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Morning Cortisol Patterns in Mental Health (Depression, Anxiety, and Stress)

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ABSTRACT

Cortisol is well known as a hormone that is released as a repones of the hypothalamic-pituitary-adrenal axis, which was found to be associated with depression, anxiety, and stress. However, the role of morning cortisol patterns, particularly the cortisol awakening response, remains unclear. This study aimed to demonstrate the association between morning cortisol levels and mental health conditions. 88 participants have been included to undergo a blood test to measure the morning blood cortisol and depression, anxiety and stress levels were measured using Depression, Anxiety and Stress Scale-21. The findings indicated that individuals with depressive symptoms not anxiety or stress showed elevated morning cortisol. This study concludes that morning blood cortisol could be used as an early detector for depression.

Keywords: Cortisol dysregulation, hypothalamic-pituitary-adrenal axis, depression, anxiety, stress, cortisol awakening response.

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Introduction

The hypothalamic pituitary adrenal axis (HPA axis) releases the cortisol hormone and is essential for controlling the body's stress response. Levels peak shortly after awakening an event referred to as the cortisol awakening response (CAR), and they decline throughout the day (Clow et al., 2004). In particular high morning cortisol is associated with various psychological disorders such as depression, anxiety, and stress (Doolin et al., 2017). Because these conditions are so common, knowing how cortisol dynamics are involved in mood disturbances can be useful in identifying early biomarkers for diagnosis and treatment.

Many reports have discovered the relationship between cortisol and psychological disorders with diverse results. Many CAR studies have been focused on assessing its potential as an indicator of stress related psychopathology. Possibly consistent with the theory that lack of regulation of the HPA axis underlies the onset and maintenance of depressive symptoms, Mikulska et al. (2021) found that major depressive disorder patients often have elevated morning cortisol. Taken within this context, hypercortisolemia may intensify the neurobiological mechanisms underlying the pathophysiology of both depression and anxiety, thereby potentially function as a bio-marker for these conditions. In addition, stress is known to be an essential element of the dysregulation of cortisol: while chronic stress is reflected by both elevated and suppressed cortisol responses, stress per se does modify the responses to stimulation of the hypothalamic-pituitary-adrenal system. According to Biggio and Mostallino (2009), prolonged stress can alter neuronal plasticity promoting changes in structural brain alterations that promote vulnerability for mood disorder. Farrell et al (2017) found that high levels of sustained cortisol are linked with more stress, anxiety, and depression, and these findings supporting their own. This adds further support for the use of cortisol as a potential stress related psychopathology marker.

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While some studies, however, counter the consistency of this linkage. For example, Kurina et al. (2001) found no association between cortisol levels and anxiety symptoms in older adults, even when the HPA axis function is affected by stress research. Mikulska et al. (2021) also found that the HPA axis is related to mood disorders such as depression, and those who have difficulty going through this process sometimes respond to specific psychological symptoms in different ways, and therefore, a relationship is not well established. The disorder's variations may depend on genetic predisposition, the nature of coping with stress, and the severity of the disorder.

Additionally, several studies provided contradictory results concerning the relationship of cortisol with depression. While elevated morning cortisol levels were linked with depressive symptoms in some, others had lower levels, making it difficult to understand how the HPA axis interacts with mood disorders, Vreeburg et al., 2010. In a study by Bhagwagar et al. (2005), patients with remitted depression showed inconsistent cortisol patterns, which would suggest an inconsistent cortisol and depression relationship dependent on the phase of the disorder or individual biological signature.

However, emerging evidence for such a relationship has yet to resolve the inconsistencies about the nature of the link between cortisol and psychological states. As a result of this, this study tried to clarify further the relationship between morning levels of cortisol on the one side and symptoms of depression, anxiety and stress on the other. This research looks at cortisol as the biological marker of these psychological disorders to contribute to understanding how HPA axis dysregulation plays a role in mental health. It will specifically examine whether alterations of the cortisol awakening response can reliably predict the severity of mood disturbances in clinical populations.

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Methods

Study participants:

A cross-sectional study used 88 healthy participants from the general public referred for a morning cortisol serum test. Demographic information was also gathered, and a validated scale was used to measure Depression Anxiety Stress. After a complete explanation of the objectives and procedures of the study, all participants gave informed consent.

The inclusion criteria for the study were as follows: (1) Age 18 to 65 years; (2) history of no psychiatric or neurological disorders; (3) use of no current psychotropic medications; (4) no substance abuse or dependence. The exclusion criteria were

1. Participants outside the age range of 18 to 65 years,
2. Patients with a current neurodegenerative or psychiatric condition,
3. Patients currently using any medications that may affect cortisol levels, such as corticosteroids and
4. chronic medical conditions.

Blood Sampling

Morning cortisol levels were measured by blood sampling using consistent procedures and timing for all subjects. Participants were asked to stop physical exercise, nicotine, and caffeine at least 24 hours before a blood test to decrease the likelihood that such factors would influence cortisol levels. A certified nurse obtained blood samples one hour after waking up in each participant's home. All samples were taken between 7:00 AM and 9:00 AM to ensure consistency.

Venipuncture was performed, and samples were sent to the laboratory promptly, from where they were stored at 4–8°C. The levels of a hormone known as cortisol were tested in blood serum using an enzyme-linked immunosorbent assay, which is a susceptible technique for detecting how much cortisol is in blood serum in the

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laboratory. The test is accurate, with a sensitivity of 0.3 µg/dL and an intra-assay coefficient of variation of 5 and inter-assay of 7.

Questionnaires

The Depression, Anxiety, Stress Scale-21 (DASS-21), Arabic version, was used to assess participants' emotional states in three key areas: This leaves you complaining of depression, anxiety and stress. The widely used DASS 21 has been validated in many studies. It has 21 items with 7 questions per emotional state. We asked participants to rate each statement on a scale from 0 (did not apply to me at all) to 3 (applied to me very much or most of the time).

It was shown that the DASS-21 has had convergent solid validity with other scales (i.e., Beck Depression Inventory, Beck Anxiety Inventory), showing reliability and accuracy in the assessment of these emotional states (Brown et al., 1997; Antony et al., 1998). Cronbach's alphas of .91, .84, and .90 for depression, anxiety, and stress in the Arabic version of the DASS-21, respectively, support high internal consistency and cultural validation of the Arabic version of the DASS-21 as a reliable measure of emotional states in Arabic-speaking populations.

Analysis

The analysis used SPSS (version 27) and a $p < 0.05$ significance level. Demographic variables and primary study measures were calculated using descriptive statistics, such as means, standard deviations and frequencies. ANOVA tests were used to test the association of depression, anxiety, and stress on morning blood cortisol levels between the groups. Participants were divided into two groups (low and high) based on the median split for each independent variable: anxiety, depression, and stress. We evaluated whether these groups had significant differences in morning cortisol levels using the ANOVA analysis.

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Second, the impact of depression, anxiety, and stress on blood cortisol levels was investigated using multiple regression analysis. Before regression analysis, assumptions of normality, linearity, homoscedasticity, and non-collinearity were tested. Variance inflation factors were used to evaluate multicollinearity; linearity and homoscedasticity were investigated using scatterplots of residuals. The Shapiro-Wilk test was used to verify normality.

SPSS ran a multiple regression model to investigate how each of the independent variables—depression, anxiety, and stress—might influence the dependent variable, blood cortisol levels. Interpretation of the regression results helped one grasp these connections' significance and direction. R-squared values let one assess the general fit of the regression model.

Results

The sample's descriptive statistics N = 88 are shown in Table 1. With an average education level of 14.38 years (SD = 3.70), 60 men and 28 women comprised the 42.06-year mean age of participants. With SD = 9.47, the mean Body Mass Index (BMI) was 33.35.

Table 1 Descriptive Statistics of Study Participants (N = 88)

Variables	**N**	**Mean**	**Std. Deviation**
Male	60		
Female	28		
Age	88	42.06	12.75
Education	88	14.38	3.69
BMI	88	33.35	9.46

BMI: Body Mass Index**, SD:** Standard Deviation.

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The associations between stress, anxiety, and depression on blood cortisol levels were investigated using multiple regression analysis. The findings show a strong correlation between anxiety and blood cortisol levels, implying that those with more depressed symptoms usually have higher cortisol levels ($p < 0.05$). This result captures the complicated interaction of stress reactions and mood disorders. By contrast, neither stress nor anxiety revealed any significant correlation with blood cortisol levels. This data shows that while stress and anxiety are usually associated with cortisol dysregulation, this research did not provide statistically significant findings.

Table 2 Regression Coefficients for Depression, Anxiety, and Stress on Blood Cortisol Levels**.**

Variables	**R^2**	**P-value**
Depression	0.32	***0.02**
Anxiety	0.01	0.21
Stress	0.01	0. 21

R^2 = Coefficient of Determination, **p-value**: Probability Value, *****= Significant.

Table 3 demonstrates that the ANOVA test revealed a statistically significant elevation in morning cortisol levels across depression groups ($p = 0.04$), accompanied by a small-to-moderate impact size. No statistically significant difference was found for anxiety groups ($p = 0.07$) or stress groups ($p = 0.71$), suggesting that cortisol levels did not vary substantially according to anxiety or stress levels.

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Table 3 Comparison between Morning Blood Cortisol Levels and Depression, Anxiety, and Stress Severity groups.

Variables	Severity groups (N)	Morning Cortisol Levels (Mean ± SD)	p-value
Depression	1 (High): N=40	308.58 ± 109.66	***0.04**
	2 (Low): N=48	250.00 ± 154.84	
Anxiety	1 (High): N=39	305.61 ± 122.67	0.07
	2 (Low): N=49	255.23 ± 142.62	
Stress	1 (High): N=50	288.13 ± 115.84	0.71
	2 (Low): N=38	277.48 ± 153.36	

SD: Standard Deviation, **p-value**: Probability Value, ***= Significant.

Discussion

The present work has examined the correlation among morning blood cortisol levels, depression, anxiety, and stress. The results showed that morning blood cortisol level corresponds exclusively with depression, not anxiety and stress. These results support earlier studies indicating the vital part the HPA plays in mood disorders. Remarkably, the strong correlation between depressed symptoms and cortisol levels found in this research corresponds with the meta-analysis study of Burke et al. (2005), which revealed a high degree of cortisol responses in persons with severe depressive disease. These consistent findings across studies imply that dysregulation of cortisol production is a robust biomarker of depression, indicating an overactive state of the Sympathetic Nervous System in reaction to stress. In addition, Stetler and Miller (2011) have summarized over four decades of research which suggests depressed individuals frequently have abnormal cortisol patterns, including elevated levels on waking. The CAR indicates that people with depression might have a higher

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physiological response to stress and that this high may go on to persist in depressive symptoms (Dedovic & Ngiam, 2015). The results of the current study support the hypothesis that the CAR may be a key biomarker for evaluating depression severity and for use in the development of clinical interventions.

In contrary, in the current study, we found no significant associations between anxiety or stress and morning blood cortisol levels in contrast to the literature that typically describes elevated cortisol levels in people with anxiety disorders. One example is Vreeburg et al. 2010 who demonstrated that people diagnosed with anxiety disorders exhibited elevated HPA axis activity and had abnormal cortisol profiles. Variability in anxiety presentations may lead to this inconsistency, and the sample in this current study may be heterogeneous. According to Mikulska et al. (2021), it is feasible that different susceptibilities to experiences of stress, differences in the perceived context of the threatening situation, and dissimilar coping strategies may play a role in both positive and negative research results on the relationship between anxiety and abnormality of cortisol feedback regulation.

Further, as opposed to the findings of Hellhammer et al. (2009), we did not find that chronic stress is associated with any of the variables measured. However, results from the current study are as follows: assuming that how we operationalize stress and where it is assessed to determine its effects on cortisol is central to how it affects cortisol levels. Learning from this study, future research must consider using more sophisticated measures of stress, which incorporate the multiple stressed individuals experience and which stressors elicit or exacerbate the physiologic response of the HPA axis.

Furthermore, the findings of this study suggest that depression was responsible for a moderate proportion of the variance in cortisol, and anxiety and stress made little contribution. This is in line with previous research, which suggests that depression, more often than not, is the driver of cortisol dysregulation as opposed to anxiety and

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stress. The study by Pruessner et al. (2003) showed that although the HPA axis activation as a result of stress and anxiety is similar, the effect of the magnitude of HPA axis activation may be less pronounced in anxiety than in depressive symptoms.

A critical strength of the present study is the use of morning cortisol levels as a biological marker of HPA axis function, which provides a physiological objective contribution to a psychological condition analysis. The sample was also free of psychiatric or neurological disorders to minimize confounding factors such as medication or illness-related cortisol variation. Still, many constraints have to be recognized. First, the cross-sectional design restricts the possibility of deducing causal links between psychiatric disorders and cortisol levels. Furthermore, the study's reliance on a median split to classify subjects into high and low groups for stress, anxiety, and depression might have lessened the sensitivity to identify more minute changes in cortisol reactions. Moreover, the DASS-21's stress evaluation could not adequately reflect the complexity and chronicity of actual stresses, affecting the nonsignificant stress results.

The results of the research have numerous significant therapeutic consequences. Given the vital link between depression and cortisol dysregulation, morning cortisol levels and the CAR might be helpful indicators for tracking and determining the degree of depression. Including cortisol tests in their diagnostic and therapy plans for patients experiencing depressed symptoms—especially those resistant to traditional treatments—may help clinicians. Furthermore, the absence of notable results for stress and anxiety implies that these disorders could need new biomarkers or more thorough psychophysiological tests for correct diagnosis and treatment.

In conclusion, the present research emphasizes the complexity and subtleties of anxiety and stress even as it confirms and expands earlier results connecting depression with cortisol dysregulation. The contradicting findings for these dimensions imply further investigation of their interactions with cortisol and finding

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possible mediators influencing these dynamics. The development of focused treatments that meet the particular requirements of people with different mental profiles depends on an awareness of these variations.

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