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Vitamin D levels and its impact on symptom severity and quality of life in Bipolar Depression and Major Depressive Disorder - A comparative study

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ABSTRACT

INTRODUCTION: Background - Depression is often seen as having biochemical or emotional basis, but nutrition, including Vitamin D, also plays a pivotal role in its onset, severity, and treatment response. Vitamin D deficiency has been associated with various psychiatric disorders, including depression. Both Bipolar Depression (BD) and Major Depressive Disorder (MDD) impair quality of life (QOL), which is gaining recognition as a vital measure of well-being and patient health.
Aim - To explore potential correlations between Vitamin D levels, symptom severity, and Quality of Life among patients with Bipolar Depression (BD) and Major Depressive Disorder (MDD).
Methodology - This cross-sectional observational study was conducted at the Department of Psychiatry in tertiary care hospital in North-western Rajasthan. 30 patients from each group were analysed. Informed written consent including consent for blood sample collection was taken. Socio- demographic details and clinical profiles were recorded using a semi-structured proforma; HAM- D and WHOQOL-BREF (Hindi version) scales were applied. The collected data was entered into Excel, and statistical analysis was performed using Epi Info version 7.2.1.0.
Results - The Vitamin D level in BD group ranged from 11.19 to 41.69 ng/ml with a mean of 31.50 ± 8.17 ng/ml. The Vitamin D level in MDD group ranged from 7.37 to 52.37 ng/ml with a mean of 20.49 ± 9.63 ng/ml. Considering the 30 patients in BD group in this study, moderate negative correlation was found between Vitamin D with HAM-D (r= -0.455, p=0.011). Considering the 30 patients in MDD group in this study, no significant correlation was found between Vitamin D levels with HAM-D. In BD group, moderate positive correlation was found between Vitamin D with Overall QOL (r= -0.452, p=0.012), Physical domain (r= -0.413, p=0.023), and Psychological domain (r= -0.445, p=0.014). No significant correlation was found between WHO QOL with Vitamin D in MDD group. **Conclusions** - Our study found that Vitamin D levels were lower in patients with Major Depressive Disorder (MDD) compared to those with Bipolar Depression (BD). In BD patients, lower the vitamin D levels, more was the symptom severity as indicated by higher score on HAM-D. Additionally, higher Vitamin D levels in BD patients were moderately correlated with better overall quality of life (QOL), particularly in the physical and psychological domains. However, no significant correlation was found between Vitamin D levels and QOL in the MDD group, suggesting that Vitamin D had a greater impact on QOL in BD patients than in those with MDD.

Keywords: Keywords- Bipolar Depression, Major Depressive Disorder, Vitamin D levels, Quality of life.

INTRODUCTION

Depression is often seen as primarily having biochemical or emotional basis, but nutrition also plays a crucial role in its onset, severity, duration, and response to treatment. Studies have found that Asian and American populations have diets deficient in essential nutrients, particularly vitamins, minerals, and omega-3 fatty acids. [1]

Vitamin D, a fat-soluble vitamin, is essential for vital bodily functions; enhancing calcium and phosphorus absorption by 30–40% and 80%, respectively. It has been estimated that over one billion people worldwide have insufficient or deficient Vitamin D levels. The most effective way to assess Vitamin D levels is through serum 25-hydroxyVitamin D [25(OH)D] levels. Vitamin D deficiency is defined as levels less than 30ng/mL. This widespread deficiency is a significant public health concern, as low Vitamin D levels are an independent predictor of total mortality in the general population. Emerging research suggests that Vitamin D may also have protective role against cancer, cardiovascular disorders, fractures, autoimmune diseases, influenza, and depression.[2] Neurobiological and neuroendocrinological factors have been identified, suggesting a connection between vitamin D deficiency and various psychiatric conditions, including depression. [3] Although the exact mechanism linking Vitamin D to psychiatric disorders is not fully understood, the presence of Vitamin D receptors in the hypothalamus suggests a potential role in neuroendocrine function, possibly influencing psychiatric disorders like depression. [4]

Bipolar Depression and Major Depressive Disorder (MDD) are linked to serious consequences, including increased mortality, loss of productivity and may lead to poorer health outcomes and suicide. One valuable aspect to study in differentiating these disorders is quality of life (QOL).[5] The World Health Organization (WHO) defines QOL as an individual's perception of their own position in life, considering their cultural context, values, goals, expectations, and concerns. This broad concept encompasses physical health, psychological state, personal beliefs, level of independence, social relationships, and living environment. Both somatic and mental illnesses are known to impair QOL, making it a key measure in assessing the effectiveness of mental health services. In both MDD and Bipolar Disorder, QOL is notably impaired, and growing evidence supports its importance as a target for well-being and an indicator of patient health. QOL measurements are increasingly recommended as a gauge for treatment efficacy and recurrence in depression.[6].

METHODOLOGY

Aims and Objectives

To explore potential correlations between Vitamin D levels, symptom severity, and Quality of Life among patients with Bipolar Depression and Major Depressive Disorder.

Study settings

The study was conducted at Department of Psychiatry in tertiary care hospital in North-western Rajasthan.

Study Design

A cross-sectional observational study. The sample was recruited from the patient population attending OPD/IPD of Department of Psychiatry in tertiary care hospital in North-western Rajasthan.

Study Duration

Six months- November 2023 to April 2024

Sampling Technique

All the patients fulfilling the inclusion and exclusion criteria and willing to give consent within the study duration were included in the study.

Blood Sample Collection

The blood samples for evaluation of levels of Vitamin D were taken under all aseptic conditions by post-graduate student conducting the study and were taken from right/left median cubital vein preferably in a single prick. Approximately 3 mL of blood was collected per patient in gel clot activator vial (Golden top serum separator tube). Sample collected was transported to Department of Biochemistry with ice packs in thermocol box maintaining a temperature between 2-8º C. Once the blood sample reached Biochemistry lab, it was centrifuged to obtain serum and plasma for further processing.

Technique of the Procedure for Quantitative measurement of Vitamin D

Competitive immunoassay technique was used in VITROS ECi/ECiQ/3600 Immunodiagnostic system and VITROS 5600/XT 7600 integrated system for quantitative measurement of Vitamin D in human serum, with incubation time of 16 minutes at temperature 37º C with 60 µL of serum sample.

Test Type	System *	Incubation Time	Time to first result	Test Temperature	Reaction Sample Volume
Competitive Immunoassay	ECi/ECiQ, 3600, 5600, XT 7600	16 minutes	24 minutes	37 °C	60 µL

Inclusion and Exclusion criteria for patients Inclusion criteria for patients

All the patients aged 18-59 years and of either sex willing to participate in the study and diagnosed with Major Depressive Disorder/Bipolar Depression by two Psychiatrists independently based on DSM-5 criteria were included in the study.

Exclusion criteria for patients

Patients not willing to provide informed written consent to participate in the study, with any history of psychiatric comorbidity, substance use disorders except nicotine, illness involving gastrointestinal system, renal disorders or any medical co-morbidity affecting absorption of vitamins, severe or long-term physical illness or on any supplements containing Vitamin D were excluded from the study.

Study Tools

a. Consent form

b. Semi structured data collection sheet

c. Hamilton rating scale for Depression (HAM-D)

The scale consists of 21 items, but only the first 17 are used for scoring. Each item assesses a different symptom or aspect of depression, such as mood, feelings of guilt, suicidal thoughts, insomnia, agitation, and somatic symptoms. [5]

WHOQOL-BREF (Hindi)- WHOQOL-BREF Hindi is an abbreviated version comprised of 26 items was developed by Dr. Shekhar Saxena, AIIMS New Delhi, using data from the field-trial version of the WHOQOL-100. It also aggregates all the 4 domains of quality of life Ethical approval Clearance from the Ethical Committee of tertiary care hospital in North-western Rajasthan was taken prior to the study. A detailed information sheet about the study was provided along with the informed written consent prior to the study. Consent for blood sample (3mL) collection was taken from the patients. Patients were assured of confidentiality and informed their data would be used solely for research purposes.

Statistical Analysis

Categorical variables were summarized with frequencies and percentages and analyzed using the Chi-square test. Continuous variables were summarized with means and standard deviations and compared between two groups using the independent samples t-test. The correlation between two variables was assessed using the Pearson correlation coefficient. A p-value of ≤ 0.05 was considered statistically significant. All statistical analyses were performed using Epi Info version 7.2.1.0

RESULTS

Table 1: Socio demographic characteristics of patients.

		BD		MDD		$\chi 2$	P value
		N	%	N	%		
Age (years)	<31 years	5	16.7	4	13.3	0.697	1.000
	31-40 years	5	16.7	7	23.3		
	41-50 years	11	36.7	9	30		
	51-60 years	9	30	10	33.3		
Gender	Female	11	36.7	18	60	2.403	0.121
	Male	19	63.3	12	40		
Marital status	Unmarried	4	13.3	3	10	0.234	0.890
	Married	21	70	21	70		
	Others	5	16.7	6	20		
Religion	Hindu	29	96.7	21	70	7.724	0.021 (S)
	Muslim	1	3.3	8	26.7		
	Others	0	0	1	3.3		
	Illiterate	5	16.7	10	33.3		
	Primary school	6	20	7	23.3		

Education	Middle school	5	16.7	4	13.3	3.109	0.054
	High school	9	30	5	16.7		
	Graduate & above	5	16.7	4	13.3		
Employment	Currently employed	12	40	8	26.7	2.470	0.291
	Currently not employed	8	26.7	6	20		
	Never been employed	10	33.3	16	53.3		
Occupation	Unskilled	11	36.7	3	10	6.453	0.120
	Self employed	7	23.3	8	26.7		
	Student	2	6.7	2	6.7		
	Home maker	10	33.3	17	56.6		
Type of family	Joint	17	56.7	17	56.7	1.719	0.866
	Nuclear	9	30	10	33.3		
	Extended nuclear	4	13.3	3	10		
Place of stay	Rural	20	66.7	20	66.7	0.075	0.784
	Urban	10	33.3	10	33.3		

Most of the patients in BD group were aged 41-50 years (36.7%) and 51-60 years (30%). Similarly most patients in MDD group were aged 51-60 years (33.3%) and 41-50 years (30%). No significant difference was seen in age composition of both groups (p=1.000). Most patients in BD group were males (63.3%), while in MDD group most patients were females (60%), this difference was however not found to be statistically significant (p=0.121). Most of the patients in both BD group (70%) and MDD group (70%) were married (p=0.890). Most patients in BD group were Hindu (96.7%), while 3.3% were Muslim, while in MDD group Hindu were 70% and Muslims were 26.7%. This difference in religion of both groups was found to be statistically significant (p=0.021).

In BD group most patients were educated till high school (30%), and 16.7% were graduates. Only 16.7% were illiterate. In MDD group 33.3% were illiterate and 23.3% were educated till primary school. This difference in education status in both groups was however not found to be statistically significant (p=0.054). Most patients in BD group (40%) were currently employed, while 33.3% were never employed. In MDD group most patients (53.3%) were never employed while 26.7% were currently employed. This difference in employment status in both groups was however not found to be statistically significant (p=0.291).

In BD group most patients were unskilled worker (36.7%) while 33.3% were home maker and 23.3% were self employed. In MDD group 56.6% were home maker and 26.7% were self employed. This difference in occupation in both groups was however not found to be statistically significant (p=0.120).

Most patients were from joint family in both BD (56.7%) and MDD group (56.7%). While 30% patients from BD group and 33.3% patients from MDD group had nuclear family. This difference in type of family in both groups was however not found to be statistically significant (p=0.866).

Most patients were from rural background in both BD (66.7%) and MDD group (66.7%).

Table 2 : Comparison of mean Vitamin D among study groups

Group	N	Mean ± SD	Median (Range)	P value
BD	30	31.50 ± 8.17	19.43 (11.19, 41.69)	0.663
MDD	30	20.49 ± 9.63	18.3 (7.37, 52.37)	

The Vitamin D level in BD group ranged from 11.19 to 41.69 ng/ml with a mean of 31.50 ± 8.17 ng/ml. The Vitamin D level in MDD group ranged from 7.37 to 52.37 ng/ml with a mean of 20.49 ± 9.63 ng/ml. Although a difference in mean Vitamin D levels was observed between the two groups, it was not statistically significant. (p=0. 663).

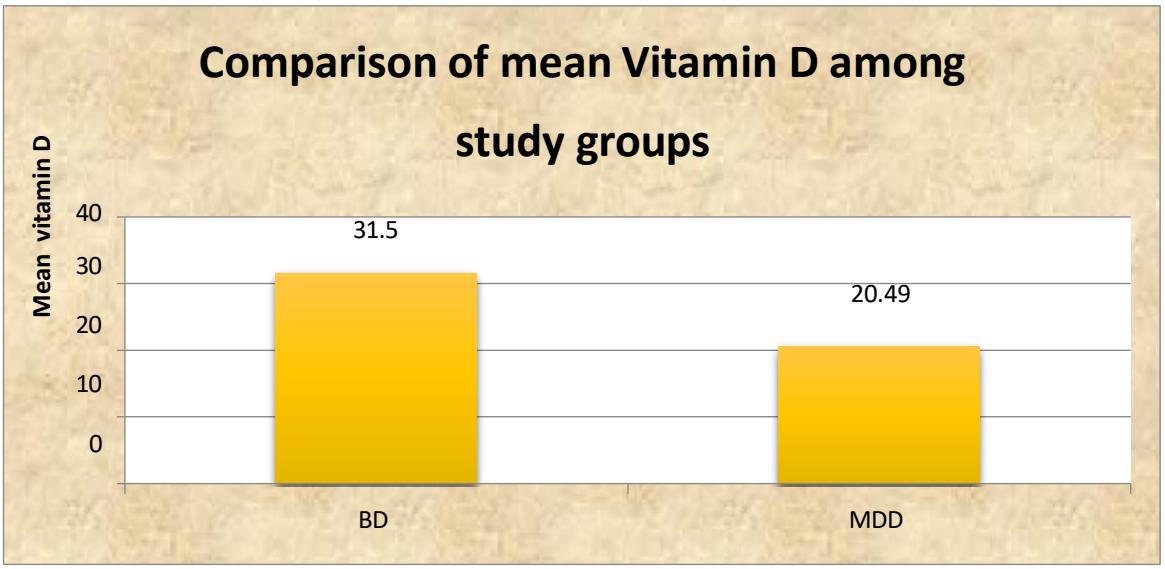

Figure 1 : Comparison of mean Vitamin D among.

Table 3 : Correlation of HAM-D with Vitamin D levels in all patients (N=60)

	Vitamin D	
	r	P value
HAM-D	-0.285	0.027 (S)

Considering all 60 patients in this study, weak negative correlation was found between Vitamin D with HAM-D (r= -0.455, p=0.027).

Table 4 : Correlation of HAM-D with Vitamin D levels in BD patients (N=30)

	Vitamin D	
	r	P value
HAM-D	-0.455	0.011 (S)

Considering the 30 patients in BD group in this study, moderate negative correlation was found between Vitamin D with HAM-D (r= -0.455, p=0.011).

Table 5 : Correlation of HAM-D with Vitamin D levels in MDD

	Vitamin D	
	r	P value
HAM-D	-0.111	0.560

Considering the 30 patients in MDD group in this study, no significant correlation was found between Vitamin D levels with HAM-D.

Table 6 : Correlation of WHO QOL with Vitamin D in BD group

	Vitamin D	
	r	P value
Q1 (Overall QOL)	0.452	0.012* (S)
Q2 (Overall health)	0.318	0.087
Domain 1 (Physical)	0.413	0.023* (S)
Domain 2 (Psychological)	0.445	0.014* (S)
Domain 3 (Social)	0.168	0.374
Domain 4 (environmental)	0.327	0.077

*= correlation is significant at the level of 0.05

**= correlation is significant at the level of 0.01

Considering the 30 patients in BD group in this study, moderate positive correlation was found between Vitamin D with Overall QOL (r= -0.452, p=0.012), Physical domain (r= -0.413, p=0.023), and Psychological domain (r= -0.445,

p=0.014).

Table 7 : Correlation of WHO QOL with Vitamin D in MDD group

	Vitamin D	
	r	P value
Q1 (Overall QOL)	0.158	0.404
Q2 (Overall health)	-0.051	0.787
Domain 1 (Physical)	-0.075	0.692
Domain 2 (Psychological)	0.001	0.953
Domain 3 (Social)	0.213	0.259
Domain 4 (environmental)	-0.081	0.669

No significant correlation was found between WHO QOL with Vitamin D

DISCUSSION

First and foremost, the socio-demographic profile of both the study groups i.e patients with Bipolar Depression and patients with Major Depressive Disorder was studied. Considering the gender of the patients in both study groups, most of the patients in Bipolar Depression group were males (63.3%), while in Major Depressive Disorder group most patients were females (60%), this difference was however not found to be statistically significant (p=0.121). Similar findings were reported in a study conducted by Xiang Y et al. (2013), which concluded that patients with Bipolar Depression were more likely to be male and married compared to those with Major Depressive Disorder.[8] Another study by Kalitha KN et al. (2017) found that 59.4% of the study population was comprised of the Bipolar Depression group. [9]

Taking into account the marital status of the patients in our study, majority of patients in both the study groups 70% for both, were constituted by married patients. These results were supported by a study by Berlim MT et al. (2004) where married groups comprised majority in both study groups. [5] However, a study by Motovsky and Pecenak (2013) found that married patients were more prone to Major Depressive Disorder. [10]

Education and employment status of the patients were studied next. Our study results revealed that majority of patients with Bipolar Depression were educated till high school i.e. 30% followed by 16.7% who were graduates and only 16.7% were illiterate. Whereas, among patients with Major Depressive Disorder majority of the patients were illiterate i.e. 33% followed by 23.3% who were educated till primary school. As the patients with Bipolar Depression had a better education status than the group with Major Depressive Disorder, this reflected in the results of the employment status of the patients in both groups. Most patients in Bipolar Depression group were currently employed (40%) and only 33.3% were never employed. On the other hand, among the patients with Major Depressive Disorder, most of the patients were never employed (53.3%) and only 26.7% were currently employed. These results are supported by a study conducted at University Hospital in Slovakia by Motovsky and Pecenak (2013), which found a strong association between patients' employment status and depressive symptoms and observed a higher number of unemployed individuals in the Major Depressive Disorder group compared to those with Bipolar Depression.[10].

Looking into the place of residence and family setup of the patients, most patients in both Bipolar Depression group and Major Depressive Disorder group were residing in rural area (66.7%) for both groups and were reported to be living in joint family. This may be due to the reason that majority of study sample was taken from the rural settings and in today's scenario joint family structure is seen to be more prevalent in rural areas as compared to urban areas. These results were in accordance to the results of a study by Kalitha KN et al. (2017) where the rural population comprised the majority in both Bipolar Depression and Major Depressive Disorder group. [9]

As per the results of our study, a statistically significant difference in the religion of both the study groups was found. 96.7% of patients with Bipolar Depression belonged to Hindu religion and 70% among the Major Depressive Disorder group belonged to the Hindu population. This aligns with the study by Kalitha KN et al. (2017), which found that the Hindu community was predominant in both the Bipolar Depression and Major Depressive Disorder groups, with a significantly higher number of subjects in the Bipolar Depression group. [9]

In our study, we considered comparison of levels of Vitamin D in both the study group patients. Our study results indicated that Vitamin D levels in BD group ranged from 11.19 to 41.69 ng/ml with a mean of 31.50 ± 8.17 ng/ml. The Vitamin D level in MDD group ranged from 7.37 to 52.37 ng/ml with a mean of 20.49 ± 9.63 ng/ml. This showed that patients with Bipolar Depression had higher levels of Vitamin D as compared to those with Major Depressive Disorder. Although a difference in mean Vitamin D levels was observed between the two groups, it was not statistically significant (p=0. 663). Study conducted by Anglin RES et al. (2013) showed an analysis of one case-control study, ten cross-sectional studies, and three cohort studies concluded that Vitamin D levels were lower in patients with depression compared to healthy controls.[11]

A study by Victor R et al. (2023) concluded that Vitamin D deficiency was majorly found in patients suffering from anxiety disorder and depressive disorder. [12]

As a part of the study, we also assessed the correlation between Vitamin D levels and HAM-D scores. Among the 60 patients included in this study, a weak negative correlation was found between Vitamin D levels and HAM-D (r= -0.455, p=0.027). This showed that lower the Vitamin D levels in the patients, more severe were the depressive and anxiety symptoms. Study by Somoza-Moncada MM et al. (2023) found that patients with depressive symptoms had lower levels of Vitamin D compared to those without depression.[13] This was in support of the results of our study.

Results of our study are in also accordance with study by Husain K et al. (2017) which concluded that the Vitamin D is significantly lower in depression group. The correlation coefficient between HAM-D score and Vitamin D level was found to be – 0.468 i.e. there is an inverse relation between Vitamin D level and HAM-D score. It was found to be significant (p value – 0.001). [14]

However, the results of a few studies were found to be in contrast to results of our study. Study by Elseesy SW (2020) stated that there was no significant correlation between Vitamin D levels and the severity of depression as measured by the HAM-D. [15] Another study whose results did not resemble our study was done by Shekar A et al. where they concluded that no association was found between Vitamin D levels and the severity of depression and anxiety.[16]

Not many studies have been done till date comparing the levels of Vitamin D in patients of Bipolar Depression and Major Depressive Disorder Furthermore, correlations between Vitamin D levels with QOL were also studied, which revealed weak positive correlations between Vitamin D levels and overall Quality of Life (QOL) (r= -0.287, p=0.026). Among the 30 patients diagnosed with Bipolar Depression, moderate positive correlations were identified between Vitamin D levels and overall QOL (r= -0.452, p=0.012), as well as the physical domain (r= -0.413, p=0.023) and psychological domain (r= -0.445, p=0.014) scores. However, no significant correlations were observed between WHO-QOL and Vitamin D levels in the Major Depressive Disorder group.

CONCLUSION

Based on our study's results, we conclude that Vitamin D levels were lower in patients of MDD group as compared to those of BD group. Considering the severity of symptoms of depression assessed with the help of HAM-D in both groups, moderate negative correlation was found between Vitamin D levels HAM-D in Bipolar Depression thus indicating that lower the vitamin D levels in patients of Bipolar Depression, more was the symptom severity as indicated by higher score on HAM-D. No such correlation was seen in patients of MDD indicating that Vitamin D levels did not affect the symptom severity in patients with MDD. The study also showed moderate positive correlation between Vitamin D and Overall QOL (r= -0.452, p=0.012) and Physical (r= -0.413, p=0.023), and Psychological (r= -0.445, p=0.014) domains of WHO-QOL. This indicated that higher the vitamin D levels in patients of BD, better was their overall QOL, Physical domain and Psychological domain of QOL. No significant correlation was found between WHO-QOL with Vitamin D in MDD group, thereby implying that Vitamin D levels in patients with MDD did not affect their quality of life.

CLINICAL IMPLICATIONS

Exploring the role of Vitamin D in mood disorders can inform personalized treatment approaches. For example, patients with lower levels of Vitamin D and B12 may benefit from supplementation alongside conventional therapies. Clinicians can also consider nutritional assessments as a part of routine investigations and incorporate dietary interventions into treatment plans.

FUTURE DIRECTIONS

- Conducting longitudinal studies that track patients over time can offer valuable insights into how nutritional factors affect the progression of disease. Long-term follow-up can also help identify predictors of treatment response and relapse, informing personalized interventions.
- Designing interventional trials to evaluate the efficacy of Vitamin D supplementation, along with psychosocial interventions, in improving clinical outcomes in patients with Bipolar Depression and MDD. Randomized controlled trials can help establish causal relationships and guide evidence-based treatment strategies.

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CONFLICT OF INTEREST-Nil**.**

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