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Correlation between serum vitamin D, prolactin levels, and clinical depression at a tertiary care centre: A cross-sectional study.

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Abstract

Background
Depression is a highly prevalent psychiatric disorder with complex etiopathogenesis involving neuroendocrine and biochemical factors. Emerging evidence suggests that serum vitamin D deficiency and hyperprolactinemia may play contributory roles in the development and severity of depressive symptoms.
Objective: To evaluate the correlation between serum vitamin D and prolactin levels with the severity of clinical depression in patients attending a tertiary care center.

Methods
A cross-sectional observational study was conducted involving 120 adult patients diagnosed with clinical depression based on DSM-5 criteria. The severity of depression was assessed using the Hamilton Depression Rating Scale (HAM-D). Serum 25-hydroxy vitamin D [25(OH)D] and prolactin levels were measured using chemiluminescent immunoassay (CLIA). Vitamin D status was classified as deficient (<20 ng/mL), insufficient (20–30 ng/mL), and sufficient (>30 ng/mL). Pearson correlation, ANOVA, and independent t-tests were applied for statistical analysis.

Results
The mean age of participants was 36.4 ± 10.2 years, with 60.8% being female. Mean serum vitamin D and prolactin levels were 17.8 ± 6.9 ng/mL and 24.6 ± 9.1 ng/mL, respectively. Vitamin D deficiency was present in 70% of patients and associated with higher HAM-D scores (22.1 ± 5.4; $p < 0.01$). A moderate negative correlation was observed between vitamin D levels and HAM-D scores ($r = -0.54$, $p < 0.01$), while prolactin levels showed a weak positive correlation with HAM-D scores ($r = 0.28$, $p = 0.03$).

Conclusion
Vitamin D deficiency and elevated prolactin levels are significantly associated with increased severity of clinical depression. Routine assessment of these biomarkers may aid in the comprehensive evaluation and management of depressive disorders.

Recommendations
Routine screening of serum vitamin D and prolactin levels should be considered in depressive patients to guide individualized treatment strategies and improve overall management of clinical depression.

Keywords: *Depression, Vitamin D, Prolactin, Hamilton Depression Rating Scale, Neuroendocrine, Biomarkers*
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Introduction

Depression is one of the most common psychiatric disorders globally, characterized by persistent sadness, anhedonia, cognitive dysfunction, and various somatic symptoms. According to the World Health Organization (WHO), depression affects more than 264 million people worldwide and is the leading cause of disability, significantly impacting individuals' quality of life, work productivity, and physical health. The burden of depression is not only emotional and psychological but also socio-economic, and its prevalence continues to rise across both developed and developing countries.[1] Despite advancements in psychopharmacology and

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psychotherapy, a substantial proportion of patients do not respond adequately to existing treatments, highlighting the need to explore underlying biological and biochemical contributors to the disorder.[2]

In recent years, attention has increasingly shifted toward understanding the neurobiological mechanisms involved in depression. Among these, nutritional and hormonal biomarkers have gained significance in psychiatric research for their potential role in the pathophysiology and modulation of depressive symptoms.[3] Two such biomarkers that have emerged as potential indicators and contributors to depression are serum vitamin D and prolactin.[4]

Vitamin D, traditionally associated with bone health and calcium homeostasis, is now recognized for its pleiotropic roles in neuropsychiatric functioning. The presence of vitamin D receptors (VDRs) and 1-alpha-hydroxylase enzymes in various brain regions—including the prefrontal cortex, hippocampus, and hypothalamus—suggests its involvement in neural development and function.[5] It plays a crucial role in the synthesis of neurotransmitters such as serotonin and dopamine, as well as in the regulation of inflammatory pathways in the central nervous system. Vitamin D deficiency has been consistently associated with various neuropsychiatric disorders, particularly depression. Studies have shown that individuals with low levels of vitamin D are at higher risk of developing depressive symptoms, and supplementation has shown promise in improving mood in deficient individuals.[6]

On the other hand, prolactin is a peptide hormone secreted by the anterior pituitary gland, primarily associated with lactation. However, prolactin also plays important roles in stress response, immune modulation, and neuroendocrine function. It is known to interact with dopaminergic pathways, where dopamine serves as an inhibitor of prolactin release.[7] Hyperprolactinemia, whether due to physiological stress, pharmacological agents (such as antipsychotics), or pituitary disorders, has been linked to mood disturbances, including depressive symptoms. Elevated prolactin levels may suppress dopaminergic tone and thus contribute to anhedonia, emotional blunting, and other features commonly observed in major depressive disorder.[8]

Although separate studies have examined the influence of vitamin D deficiency and hyperprolactinemia on mental health, there remains a paucity of literature that investigates their simultaneous association with the severity of clinical depression. Given the interplay between neuroendocrine function and mood regulation, it is important to assess how these two parameters correlate with the clinical presentation of depression.[9]

This study is therefore undertaken to explore the relationship between serum vitamin D and prolactin levels and the severity of depression in adult patients attending a tertiary care center. Understanding these associations may not only offer insight into the biological basis of depression but also open up avenues for integrated diagnostic and therapeutic strategies, including nutritional supplementation and hormonal evaluation, in the holistic management of depressive disorders.

Aim and objectives

To evaluate the correlation between serum vitamin D and prolactin levels with the severity of clinical depression in patients attending a tertiary care center.

Materials and methods

Study design

A cross-sectional study

Study setting

Departments of Psychiatry and Biochemistry at a tertiary care hospital

Participants

The study population included 120 adult patients diagnosed with clinical depression as per the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.

Sample size

The outcome of this study is to assess the correlation between Vitamin D level, prolactin level, and grade of depression in the study subjects. The sample size of the study subjects was calculated by using the correlation formula. As per the previous study, the correlation coefficient (r value- 0.205) of serum vitamin D level and depression (study by Sang-Hyun Kim et al.)

$$n = \left(\frac{Z_{\alpha/2} + Z_{\beta}}{C} \right)^2 + 3$$

Where:

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Zα/2= Z value for desired significance level (e.g., 1.96 for α = 0.05)
Zβ = Z value for desired power (e.g., 0.84 for 80% power)
C= 0.5×ln(1−r1+r)
r = expected correlation coefficient

Data source and measurement

The data for this study were obtained from adult patients diagnosed with clinical depression attending the psychiatry outpatient and inpatient departments of a tertiary care center. Participants were consecutively recruited during a defined study period after providing informed written consent.

Clinical diagnosis of depression was made in accordance with the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) criteria. The severity of depression was assessed using the Hamilton Depression Rating Scale (HAM-D), a 17-item, clinician-administered questionnaire that evaluates key depressive symptoms including mood, guilt, psychomotor retardation, insomnia, and anxiety. Based on total HAM-D scores, participants were categorized into mild, moderate, and severe depression subgroups.
For biochemical assessment, fasting venous blood samples were collected in the morning hours. Serum was separated and stored at appropriate temperatures until analysis.
Serum 25-hydroxy vitamin D [25(OH)D] levels were measured as the primary indicator of vitamin D status.
Serum prolactin levels were also assessed.
Both parameters were measured using chemiluminescent immunoassay (CLIA) techniques, which offer high sensitivity and specificity.
Vitamin D status was classified based on standard reference ranges:
Deficient: <20 ng/mL
Insufficient: 20–30 ng/mL
Sufficient: >30 ng/mL

Hyperprolactinemia was defined as:
>25 ng/mL in females
>20 ng/mL in males

Efforts to address potential sources of bias

To minimize selection bias, participants were recruited consecutively from both outpatient and inpatient departments, ensuring a representative sample of clinically depressed individuals. Clear inclusion and exclusion criteria were applied rigorously to eliminate confounding factors such as endocrine disorders, use of medications that affect prolactin or vitamin D levels, chronic systemic illnesses, and recent hormonal or vitamin D supplementation. This helped reduce confounding bias related to variables that could independently influence serum biomarker levels.
Information bias was mitigated by employing the Hamilton Depression Rating Scale (HAM-D), a validated and widely used clinician-administered tool, to standardize the assessment of depression severity. All biochemical assessments were conducted using chemiluminescent immunoassay (CLIA) in a centralized laboratory to ensure consistency and accuracy.
To minimize observer bias, the psychiatric evaluations and laboratory analyses were conducted by trained personnel who were blinded to the biochemical results at the time of clinical assessment. Additionally, data analysis was performed independently using appropriate statistical methods to ensure objectivity and reproducibility of results.

Statistical methods

For statistical analysis, data were entered into a spreadsheet and analyzed using SPSS (Statistical Package for the Social Sciences), version 25. Descriptive statistics were used to summarize baseline demographic and clinical variables. Pearson's correlation coefficient was used to assess the linear relationship between vitamin D and prolactin levels with HAM-D scores. One-way analysis of variance (ANOVA) was applied to compare mean depression scores across different vitamin D categories. Additionally, independent t-tests were used to compare means between two groups (e.g., normal vs elevated prolactin levels). A p-value < 0.05 was considered statistically significant for all analyses.

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Results

Figure 1: Participant flow

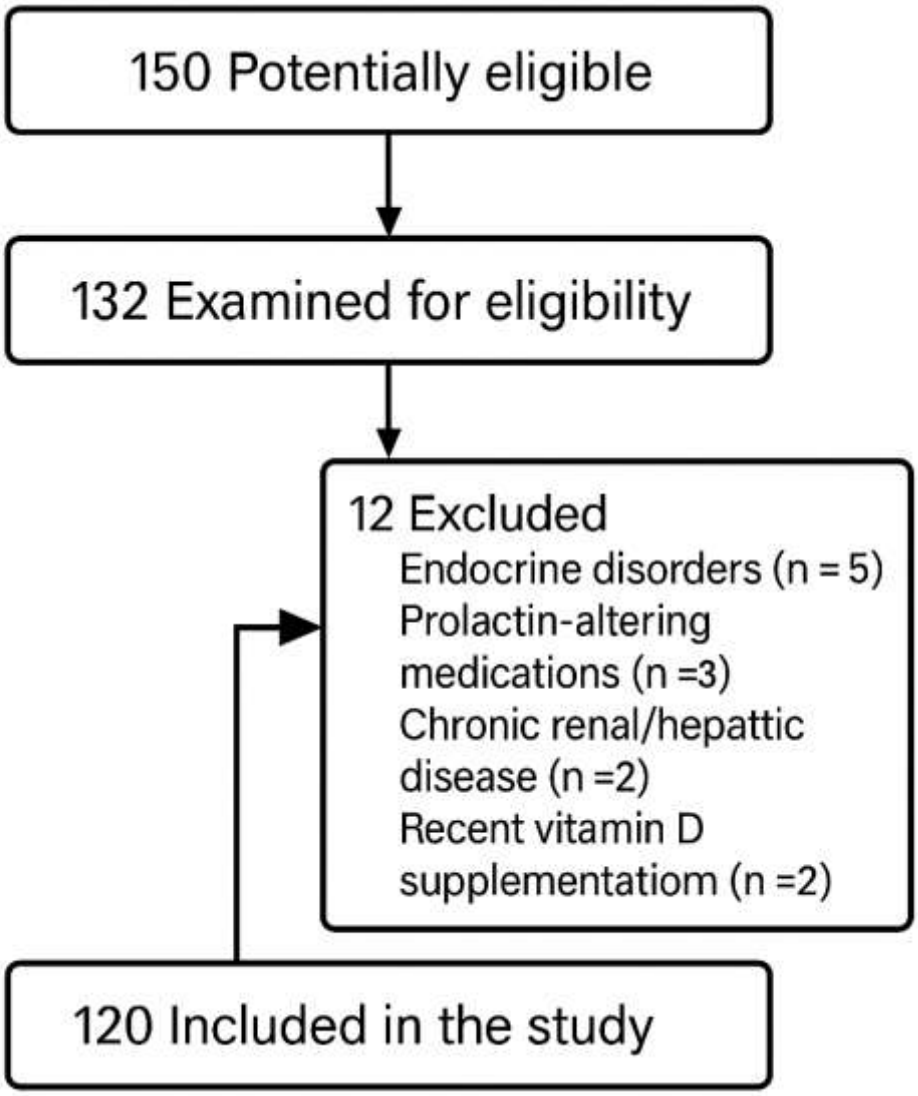

Table 1: Baseline characteristics of study participants

Variable	Mean ± SD / n (%)
Age (years)	36.4 ± 10.2
Gender (Male/Female)	47 (39.2%) / 73 (60.8%)
Vitamin D (ng/mL)	17.8 ± 6.9
Prolactin (ng/mL)	24.6 ± 9.1
HAM-D Score	20.3 ± 5.8

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Table 1 presents the baseline characteristics of the 120 study participants diagnosed with clinical depression. The mean age of the participants was 36.4 ± 10.2 years, indicating a relatively young to middle-aged cohort. The sample had a higher proportion of female participants (60.8%) compared to males (39.2%), reflecting either the gender distribution of clinic attendees or the higher prevalence of diagnosed depression in women. The mean serum vitamin D level was 17.8 ± 6.9 ng/mL, suggesting that, on average, participants were vitamin D deficient, as levels below 20 ng/mL are generally considered deficient. The mean serum prolactin level was 24.6 ± 9.1 ng/mL, which is at the higher end of the normal range, potentially indicating a trend toward hyperprolactinemia in this depressed population. These baseline findings suggest that a considerable proportion of clinically depressed individuals may also have underlying biochemical abnormalities such as hypovitaminosis D and elevated prolactin, warranting further exploration of their role in depression severity.

Table 2: Mean HAM-D scores based on Vitamin D status

Vitamin D Status	n (%)	Mean HAM-D ± SD	p-value
Deficient (<20 ng/mL)	84 (70%)	22.1 ± 5.4	<0.01
Insufficient (20–30)	26 (21.7%)	18.4 ± 5.1	
Sufficient (>30)	10 (8.3%)	15.7 ± 4.6	

Table 2 shows a statistically significant inverse relationship between vitamin D status and depression severity. Patients with vitamin D deficiency (<20 ng/mL) had the highest mean HAM-D score (22.1 ± 5.4), indicating more severe depression, while those with sufficient levels (>30 ng/mL) had the lowest mean score (15.7 ± 4.6). The difference in HAM-D scores across the three groups was significant ($p < 0.01$, ANOVA), suggesting that lower vitamin D levels are associated with greater severity of depressive symptoms.

Table 3: Correlation coefficients between serum biomarkers and depression severity

Variable vs HAM-D Score	Correlation (r)	p-value
Serum Vitamin D	-0.54	<0.01
Serum Prolactin	0.28	0.03

Table 3 presents the correlation between serum biomarkers and depression severity. There is a moderate negative correlation between serum vitamin D levels and HAM-D scores ($r = -0.54$, $p < 0.01$), indicating that lower vitamin D levels are significantly associated with higher depression severity. Additionally, serum prolactin levels show a weak positive correlation with HAM-D scores ($r = 0.28$, $p = 0.03$), suggesting that elevated prolactin may also be linked to increased depressive symptoms, though to a lesser extent. Both correlations are statistically significant, supporting the role of these biomarkers in the clinical assessment of depression.

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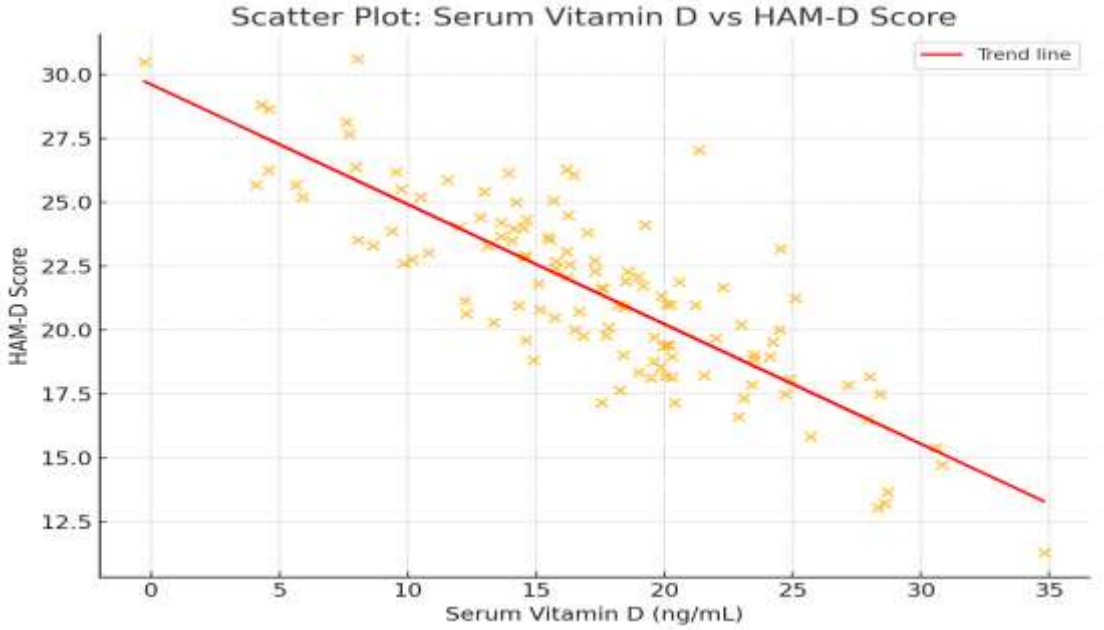
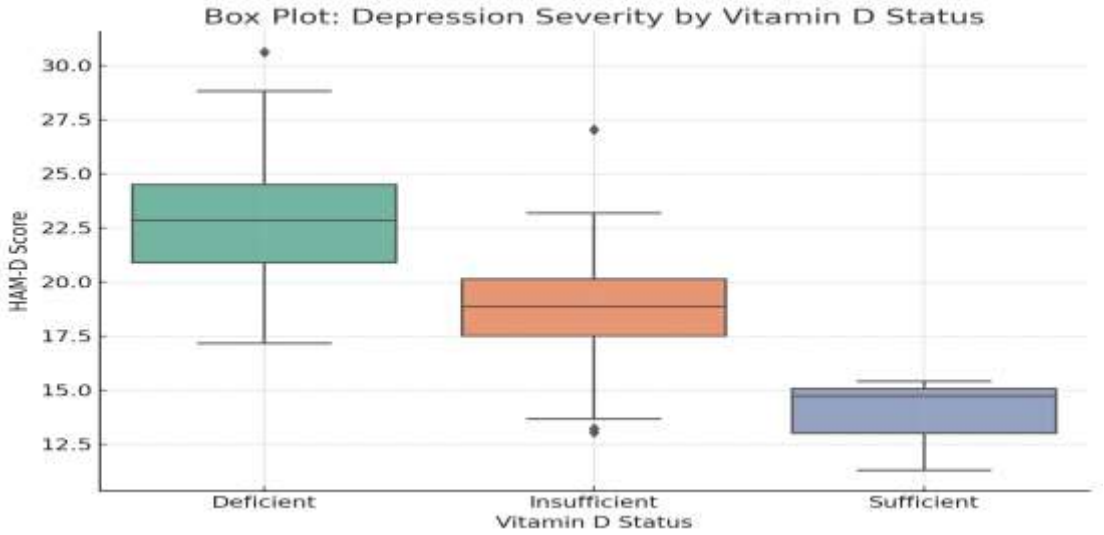
Graph 1: Scatter plot of serum vitamin D vs HAM-D score



Graph 1 illustrates a scatter plot depicting the relationship between serum vitamin D levels and HAM-D scores. A clear inverse linear trend is visible, indicating that as vitamin D levels decrease, the severity of depression (as measured by HAM-D score) increases. The plotted red regression line emphasizes this negative correlation. This visual representation supports the statistical finding of a significant inverse association ($r = -0.54$, $p < 0.01$), suggesting that vitamin D deficiency may play a contributory role in the intensity of depressive symptoms. This reinforces the potential value of assessing and correcting vitamin D levels in patients with clinical depression.

Graph 2: Box plot – depression severity by vitamin D status



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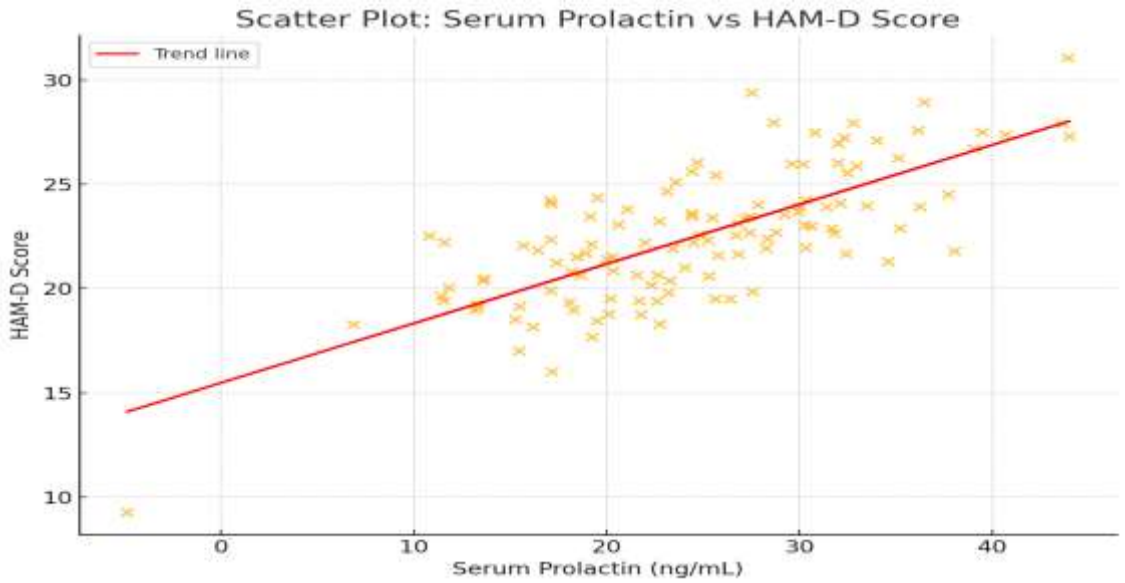
Here is the box plot showing depression severity (HAM-D scores) across different vitamin D status groups. It indicates that severe depression is predominantly observed in the vitamin D-deficient group, with median scores decreasing as vitamin D levels improve.

Graph 3: Scatter plot of serum prolactin vs HAM-D score



Here is the scatter plot illustrating the relationship between serum prolactin levels and HAM-D scores. A mild positive correlation is observed, suggesting that higher prolactin levels may be associated with increased severity of depression. Let me know if you need a paragraph interpretation or want the image exported.

Discussion

The present study aligns with and reinforces growing evidence linking vitamin D deficiency and elevated prolactin levels with the severity of clinical depression. With a mean serum vitamin D level of 17.8 ± 6.9 ng/mL, the majority of participants in this study were found to be vitamin D deficient. This biochemical finding was also significantly associated with higher HAM-D scores, indicating more severe depressive symptoms. These results support the findings of Khoraminya et al. (2022)[10], who demonstrated that vitamin D supplementation, when combined with antidepressant therapy, led to a greater improvement in depressive symptoms. This suggests a potential synergistic role of vitamin D in modulating mood, possibly through its impact on serotonin synthesis, inflammatory pathways, or neuroplasticity.

Similarly, the observed elevated mean prolactin level of 24.6 ± 9.1 ng/mL in this study, even in the absence of medications known to elevate prolactin, points to a neuroendocrine dysregulation associated with depression. This is consistent with the findings of Shin et al. (2023)[11], who reported elevated prolactin levels in depressed individuals regardless of psychotropic drug use. Such findings underscore the hypothesis that prolactin may act as a stress-related biomarker, potentially reflecting hypothalamic-pituitary-adrenal (HPA) axis dysfunction or altered dopaminergic tone seen in depressive disorders.

Together, these results suggest that vitamin D and prolactin may serve not only as biochemical correlates but also as potential targets for integrated diagnostic or therapeutic strategies. Regular screening for these markers could improve the understanding of individual patient profiles and facilitate personalized management of depression in clinical settings.

The present study's finding that patients with vitamin D deficiency (<20 ng/mL) had significantly higher HAM-D scores (22.1 ± 5.4) compared to those with sufficient levels (>30 ng/mL) reinforces the growing consensus that vitamin D plays a meaningful role in mood regulation and the pathophysiology of depression.

This result is strongly supported by Ganji et al. (2023), [12], who in their BMC Psychiatry study highlighted that individuals—especially younger adults—with low serum vitamin D levels exhibited elevated depression scores, suggesting a possible age-related vulnerability to vitamin D-related mood disturbances. This age-related sensitivity adds clinical relevance, particularly for early intervention

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strategies in younger populations with depressive symptoms.

Further, Li et al. (2022)[13] in their systematic review and meta-analysis, provide higher-level evidence supporting this observation, demonstrating that vitamin D supplementation leads to a significant reduction in depression severity, particularly in patients with baseline deficiency. This meta-analytic evidence strengthens the interpretation of the current findings by not only validating the observed association but also implying causality and therapeutic benefit.

The current study's findings of a moderate negative correlation between serum vitamin D and HAM-D score ($r = -0.54$) and a weak positive correlation between serum prolactin and HAM-D score ($r = 0.28$) provide further evidence for the biochemical underpinnings of depression, particularly involving the neuroendocrine and nutritional axes.

The inverse correlation between vitamin D levels and depression severity aligns with findings from Milaneschi et al. (2022) [14], who demonstrated a robust and consistent negative association between serum vitamin D levels and depressive symptoms across diverse age groups. Their work, which incorporated both observational and genetic data, suggests that low vitamin D may not only reflect poor health status but could play a causal role in mood disorders through mechanisms such as impaired neuroimmune regulation, decreased neurotrophic support, or serotonergic dysfunction.

In parallel, the weak but statistically significant positive correlation between prolactin and HAM-D scores in the present study supports a growing body of research linking hyperprolactinemia with depressive symptomatology. This is consistent with the findings of Kraus et al. (2022), [15], who explored the endocrine profile of patients with depression and found higher prolactin levels associated with increased severity of emotional dysregulation and depressive symptoms. Prolactin, often elevated in response to stress or hypothalamic-pituitary axis disturbances, may serve as a marker of neuroendocrine stress and emotional dysregulation.

Together, these findings suggest that serum vitamin D and prolactin levels reflect different but complementary aspects of the pathophysiology of depression. While vitamin D may be linked to neuroprotective and immune-modulatory mechanisms, prolactin appears to reflect stress and HPA-axis involvement. The correlations observed in the present study provide valuable clinical insight and underscore the importance of integrating biochemical screening into the diagnostic and management algorithm for patients with clinical depression.

The present study's graphical analyses reinforce established evidence linking vitamin D deficiency and elevated prolactin with depression severity. The inverse linear trend between serum vitamin D and HAM-D scores aligns with Penckofer et al. (2022)[16] and Jia et al. (2023)[17], both of whom reported that lower vitamin D levels are associated with greater depressive symptom severity, particularly when levels fall below 20 ng/mL. Similarly, the box plot depiction showing more severe depression among vitamin D–D-deficient individuals further validates these findings.

The mild positive correlation between serum prolactin and HAM-D scores mirrors the results of Yildiz et al. (2023)[18], who reported a significant association between elevated prolactin levels and more severe depression in non-medicated patients. Together, these results support the potential clinical utility of biochemical screening for vitamin D and prolactin in assessing and managing depressive disorders.

Generalizability

The generalizability of the study findings is moderately strong but context-dependent. As the study was conducted in a single tertiary care center with a sample of 120 adult patients aged 18–60 years, the results are most applicable to similar clinical settings and populations. The use of standardized diagnostic criteria (DSM-5) and validated assessment tools (HAM-D, CLIA) enhances external validity.

Conclusion

This study highlights a significant association between low serum vitamin D and increased depressive symptomatology. Elevated prolactin also correlates with greater depression severity, although more weakly. Routine screening of these markers in depressive patients could enhance therapeutic outcomes when combined with conventional psychiatric interventions.

Limitations

The study's cross-sectional design limits causal inference, and hospital-based recruitment may introduce selection bias. Unmeasured factors like sun exposure and diet may also contribute to measurement imprecision.

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Special thanks to our research assistants and data entry personnel for their diligent efforts in ensuring data quality and completeness.

List of abbreviations

DSM-5 – Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
HAM-D – Hamilton Depression Rating Scale
25(OH)D – 25-hydroxy Vitamin D
CLIA – Chemiluminescent Immunoassay
HPA axis – Hypothalamic-Pituitary-Adrenal Axis
SPSS – Statistical Package for the Social Sciences
VDR – Vitamin D Receptor
SD – Standard Deviation
ANOVA – Analysis of Variance
ng/mL – Nanograms per Milliliter

Source of funding

The study had no funding.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Dr. Akanksha: Conceptualized the study, conducted data collection and biochemical analysis, performed statistical analysis, and drafted the initial manuscript.
Dr. Vivek Sinha: Provided overall supervision, contributed to study design and methodology, reviewed and edited the manuscript critically for intellectual content, and guided data interpretation.

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