



PSYCHIATRIC MANIFESTATIONS OF VITAMIN D-3 DEFICIENCY

Dr. Ujjwal Bandyopadhyay¹, Dr. Supti Mukhopadhyay (Banerjee)²

¹MBBS, DPM, MD (Psychiatry) Professor & Head, Department of Psychiatry, ESI-PGIMS, ESIC Medical College & Hospital, Kolkata.

²MBBS, MD (Pathology) Senior Consultant Pathologist, Associate Professor, Department of Pathology, ICARE Institute of Medical Science and Research, Haldia, Proprietor - Rishi Pathological Laboratory, Kolkata.



Correspondence:

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Abstract

Vitamin D₃ (cholecalciferol) is a fat-soluble secosteroid hormone that plays a crucial role not only in calcium and bone metabolism but also in multiple non-skeletal physiological processes, including immune modulation, cardiovascular health, and neuropsychiatric functioning [1]. Vitamin D deficiency has emerged as a major global public health concern, affecting nearly one billion people worldwide, with particularly high prevalence in developing countries despite abundant sunlight [2]. In India, widespread hypovitaminosis D has been reported across all age groups due to factors such as limited sun exposure, skin pigmentation, dietary insufficiency, urbanization, and lifestyle changes

Keywords: Vitamin D secosteroid cardiovascular health neuropsychiatric functioning



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INTRODUCTION

Vitamin D₃ (cholecalciferol) is a fat-soluble secosteroid hormone that plays a crucial role not only in calcium and bone metabolism but also in multiple non-skeletal physiological processes, including immune modulation, cardiovascular health, and neuropsychiatric functioning [1]. Vitamin D deficiency has emerged as a major global public health concern, affecting nearly one billion people worldwide, with particularly high prevalence in developing countries despite abundant sunlight [2]. In India, widespread hypovitaminosis D has been reported across all age groups due to factors such as limited sun exposure, skin pigmentation, dietary insufficiency, urbanization, and lifestyle changes [3].

Over the past two decades, growing evidence has highlighted the role of vitamin D in brain development and function. Vitamin D receptors (VDRs) and the enzyme 1- α -hydroxylase, required for conversion of vitamin D into its active form, are widely distributed in various regions of the brain, including the prefrontal cortex, hippocampus, amygdala, and cerebellum—areas critically involved in mood regulation, cognition, and behavior [4]. Vitamin D is known to influence neurotrophic factors, neuronal differentiation, synaptic

plasticity, and neurotransmitter synthesis, particularly serotonin and dopamine pathways, which are central to psychiatric health [5].

Psychiatric manifestations associated with vitamin D₃ deficiency have gained increasing attention in clinical and research settings. Several observational and interventional studies have reported associations between low serum vitamin D levels and a wide range of psychiatric disorders, including depression, anxiety disorders, schizophrenia, bipolar disorder, cognitive impairment, and dementia [6]. Among these, depressive disorders have been most consistently linked with vitamin D deficiency, with low levels correlating with increased severity of depressive symptoms, poor treatment response, and higher relapse rates [7].

Anxiety symptoms, including generalized anxiety, panic attacks, and somatic anxiety, have also been observed more frequently in individuals with vitamin D deficiency. Proposed mechanisms include dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis, increased inflammatory cytokines, and altered calcium homeostasis affecting neuronal excitability [8].

Furthermore, vitamin D deficiency has been implicated in psychotic disorders, particularly schizophrenia, where prenatal and early-life deficiency has been associated with increased disease risk, suggesting a neurodevelopmental role of vitamin D [9].

Cognitive dysfunction is another important psychiatric manifestation linked to vitamin D deficiency. Low vitamin D levels have been associated with impaired attention, memory deficits, executive dysfunction, and increased risk of mild cognitive impairment and Alzheimer's disease. Vitamin D's neuroprotective effects, including antioxidant activity, regulation of neuroinflammation, and clearance of amyloid plaques, are thought to underlie these associations [10].

Despite increasing recognition of the neuropsychiatric implications of vitamin D deficiency, it often remains underdiagnosed and untreated in patients presenting with psychiatric symptoms. Given that vitamin D deficiency is a potentially reversible and easily correctable condition, early identification may have significant therapeutic implications. Screening for vitamin D levels in patients with psychiatric disorders may help improve clinical outcomes, reduce symptom burden, and enhance overall quality of life.

The aim of this study is to evaluate the association between vitamin D₃ deficiency and various psychiatric manifestations. The study seeks to assess the prevalence and pattern of psychiatric symptoms among individuals with vitamin D₃ deficiency and to analyze the relationship between serum vitamin D₃ levels and the severity of psychiatric presentations. By identifying this correlation, the study aims to emphasize the importance of early detection and correction of vitamin D₃ deficiency in patients presenting with psychiatric disorders.

MATERIALS AND METHODS

Study Design: Hospital-based, observational, cross-sectional study.

Study Investigators

- Dr. Ujjwal Bandyopadhyay, MBBS, DPM, MD (Psychiatry), Professor & Head, Department of

Psychiatry, ESI-PGIMSR, ESIC Medical College & Hospital, Kolkata.

- Dr. Supti Mukhopadhyay (Banerjee), Senior Consultant Pathologist, Associate Professor, Department of Pathology, ICARE Institute of Medical Science and Research, Haldia; Proprietor, Rishi Pathological Laboratory, Kolkata.

Study Place: Rishi Pathological Laboratory, Kolkata.

Study Duration: One year.

Sample Size: Total of 30 participants.

Study Population: Adult patients referred for serum vitamin D₃ estimation and presenting with psychiatric symptoms.

Inclusion Criteria

- Age ≥ 18 years.
- Patients with psychiatric symptoms attending outpatient or laboratory referral.
- Patients with serum vitamin D₃ deficiency.
- Patients providing informed written consent.

Exclusion Criteria

- Patients with known neurological disorders (e.g., epilepsy, stroke).
- Patients with severe medical illnesses affecting vitamin D metabolism (chronic kidney disease, chronic liver disease).
- Patients on vitamin D supplementation within the previous 3 months.
- Pregnant and lactating women.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. The unpaired t-test was used to compare continuous variables between independent groups, and the paired t-test was applied for within-group comparisons. Categorical variables were analyzed using the Chi-square test or Fisher's exact test as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Age Distribution of Study Subjects (n = 30)

Age group (years)	Number (%)
18–30	6 (20.0)
31–45	12 (40.0)
46–60	8 (26.7)
>60	4 (13.3)
Total	30 (100)

Table 2: Gender Distribution

Gender	Number (%)
Male	14 (46.7)
Female	16 (53.3)
Total	30 (100)

Table 3: Serum Vitamin D₃ Level Distribution

Vitamin D ₃ level (ng/mL)	Number (%)
<10 (Severe deficiency)	9 (30.0)
10–19 (Deficiency)	21 (70.0)
Mean ± SD	12.4 ± 4.1

Table 4: Distribution of Psychiatric Diagnoses

Psychiatric diagnosis	Number (%)
Depressive disorder	12 (40.0)
Anxiety disorder	8 (26.7)
Mixed anxiety & depression	5 (16.7)
Psychotic disorder	3 (10.0)
Cognitive impairment	2 (6.6)
Total	30 (100)

Table 5: Vitamin D₃ Deficiency Severity vs Psychiatric Diagnosis

Diagnosis	<10 ng/mL	10–19 ng/mL	Total
Depression	6	6	12
Anxiety	1	7	8
Mixed anxiety–depression	1	4	5
Psychotic disorder	1	2	3
Cognitive impairment	0	2	2
Total	9	21	30

Table 6: Mean Vitamin D₃ Levels in Common Psychiatric Conditions

Psychiatric condition	Mean Vitamin D ₃ (ng/mL) ± SD
Depressive disorder	10.8 ± 3.2
Anxiety disorder	13.6 ± 3.8
Psychotic disorder	9.4 ± 2.1
Cognitive impairment	8.9 ± 1.9

Figure:1. Distribution of Psychiatric Diagnoses

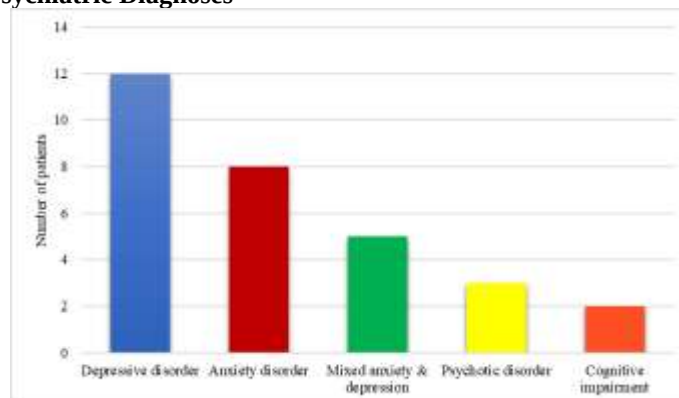
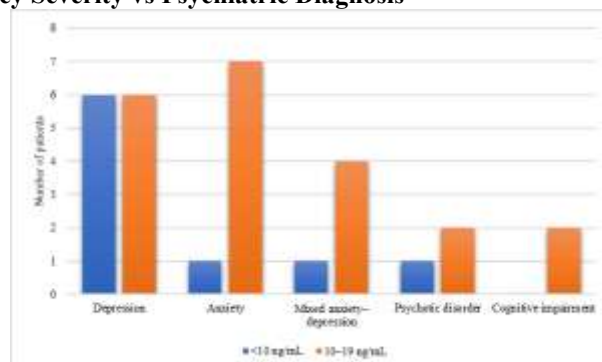


Figure:2. Vitamin D₃ Deficiency Severity vs Psychiatric Diagnosis



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A total of 30 subjects were included in the present study. The majority of participants belonged to the 31–45 years age group (40%), followed by 46–60 years (26.7%), 18–30 years (20%), and those above 60 years (13.3%). Females constituted a slightly higher proportion of the study population (53.3%) compared to males (46.7%).

All study subjects were found to have vitamin D₃ deficiency. Severe deficiency (serum vitamin D₃ <10 ng/mL) was observed in 30% of cases, while 70% had vitamin D₃ levels between 10–19 ng/mL. The mean serum vitamin D₃ level of the study population was 12.4 ± 4.1 ng/mL.

Regarding psychiatric diagnoses, depressive disorder was the most common presentation, observed in 40% of patients, followed by anxiety disorders (26.7%) and mixed anxiety and depressive disorder (16.7%). Psychotic disorders were seen in 10% of cases, while cognitive impairment was noted in 6.6% of subjects.

On comparing the severity of vitamin D₃ deficiency with psychiatric diagnoses, depressive disorder was more frequently associated with severe vitamin D₃ deficiency (<10 ng/mL), whereas anxiety disorders were more commonly seen in patients with moderate deficiency (10–19 ng/mL). Psychotic disorders and cognitive impairment were predominantly observed in patients with lower serum vitamin D₃ levels.

The mean serum vitamin D₃ levels were lowest among patients with cognitive impairment (8.9 ± 1.9 ng/mL) and psychotic disorders (9.4 ± 2.1 ng/mL), followed by depressive disorder (10.8 ± 3.2 ng/mL). Patients with anxiety disorders had comparatively higher mean vitamin D₃ levels (13.6 ± 3.8 ng/mL).

DISCUSSION

The present study highlights a significant association between vitamin D₃ deficiency and various psychiatric manifestations, with depressive disorders emerging as the most common clinical presentation. This finding is consistent with earlier studies that have demonstrated a high prevalence of depression among individuals with low serum vitamin D levels. A study by Anglin et al. reported a strong inverse relationship between vitamin D status and depressive symptoms, suggesting that deficiency may contribute to both the onset and severity of depression [11]. Similarly, Parker et al. observed that patients with depression frequently exhibit lower serum vitamin D levels compared to healthy controls, reinforcing the biological plausibility of this association [12].

In the current study, anxiety disorders constituted the second most common psychiatric diagnosis. Comparable findings were reported by Ganji et al., who demonstrated a significant association between low vitamin D levels and increased anxiety symptoms in young adults [13]. The proposed mechanisms include dysregulation of the hypothalamic–pituitary–adrenal axis, increased neuroinflammation, and impaired calcium signaling within neurons, all of which may contribute to heightened anxiety states [14]. Our observation that anxiety disorders were more prevalent in patients with moderate vitamin D deficiency aligns with these findings and suggests a dose-dependent relationship.

Psychotic disorders, although less frequent in the present study, were predominantly associated with severe vitamin D₃ deficiency. This observation parallels findings from McGrath et al., who reported that vitamin D deficiency, particularly during early life and adulthood, may increase vulnerability to schizophrenia and other psychotic disorders [15]. The

neurodevelopmental hypothesis of vitamin D suggests that deficiency may affect brain maturation, neurotransmission, and immune modulation, thereby contributing to psychosis risk [16].

Cognitive impairment was observed in a small proportion of patients but was associated with the lowest mean vitamin D₃ levels in the study. This is consistent with the work of Annweiler et al., who demonstrated that low serum vitamin D levels are associated with impaired cognitive performance and increased risk of dementia [17]. Vitamin D is believed to exert neuroprotective effects by reducing oxidative stress, regulating neuroinflammation, and facilitating amyloid clearance, mechanisms that may explain its role in cognitive function [18].

The overall pattern observed in this study supports the findings of a large systematic review by Ju et al., which concluded that vitamin D deficiency is associated with a wide spectrum of psychiatric disorders, including depression, anxiety, psychosis, and cognitive decline [19]. However, unlike larger population-based studies, the present study involved a small sample size and a cross-sectional design, limiting causal inference. Nevertheless, the consistency of findings with existing literature strengthens the validity of the observed associations.

Given that vitamin D₃ deficiency is a modifiable and treatable condition, the findings of this study underscore the importance of routine screening for vitamin D levels in patients presenting with psychiatric symptoms. Early identification and correction of deficiency may serve as an adjunctive strategy in the management of psychiatric disorders and potentially improve treatment outcomes, as suggested by intervention studies demonstrating

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symptom improvement following vitamin D supplementation [20].

CONCLUSION

The present study demonstrates a significant association between vitamin D₃ deficiency and a range of psychiatric manifestations, with depressive disorders being the most frequently observed, followed by anxiety disorders, psychotic disorders, and cognitive impairment. Lower serum vitamin D₃ levels were more commonly associated with severe psychiatric presentations, indicating a possible relationship between the degree of deficiency and symptom severity. These findings support existing evidence suggesting that vitamin D plays an important role in brain function through its effects on neurotransmission, neuroinflammation, and neuroprotection. Considering the high prevalence, ease of diagnosis, and reversibility of vitamin D₃ deficiency, routine screening for vitamin D₃ levels in patients presenting with psychiatric symptoms may be clinically beneficial. Early identification and appropriate correction of deficiency could serve as an effective adjunct to conventional psychiatric management and may contribute to improved clinical outcomes. However, further large-scale, longitudinal, and interventional studies are required to establish a causal relationship and to clarify the therapeutic role of vitamin D supplementation in psychiatric disorders.

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