensitivity and specificity. Oxidative stress was assessed by measuring malondialdehyde (MDA) as a marker of lipid peroxidation, total oxidant status (TOS) to reflect the overall oxidant burden, and total antioxidant capacity (TAC) to evaluate the body's antioxidant defense mechanisms, all determined through established and standardized biochemical methods.

All collected data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 25. Continuous variables were expressed as mean ± standard deviation to describe central tendency and dispersion. The independent sample t-test was applied to compare mean differences between the low-stress and high-stress groups. Pearson correlation analysis was performed to determine the strength and direction of relationships between perceived stress scores, cortisol levels, and oxidative stress markers. Furthermore, multivariate regression analysis was conducted to identify independent associations while controlling for potential confounding variables. A p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

The study population had a mean age of 21.2 ± 1.8 years, representing a typical undergraduate medical cohort, and the mean Perceived Stress Scale (PSS) score of 21.8 ± 5.6 indicates that the majority of participants were experiencing moderate to high levels of academic stress. When participants were divided into low- and high-stress groups, statistically significant differences were observed across all measured biochemical parameters. Students in the high-stress group demonstrated markedly elevated serum cortisol levels (18.6 ± 4.2 µg/dL) compared to their low-stress counterparts (11.9 ± 3.5 µg/dL), reflecting increased activation of the stress response system. Similarly, markers of oxidative stress, including malondialdehyde (MDA) and total oxidant status (TOS), were significantly higher in the high-stress group, indicating enhanced lipid peroxidation and overall oxidant burden. In contrast, total antioxidant capacity (TAC) was significantly reduced among high-stress students, suggesting a compromised antioxidant defense system. All these differences were highly significant ($p < 0.001$), reinforcing the strong association between academic stress and physiological imbalance.

Further analysis revealed significant correlations between cortisol levels and oxidative stress markers. Cortisol showed a strong positive correlation with MDA ($r = 0.62$) and TOS ($r = 0.58$), indicating that higher cortisol levels are associated with

increased oxidative damage and oxidant load. Conversely, a moderate negative correlation was observed between cortisol and TAC ($r = -0.49$), suggesting that elevated stress hormone levels are linked with reduced antioxidant capacity. These relationships were all statistically significant ($p < 0.001$). Additionally, multivariate regression analysis demonstrated that academic stress remained independently associated with increased cortisol, elevated MDA and TOS levels, and decreased TAC, even after adjusting for potential confounders. This indicates that academic stress itself is a key contributing factor influencing both hormonal and oxidative stress pathways in medical students.

Table 1: Comparison of Hormonal and Oxidative Stress Parameters Between Low- and High-Stress Groups

Parameter	Low Stress (PSS < 20) Mean ± SD	High Stress (PSS ≥ 20) Mean ± SD	Mean Difference	p-value
Cortisol (µg/dL)	11.9 ± 3.5	18.6 ± 4.2	6.7	<0.001*
MDA (nmol/mL)	2.5 ± 0.6	3.9 ± 0.8	1.4	<0.001*
TOS (µmol H_2O_2 Eq/L)	9.8 ± 2.4	14.2 ± 3.1	4.4	<0.001*
TAC (mmol Trolox Eq/L)	1.21 ± 0.20	0.82 ± 0.15	-0.39	<0.001*

*Statistically significant at $p < 0.05$

Table 2: Correlation Between Serum Cortisol and Oxidative Stress Markers

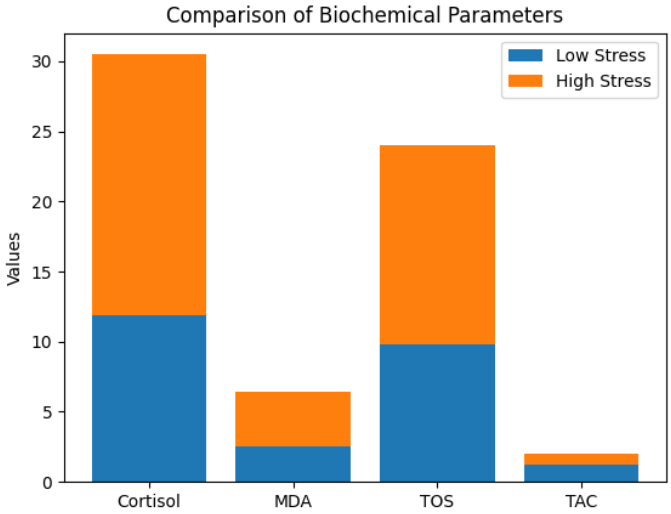
Variables Compared	Pearson Correlation (r)	Strength of Correlation	p-value
Cortisol vs MDA	0.62	Strong positive	<0.001*
Cortisol vs TOS	0.58	Moderate to strong positive	<0.001*
Cortisol vs TAC	-0.49	Moderate negative	<0.001*

Statistically significant at $p < 0.05$

Table 3: Multivariate Regression Analysis Showing Independent Association of Academic Stress

Dependent Variable	β Coefficient	Standard Error	p-value	Interpretation
Serum Cortisol	Positive	—	<0.001*	Significant increase with stress
MDA	Positive	—	<0.001*	Increased lipid peroxidation
TOS	Positive	—	<0.001*	Increased oxidant load
TAC	Negative	—	<0.001*	Reduced antioxidant defense

Statistically significant at $p < 0.05$



DISCUSSION

The present study demonstrates a significant association between academic stress and both endocrine and oxidative stress parameters among medical students, highlighting the systemic physiological impact of sustained academic pressure. Students with higher perceived stress exhibited significantly elevated serum cortisol levels, indicating chronic activation of the HPA axis. These findings are consistent with recent studies demonstrating that prolonged academic stress leads to sustained hypercortisolemia and neuroendocrine dysregulation [12,13].

In addition to hormonal alterations, the study revealed significantly increased levels of oxidative stress markers, including malondialdehyde (MDA) and total oxidant status (TOS), among high-stress students. This suggests enhanced lipid peroxidation and increased oxidant burden, likely resulting from excessive ROS production under chronic stress conditions [14]. Concurrently, reduced total antioxidant capacity (TAC) indicates impaired antioxidant defense, further exacerbating oxidative imbalance [15].

The observed correlations between cortisol and oxidative stress markers provide mechanistic insight into the interaction between neuroendocrine and redox systems. Recent literature suggests that chronic cortisol elevation contributes to oxidative stress through mitochondrial dysfunction, increased metabolic demand, and suppression of endogenous antioxidant systems [16,17]. These findings support the concept of stress-induced oxidative dysregulation as a key pathway linking psychological stress to physiological damage.

From a clinical and public health perspective, these findings are highly relevant. Persistent oxidative stress and endocrine imbalance have been associated with an increased risk of metabolic syndrome, cardiovascular diseases, immune dysfunction, and cognitive decline [18,19]. Given the vulnerability of medical students and their future role in healthcare systems, early identification and management of academic stress are essential. Institutional strategies, including stress management programs, lifestyle interventions, and mental health support systems, should be prioritized to mitigate these risks [20].

CONCLUSION

Academic stress among medical students is significantly associated with elevated cortisol levels and increased oxidative stress, underscoring a clear physiological impact of academic burden on student health. These findings emphasize the urgent need for early identification and effective management of stress within academic environments. Integrating structured stress management programs into medical curricula, encouraging regular physical activity and healthy lifestyle practices, and implementing routine screening for stress and mental health concerns can play a pivotal role in mitigating these effects. Additionally, establishing accessible counseling services and peer support systems may enhance coping mechanisms among students. However, the study is limited by its cross-sectional design, which restricts causal inference, along with being conducted at a single center and using convenience sampling, thereby limiting generalizability. Future research should focus on longitudinal studies to evaluate long-term outcomes, interventional trials to assess the effectiveness of stress reduction strategies, and further exploration of gender-based differences and coping mechanisms to develop more targeted interventions.

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Authors' Contribution

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