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IMMUNOLOGICAL AND HORMONAL ALTERATIONS IN ADULTS SUFFERING FROM DEPRESSION

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ABSTRACT

Depression is a widespread mental health concern with multifaceted etiological factors, including potential hormonal and immunological alterations. This cross-sectional study aims to investigate the relationships between depression and markers of hormonal and immunological status in adults. A total of 146 adults, aged 18 to 65, were recruited for this study, comprising 73 individuals diagnosed with depression and 73 age-matched healthy controls. Hormonal assessments included thyroid-stimulating hormone (TSH), and prolactin, while immunological parameters encompassed C-reactive protein (CRP) and Fasting blood glucose. The severity of depression was evaluated using standardized psychometric tools. Preliminary findings reveal significant alterations in TSH and prolactin were observed in the depressed group compared to controls ($p<0.01$), suggesting perturbations in thyroid function and reproductive hormones. Immunological assessments demonstrated elevated CRP levels in depressed individuals ($p<0.001$), indicative of an inflammatory response associated with depression. This cross-sectional study provides initial insights into the hormonal and immunological alterations associated with depression in adults. The observed dysregulations in TSH, prolactin, FBS and CRP emphasize the intricate interplay between the endocrine and immune systems in depressive disorders. Further exploration of these associations may contribute to a better understanding of the pathophysiological mechanisms underlying depression and facilitate the development of targeted therapeutic interventions.

Key words: Depression, Hormonal Alterations, Immunological Changes, Cross-Sectional Study, Psychiatric Morbidity.

INTRODUCTION

Depression, a pervasive and multifaceted mental health disorder, continues to be a leading cause of global disability, impacting millions of individuals across diverse demographics. The intricate interplay of biological, psychological, and social factors contributes to the heterogeneity of this condition, prompting an ongoing quest to unravel its underlying mechanisms [1-3]. Recent research suggests that beyond the conventional understanding of depression as a purely neurochemical imbalance, hormonal and immunological alterations may play pivotal roles in the etiology and manifestation of depressive disorders [4]. This cross-sectional study delves into the intricate relationships between depression and specific markers of hormonal and immunological status in adults. The exploration of these facets is essential for a comprehensive understanding of the complexities inherent in depression, potentially opening new avenues for targeted therapeutic interventions [5].

The hormonal milieu in depression is a subject of increasing interest, with studies implicating dysregulations in the hypothalamic-pituitary-adrenal (HPA) axis and other endocrine systems.

Cortisol, a key stress hormone regulated by the HPA axis, has been widely studied in the context of

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depression, with inconsistent findings that warrant further investigation. Additionally, thyroid hormones and reproductive hormones, such as prolactin, may contribute to the nuanced endocrine landscape of depressive disorders[6-7]. Concurrently, emerging evidence underscores the involvement of the immune system in depression. Systemic inflammation, reflected by elevated levels of C-reactive protein (CRP), has been posited as a potential contributor to the pathophysiology of depression. However, the intricate dynamics between the immune system and depression remain a topic of ongoing exploration[8]. This cross-sectional study seeks to bridge existing knowledge gaps by systematically examining hormonal and immunological alterations in adults diagnosed with depression. The integration of detailed interpreted data will contribute to a more nuanced understanding of the interconnections between these biological systems and depressive symptomatology[9]. Insights gained from this research may pave the way for novel diagnostic markers and therapeutic strategies, offering hope for improved outcomes in individuals grappling with depression. As we embark on this investigative journey, the results of our study aim to shed light on the intricate tapestry of hormonal and immunological alterations in depression, fostering a more holistic approach to the management of this prevalent mental health condition [10].

MATERIALS AND METHODS

This methodological framework was designed to systematically investigate the hormonal and immunological landscape in adults suffering from depression, providing a robust foundation for the subsequent interpretation and discussion of findings in our cross-sectional study.

a. **Study design and Participants:** This cross-sectional study involved 146 adults aged 18 to 65 years, recruited from Sri Lakshmi Narayana Institute of Medical sciences, Pondicherry between Feb 2015 and Jan 2016. The sample comprised 73 individuals diagnosed with depression and 73 age-matched healthy controls. Participants were recruited from psychiatric clinics, community centres, and through advertisements.
b. **Inclusion and Exclusion Criteria:** Inclusion criteria for the depressed group included a clinical diagnosis of major depressive disorder based on CES-D criteria. Healthy controls had no history of psychiatric disorders or chronic medical conditions. Exclusion criteria for all participants included pregnancy, autoimmune disorders, chronic inflammatory conditions, and recent significant medical illnesses[11].
c. **Ethical Considerations:** Ethical approval was obtained from the Institutional Ethical committee. Informed consent was obtained from all participants, emphasizing voluntary participation, confidentiality, and the right to withdraw at any point.
d. **Clinical Assessments:** Depression severity was assessed using the CES-D Scale. Socio demographic information, medical history, and medication use were collected through structured interviews and medical records.
e. **Sample collection:** Fasting blood samples (5 ml) were collected for assessment of Prolactin, TSH, FBS, CRP. Body mass index (BMI) was calculated as body weight in 2 kilograms divided by standing height in meters squared (kg/m).
f. **Hormonal Assays:** Polactin levels were measured using enzyme-linked immunosorbent assay (ELISA). Thyroid-stimulating hormone (TSH) and prolactin levels were determined by chemiluminescent immunoassay.
g. **Immunological Assays and FBS:** Serum levels of C-reactive protein (CRP) and Fasting blood glucose levels
h. **Statistical Analysis:** Data were analysed using SPSS, and results were expressed as mean ± standard deviation or median (interquartile range) depending on the distribution. Group differences in hormonal and immunological markers were assessed using ANOVA test
i. **Sample Size Justification:** The sample size was determined based on power calculations considering effect sizes from previous studies and maintaining a power of 80% and a significance level of 0.05.
j. **Quality Control:** Rigorous quality control measures were implemented throughout the study, including standardization of sample collection procedures, calibration of laboratory equipment, and regular internal and external quality assurance assessments.
k. **Data Interpretation:** Results will be interpreted with a focus on identifying patterns of hormonal and immunological alterations associated with depression, considering potential confounding factors and covariates.

The CES-D Score: The CES-D (Center for Epidemiologic Studies Depression) Scale consists of 20 items, and respondents are asked to rate how often they experienced each symptom over a specified time period, commonly the past week. The items cover a range of depressive symptoms. Here are the 20 items from the CES-D Scale [12-13]:

1. I felt hopeful about the future.
2. I was bothered by things that usually don't bother me.
3. I had trouble shaking off the blues, even with help from my friends or family.
4. I felt fearful.
5. My sleep was restless.
6. I was happy.
7. I felt lonely.

8. People were unfriendly.
9. I enjoyed life.
10. I felt sad.
11. I could not "get going."
12. I felt like a failure.
13. I felt that people disliked me.
14. I had trouble keeping my mind on what I was doing.
15. I felt like everything I did was an effort.
16. My sleep was restless.
17. I was happy.
18. I felt lonely.
19. People were unfriendly.
20. I enjoyed life.

Respondents typically rate each item on a scale from 0 to 3, where 0 represents rarely or none of the time, and 3 represents most or all of the time. The total score is obtained by summing the individual item scores, with higher scores indicating a higher level of depressive symptoms

RESULTS

1. **CES-D Score Categories:** The categorization of study groups based on CES-D scores provides a clear delineation of depressive symptom severity. Groups A and B exhibit minimal symptoms (CES-D < 16), while Groups C and D manifest moderate to severe symptoms, suggesting a diverse representation of depression across the study.
2. **Number of Subjects:** The varying number of subjects in each group reflects the distribution of participants across different severity levels of depression. The control group is notably larger, providing a robust comparison base for understanding hormonal and immunological alterations in depression.
3. **Sex Ratio:** The sex ratios within each group highlight potential gender disparities in depression. Groups A and D show a higher proportion of females, indicating a potential gender association with depressive symptom severity.
4. **Mean Age:** The progressive increase in mean age from Groups A to D and the control group suggests a potential association between age and the severity of depressive symptoms. This aligns with existing literature that indicates an increased risk of depression in older age.

BMI (Body mass Index):

The mean BMI values exhibit a noteworthy rise in more severe depression categories (Groups C and D). This aligns with the known relationship between depression and weight changes, with higher BMI potentially contributing to the severity of depressive symptoms.

1. **Thyroid Stimulating Hormone**
   - **Group A (CESD < 16):** The TSH levels are within the normal range (4.0±1.00), suggesting typical thyroid function in individuals with minimal depressive symptoms.
   - **Group B (CESD 16-32):** A moderate increase in TSH levels (6.05±0.78) indicates a potential shift towards hypothyroidism in individuals with mild to moderate depressive symptoms.
   - **Group C (CESD 32-48):** TSH levels continue to rise (6.33±0.39), indicating a possible correlation between higher depressive symptom severity and thyroid dysfunction.
   - **Group D (CESD 48-64):** Substantially elevated TSH levels (13.64±2.34) suggest a pronounced association between severe depression and hypothyroidism.
   - **Controls:** The control group demonstrates TSH levels within the normal range (8.31±0.14).

2. **Prolactin**
   - **Group A (CES-D < 16):** Prolactin levels are within the normal range (8.41±0.95) in individuals with minimal depressive symptoms.
   - **Group B (CES-D 16-32):** A slight increase in prolactin levels (9.58±1.62) suggests a potential association with mild to moderate depressive symptoms.
   - **Group C (CES-D 32-48):** Further elevation in prolactin levels (10.69±1.81) indicates a potential correlation with higher depressive symptom severity.
   - **Group D (CES-D 48-64):** Significantly elevated prolactin levels (15.2±0.23) suggest a pronounced link between severe depression and hyperprolactinemia.
   - **Controls:** The control group shows prolactin levels within the normal range (12.28±2.42).

1. **Fasting Blood Glucose**
   - **Group A (CES-D < 16):** The mean FBS level is 90.12±12.17, falling within the normal range, indicating no significant alteration in blood sugar levels in individuals with minimal depressive symptoms.
   - **Group B (CES-D 16-32):** The FBS level remains within the normal range (93.76±16.7), suggesting that mild to moderate depressive symptoms do not have a pronounced impact on fasting blood sugar.
   - **Group C (CES-D 32-48):** The mean FBS level is 99.78±14.01, still within the normal range but showing a trend toward higher values in individuals with more severe depressive symptoms.
   - **Group D (CES-D 48-64):** The FBS level is substantially elevated (136.11±18.31), indicating a potential association between severe depressive symptoms and higher fasting blood sugar levels.

- **Controls:** The control group demonstrates a mean FBS level of 96.67±12.71, within the normal range.

2. C-Reactive Protein:

- **Group A (CES-D < 16):** The mean CRP level is 0.18±0.029, indicating a low level of systemic inflammation in individuals with minimal depressive symptoms.
- **Group B (CES-D 16-32):** CRP levels remain relatively low (0.29±0.028) in those with mild to moderate depressive symptoms.
- **Group C (CES-D 32-48):** A slight increase in CRP levels (0.35±0.032) suggests a potential association between more severe depressive symptoms and increased inflammation.
- **Group D (CES-D 48-64):** The CRP level is further elevated (0.88±0.049), indicating a significant association between severe depressive symptoms and heightened systemic inflammation.
- **Controls:** The control group demonstrates a mean CRP level of 0.22±0.032, within the expected range for healthy individuals.

Table 1: Demographic characteristic of the study group

	CES-D	Number of subjects	Sex ratio	Mean age	BMI (Mean±SD)
<16	A	14	1:2	43	26.82±6.18
16-32	B	18	1:1	45	28.3±5.12
32-48	C	25	2:3	50	31.9±2.06
48-64	D	16	1:2	55	29.62±3.16
	Controls	73	3:2	49	26.8±3.97

Table 2 Showing hormonal levels in different groups

CES-D	TSH(Mean±SD)	PROLACTIN(Mean±SD)
A(n=14)	4.0±1.00	8.41±0.95
B(n=18)	6.05±0.78	9.58±1.62
C(n=25)	6.33±0.39	10.69±1.81
D(n=16)	13.64±2.34	15.2±0.23
Controls (73)	8.31±0.14	12.28±2.42

Table 3: Fasting blood sugar and C - reactive protein Levels in Different Groups

CES-D	FBS (Mean±SD)	CRP(Mean±SD)
A(n=14)	90.12±12.17	0.18±0.029
B(n=18)	93.76±16.7	0.29±0.028
C(n=25)	99.78±14.01	0.35±0.032
D(n=16)	136.11±18.31	0.88±0.049
Controls (73)	96.67±12.71	0.22±0.032

DISCUSSION

The demographic characteristics outlined in this study provide a holistic perspective on the study population, laying the groundwork for examining potential correlations with hormonal and immunological alterations in depression. Previous research studies have consistently highlighted the importance of considering demographic factors in understanding the multifaceted nature of depression. Trends observed in age, gender, and BMI underscore the complex interplay of socio demographic factors in the manifestation and severity of depression, as corroborated by existing literature [14-16].

The inclusion of a control group is instrumental in this research, acting as a crucial reference for meaningful comparisons and facilitating the identification of specific patterns associated with depression. Previous studies have emphasized the significance of well-structured control groups in enhancing the validity and reliability of findings related to depression and its various dimensions [8]. As the study progresses, the correlation between demographic factors and hormonal and immunological alterations becomes paramount. This aligns with prior research, which has emphasized the need to elucidate the intricate relationship between psychological and physiological aspects of depression in adults. Future analyses will delve into the associations between CESD scores, demographic variables, and measured hormonal and immunological parameters, contributing to a more comprehensive understanding of depression in this cross-sectional study [17-18]. The observed hormonal alterations, such as changes in TSH and prolactin levels across different depressive symptom severity groups, echo findings from earlier studies [19]. Elevated TSH levels suggest thyroid dysfunction, supporting the concept of the hypothalamic-pituitary-thyroid (HPT) axis involvement in depression, as elucidated in previous research. Furthermore, hyperprolactinemia in severe depression implies disruptions in the hypothalamic-pituitary-gonadal (HPG)

axis, aligning with studies that propose a link between altered reproductive hormone regulation and mood disturbances.

The progressive increase in FBS levels across depression severity groups suggests a potential association between more severe depressive symptoms and higher fasting blood sugar as identified by [Lukaschek et al., 2013], corroborating findings from existing literature on the complex relationship between depression and glucose metabolism. These results point to the importance of investigating both glucose metabolism and inflammatory markers in understanding depressive symptoms, as noted in prior research [20-21]. The link between increased inflammation and depression was detected in the early 1990s, Elevated CRP levels in more severe depression categories support the immune-inflammatory hypothesis in depression, as established in earlier studies. Integrating these findings with hormonal data from previous analyses will contribute to a more comprehensive understanding of the intricate relationships between psychological and physiological aspects of depression in this cross-sectional study [22].

The increase in prolactin levels, particularly in more severe depression categories, further suggests a potential association between depressive symptoms and alterations in reproductive hormone regulation. This finding aligns with previous research that has linked elevated prolactin levels to stress and altered hypothalamic-pituitary-gonadal axis functioning, emphasizing the relevance of considering reproductive hormones in the context of depression.

CONCLUSION

In our cross-sectional study, we gained valuable insights into the intricate interplay of hormonal and immunological alterations in adults with depression. The comprehensive examination of diverse parameters revealed patterns that contribute to understanding the complex relationship between psychological and physiological dimensions of depression. Regarding hormonal markers, such as thyroid-stimulating hormone (TSH) and prolactin, our findings indicate a gradient of dysregulation corresponding to the severity of depressive symptoms. Elevated TSH levels in more severe depression suggest potential disruptions in thyroid function, while increased prolactin levels, particularly in severe cases, suggest disturbances in the reproductive hormone axis, highlighting the role of the endocrine system in depressive disorders. The investigation into immunological markers, specifically C-reactive protein (CRP), revealed a significant association between depression severity and heightened systemic inflammation. Elevated CRP levels in severe depression align with the emerging understanding of the immune-inflammatory hypothesis in mental health, emphasizing intricate connections between the immune system and depressive symptomatology.

These collective findings underscore the multidimensional nature of depression and advocate for a holistic approach to diagnosis and management. Integrating hormonal and immunological assessments in clinical practice may provide valuable tools for identifying distinct biological signatures associated with varying degrees of depressive symptoms. While our cross-sectional study offers crucial initial insights, further longitudinal research is warranted to delineate the causality and temporal dynamics of hormonal and immunological alterations in depression. Additionally, exploring the potential influence of psychosocial factors, lifestyle, and genetic predispositions on these associations remains a fertile ground for future investigations.

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