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Clinical correlation of vitamin D in depression

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ABSTRACT

Background: Literature has substantially advanced our understanding of the action of vitamin D in depression, much is still unknown concerning how vitamin D relates to dimensions of depression. Hence, authors aimed to examine the relationship of vitamin D in patients of depression, its correlation with the severity of depression and different symptom domains of depression.

Methods: This Hospital based case control study included 75 patients with depression and 50 controls who were age and gender matched. Beck's Depression Inventory II was used to assess the severity and symptom domains of depression. Vitamin D levels was assessed using Enhanced Chemiluminescence Technique.

Results: Vitamin D deficiency was found significantly (<0.001*) among cases than controls. Significant (0.003*) inverse correlation was observed between severity of depression and vitamin D level.In cognitive symptoms, pessimism, punishment feeling, self-criticism, suicidal thoughts and worthlessness were found significantly higher among vitamin D deficient patients. However, in somatic-affective symptoms, crying, indecisiveness, loss of energy, irritability, concentration difficulty and being tired were the significant by prominent symptoms in vitamin D deficient patients.

Conclusions: Vitamin D (<50 nmol/L) was found to be significantly associated with depressive symptoms with cognitive and somatic-affective symptoms being affected by vitamin D deficiency.

Keywords: Cognitive domain, Depression, Somatic-affective domain, Vitamin D

INTRODUCTION

Depression is a highly prevalent and debilitating chronic mental illness that can be difficult to treat, and both depressive disorders and sub-threshold depressive symptoms are associated with significant disability, mortality, and health care costs. Illnesses that are more common among the ageing populations include depression, cardiovascular disease and diabetes. Though, there are various advanced theories including the biological, psychological and environmental processes, however the underlying etiology and pathophysiological phenomena of depression are not yet fully enlightened and there is a possibility that several different

mechanisms are involved in development of depression.² A bidirectional relationship has been observed between depression and poor dietary nutrients.³⁻⁵ Clinician routinely prescribe omega-3 fish oils, S-adenosylmethionine (SAMe), L-tryptophan, and folic acid as adjuvants to antidepressant treatment.⁶ Vitamin D is a novel hormone. It appears that Vitamin D may play a role in brain function, acts as a neurosteroid and has impact on brain serotonin; suggesting its possible role in mood regulation.^{7,8} Active metabolites of Vitamin D can cross blood brain barrier and it is observed that receptors for vitamin D are present in neuronal and glial cells of central nervous system, specifically the cingulate cortex and hippocampus, known areas to be involved in pathophysiology of depression.^{7,9} A number of literature

have found the association between serum Vitamin D levels and mood disorder including major depressive disorder, seasonal affective disorder and that its supplementation might play an important part in the depression. 10-13 treatment of Furthermore. psychopathology of depression is a heterogeneous concept regarding its symptom dimensions. Studies have shown that depressive symptoms like cognitive, somatic and neurovegetative depressive symptoms relate differently to a variation in health outcomes, including biological ones. 14,15 A recent study has reported the association of vitamin D deficiency or insufficiency with specific psychopathology in schizophrenia patients, including grandiosity, social anhedonia and irregular speech.¹⁶ In our knowledge, so far in India, no study had examined the correlation between depressive symptom domains and vitamin D. Therefore, we planned to assess the association of vitamin D levels with depression. We had also explored any relationship between Vitamin D levels and different severity grades of depression. Further to this, we also investigated the association between Vitamin D level and different symptom domains of depression.

Keypoints

- The objective was to evaluate vitamin D among patients with depression and find the association with severity and symptom domains of depression.
- Vitamin D was found to be depleted significantly among severely depressive patients.
- Cognitive symptoms particularly suicide thoughts, punishment feeling, self-criticism, worthlessness and somatic-affective symptoms such as concentration difficulty, tiredness, indecisiveness, irritability, crying and loss of energy were significantly higher among vitamin D depleted patients.
- Intervention studies are urgently required to determine for whether vitamin D can improve depressive symptoms.

METHODS

Selection of cases

After getting the Institutional Human ethics committee approval, males and females patients were recruited from Department of Psychiatry at Era Lucknow Medical College with primary diagnosis of current depressive episode (n-75) as per ICD-10 guidelines between 15 April 2017 till 17 May 2018. Patients aged between 16-60 years and willing to give informed consent were included in the study. Patients who had severe depression with psychotic symptoms or associated comorbid psychiatric illness or chronic medical or surgical condition or had mental retardation and pregnant or lactating females were excluded from the study. A total of 87 participants were assessed but only 75 were included in the study. Those who were excluded from the

study, 5 of them had comorbid substance abuse disorder, 6 had other psychiatric disorders and 1 had associated medical condition.

Selection of controls

Healthy Caregivers (n - 50) assisting the patients in psychiatry OPD/IPD were taken as controls. Age and sex matched caregivers who had given informed consent were taken in the study. Those controls were excluded from the study if they had any psychiatric illness, mental retardation, any acute or chronic medical or surgical illness and pregnant or lactating females.

Evaluation of psychiatric disorders and depression

Socio-demographic profile of the participants were gathered using as a semi-structured performa. Besides this, in order to rule out any psychiatric comorbidity Mini International Neuropsychiatric Interview (M.I.N.I) was employed over participants. Later, severity of depression among cases was assessed be applying Becks Depression Inventory II (BDI II).

Mini International Neuropsychiatric Interview (MINI)

The Mini International Neuropsychiatric Interview (MINI) is a brief structured interview for the major Axis I psychiatric disorders including depression in DSM-IV and ICD-10. The results of recent studies showed that M.I.N.I. had acceptably high validation and reliability scores. ¹⁷

Becks depression inventory II (BDI II)

A 21-item scale covering the severity of depressive mood over the last two weeks, including present day. ^{18,19} Scoring is done with a value between 0 and 3, with extreme score between 0 and 63. The cut-off point to identify participants with 'no depression' (score 0–13) versus 'mild to severe depression' (14-63). ¹⁹ A recent study had re-evaluated the validity of the scale. ²⁰ The scale was obtained from a previous literature who used it after translating the standardized English version into Hindi language. ²¹

Evaluation of Depressive Symptoms Domains

The Beck's depression Inventory II (BDI-II) items was divided into cognitive and somatic/affective subscales based on previous work on factor structure model. ¹⁹ The cognitive domain include sadness, pessimism, past failure, guild feeling, punishment feeling, self-dislike, self-criticism, worthlessness and suicidal thoughts or wishes.

However, the somatic-affective domains include loss of pleasure, crying, agitation, loss of interest, indecisiveness, loss of energy, changes in sleeping pattern, irritability, change in appetite, concentration

difficulty, tiredness or fatigue and loss of interest in sex. The validity of these subscales has recently been reevaluated.²⁰

Assessment of vitamin D levels

Blood samples of the cases and controls were collected from an intravenous route in a Plain vial and minimum of 3 ml of the blood was collected and immediately sent for assay Vitamin D in Hospital Laboratories Services (HLS) of Era's Lucknow Medical College and Hospital. Enhanced Chemiluminescence Technique was used to measure Vitamin D levels. Lower limits of detection are 10 nmol/l for the first assay and 20.3 nmol/l for the second one. To account for the different techniques, the applied vitamin D assay method was dummy coded and was then analysed. Following the previous guidelines for the definition of vitamin D status, vitamin D concentrations >75 nmol/l were considered sufficient vitamin D. Levels between 50 and 75 nmol/l and <50 nmol/l of vitamin D were defined insufficient and deficient vitamin D levels, respectively.²²

Methodology

Results were analysed using descriptive statistics and making comparisons between groups with respect to

growth parameters. Discrete (categorial) data were summarized as in proportions and percentages (%) while quantitative data were summarized as mean and SD. Proportions were compared using chi-square (x^2) test. Unpaired student's t-test was used to compare mean values of quantitative parameters between cases and controls. A two-sided ($\alpha = 2$) p <0.05 was considered statistically significant. Software's MS-Excel and Statistical Package for Social Sciences (SPSS) v 18 were used for analysis.

RESULTS

Sociodemographic variables

Table 1 shows the mean age of the study cases was 36.68±11.64 years which was matched with control group mean age 36.04±3.54 and same ratio of both males and females was taken that was 44% and 56% respectively. Out of 75 cases and 50 controls, majority of cases and controls attended the study were Muslim 56.0% and 54.0% respectively and were from rural region of the country. On comparing, significant (p-<0.001*) number of cases (48.0%) were found to be unmarried. Majority of cases were studied below 10th standard (42.7%) and low earning income i.e. less than 10000 per annum (60.0%) and were found to be underweight (49.3%).

Table 1: Demographic profile of the participants.

Variables	Category	Controls n (%)	Cases n (%)	Kruswall-Wallis Chi Sq	p-value
Age (Mean±SD)		36.04±3.54	36.68±11.64	9.711	0.821
Gender	Male	22 (44.0)	33 (44.0)	0.000	1.000
	Female	28 (56.0)	42 (56.0)	0.000	1.000
	Hindu	22 (44.05) 31 (41.3)		_	
Religion	Muslim	27 (54.0)	42 (56.0)	0.128	0.938
	Sikh	1 (2.0)	2 (2.7)	_	
	Married	34 (68.0)	37 (49.3)		
Marital Status	Unmarried	7 (14.00	36 (48.0)	19.95	<0.001*
Maritai Status	Divorced	5 (10.0)	1 (1.3)	19.93	<0.001**
	Widow (er)	4 (8.0)	1 (1.3)		
	Uneducated	19 (38.0)	19 (25.3)		
	Below 10th Standard	13 (26.0)	32 (42.7)		
Education	Below 12th Standard			5.075	0.280
	Graduate	8 (16.0)	8 (10.7)		
	Post-graduate	3 (6.0)	7 (9.3)		
	Urban	17 (34.0)	22 (29.3)	_	
Place	Semi-urban	7 (14.0)	9 (12.0)	0.541	0.763
	Rural	26 (52.0) 44 (58.7)			
Family Income	<10000	34 (68.0)	45 (60.0)	0.826	0.264
(Monthly)	>10000	16 (32.0)	30 (40.0)	0.826	0.364
Body Mass Index (BMI, Kg/m²) (Misra et al)	Underweight (<21.0)	10 (20.0)	37 (49.3)		
	Normal weight (21-22.9)			11.462	0.009*
	Overweight (23-24.09)	12 (24.0)	10 (13.3)		
	Obese (>25)	9 (18.0)	11 (14.7)		

Variable	Category		Control	Case	Kruswall-Wallischi sq	p-value
Vitamin D Status	Deficient (c50mmal/l)	No.	7	50	44.315	<0.001*
	Deficient (<50nmol/l)	%	14.0%	66.7%		
	I (C (50. 75 1/1)	No.	13	18		
	Insufficient (50-75 nmol/l)	%	26.0%	24.0%		
	C CC (2.75	No.	30	7		
	Sufficient (>75nmol/l)	%	60.0%	9.3%		

Table 2: Comparison of Mean Vitamin D3 Level between Cases and Control.

Vitamin D level among cases and controls

Table 2 show that the mean Vitamin D level between cases and control, it was found that the among the cases, 66.7% were Vitamin D deficient while among the control only 14% had Vitamin D deficiency. Approximately similar number of cases and controls had Vitamin D insufficient values. However, majority of the controls had sufficient level of Vitamin D. Conclusively, cases were found significantly more (p<0.001) Vitamin D deficient than the control.

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Distribution of subjects according to severity of depression

Figure 1 show that in our study, 60% of the cases had severe depression, followed by moderate depressive patients 32% and then mild depressive patients 8%.

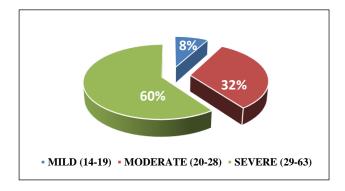


Figure 1: Severity of depression.

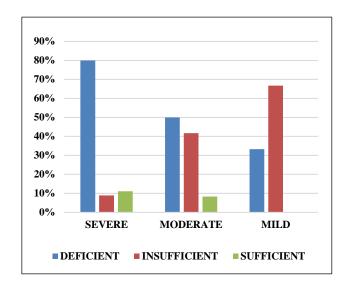


Figure 2: Association of vitamin D deficiency with severity of depression.

Association of Vitamin D levels with severity of depression

Figure 2 show that there was a significant inverse correlation (p- 0.003) between severity of depression and Vitamin D level. 80% of patients with severe depression and 50% of that with moderate depression had vitamin D deficiency. However, 66.7% mild depressive patients had insufficient vitamin D level.

Association of Vitamin D levels with BDI II scores and symptom domains of depression

Correlation of Vitamin D level deficiency with BDI II and depressive symptom domains.

Figure 3 show that, based upon Becks Depression Inventory scoring it was found that Vitamin D deficient patients (mean 36) scored significantly higher (p <0.001) on BDI II scale than those with insufficient (mean 27.82) or sufficient (mean 25.75) levels of vitamin D. Also, patients had significant scoring on BDI II cognitive symptoms (<0.001), and somatic/affective symptoms (0.002).

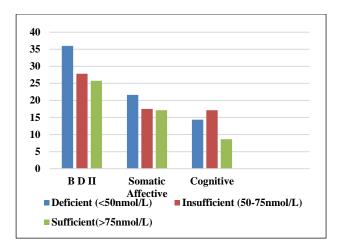


Figure 3: Association of Vitamin D Deficiency with Severity of Depression according to BDI II, Cognitive and Somatic-Affective domains.

Correlation of vitamin D deficiency with cognitive symptom domains of depression

Table 3 show that upon assessing the cognitive symptom, it was observed that symptoms such as pessimism (p-0.026), punishment feeling (p-0.000), self-criticism (p-0.017), suicidal thoughts or wishes (p-0.003) and worthlessness (p-0.016) were significantly found in greater severity in Vitamin D depleted patients.

Correlation of vitamin D deficiency with somaticaffective symptom domains of depression

Table 4 show that after exploring the somatic/affective symptoms according to BDI II, patient with Vitamin D depleted values scored significantly higher grades on symptoms of concentration difficulty (P-0.011), tiredness (P-0.021), indecisiveness (P-0.025), irritability (P-0.027), crying (p-0.032) and loss of energy (p-0.033).

Table 3: Corelation of vitaming	ı D levels a	nd cognitive symptom	s domains of	depression.
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	Vitamir	Vitamin D levels							
Cognitive symptoms domain	Deficient <50 nmol/L			Insufficient 50-75 nmol/L		ent nol/L	Kruskal- Wallis Chi sq.	Df	p- value
domani	Mean SD		Mean			SD	wams em sq.		
Sadness	2.02	0.68	1.72	0.67	1.57	0.53	4.35	2	0.114
Pessimism	1.60	0.99	0.94	0.80	1.00	0.82	7.29	2	0.026*
Past failure	1.44	1.05	1.22	1.11	1.14	0.69	0.82	2	0.665
Guilt feeling	1.02	0.84	0.78	0.65	0.29	0.49	5.61	2	0.061
Punishment feeling	1.82	1.00	1.11	1.08	0.29	0.49	17.05	2	0.000*
Self-dislike	1.46	0.79	1.22	0.81	0.86	0.69	4.45	2	0.108
Self-criticism	1.38	0.99	0.89	0.76	0.43	0.53	8.16	2	0.017*
Suicidal thoughts or wishes	1.24	0.89	0.56	0.78	0.57	0.79	11.76	2	0.003*
Worthlessness	2.40	0.76	2.00	0.59	1.86	0.38	8.23	2	0.016*

Table 4: Correlation of Vitamin D deficiency and somatic-affective symptoms domains of depression.

	Vitamin D levels						Kruskal-		p-
Somatic-affective symptom domain	Deficient <50 nmol/L			Insufficient 50-75nmol/L		Sufficient >75nmol/L		Wallis df Chi sq.	
	Mean	SD	Mean	SD	Mean	SD			
Loss of pleasure	1.84	0.71	1.83	0.71	1.57	0.53	0.99	2	0.610
Crying	1.60	0.97	0.94	0.73	1.71	1.11	6.92	2	0.032*
Agitation	1.80	0.67	1.78	0.55	1.29	0.49	4.67	2	0.097
Loss of interest	1.62	0.64	1.33	0.59	1.29	0.69	4.43	2	0.109
Indecisiveness	1.74	0.75	1.61	0.78	0.86	0.69	7.38	2	0.025*
Loss of energy	2.16	1.02	1.50	0.92	2.14	0.69	6.80	2	0.033*
Changes in sleeping pattern	1.56	0.99	1.33	0.84	1.14	0.69	2.13	2	0.344
Irritability	2.00	1.01	1.56	1.04	1.00	0.82	7.20	2	0.027*
Change in appetite	1.84	0.71	1.89	0.47	1.86	0.38	0.03	2	0.983
Concentration difficulty	2.50	0.71	2.11	0.76	1.86	0.38	8.98	2	0.011*
Tiredness or Fatigue	1.60	1.01	0.94	0.80	0.86	0.69	7.73	2	0.021*
Loss of interest in sex	1.36	0.78	0.89	0.83	1.00	0.58	4.79	2	0.091

DISCUSSION

In the present study, authors have found that depression was found significantly higher among unmarried cases. This was probably because of the less psychosocial support. in addition to this, we had also found that cases with depression were significantly (p- <0.001*) vitamin D deficient (<50 nmol/L) and insufficient (50-75 nmol/L) in comparison to healthy subjects. Our findings were in consistent with the previous literature conducted by Hoogendijk WJ et al, who had investigated the relationship of 25 (OH) D with prevalent depression and found that participants with major depressive disorder and mild depression had significant lower (p- <0.001) 25(OH) D level than the non-depressed individuals.²³ However, there are several other studies which deny this association.²⁴⁻²⁶ In our view the above findings may be of immense importance because the Vitamin D has been increasingly measured among nonresponding depressive patients who require inpatients facility with the expectation to offer a new therapeutic option for depression.²⁷ Furthermore, we have also found that vitamin D deficient participants had scored higher (more severity) on BDI II scale compared with those having sufficient vitamin D levels (>75 nmol/L). The results were in accordance to the previous work done by Penckofer S et al and Armstrong DJ et al .^{28,29}In contrast, Zhao G et al in his survey had found no significant association between Vitamin D concentration and depression severity. 30

We don't know whether vitamin D deficiency acts as an etiological factor leading to depression or it is a consequence of depression. It is plausible this inverse association can be possibly because of the fact that subjects with depression have less-nutritious diets, lives a sedentary lifestyle, have diminished social interactions. Also, their psychomotor activity is retarded leading to less involvement in less physical activity and have fewer opportunities for exposure to sunlight. Also, their psychomotor activity and have fewer opportunities for exposure to sunlight. Also, their psychomotor activity and have fewer opportunities for exposure to sunlight.

Moreover, activated form of vitamin D augments the metabolism of glutathione in neurons in brain, and thereby, enhances the antioxidant properties which have the pivotal role in protection of brain neurons from oxidative degenerative processes. In addition to this, it has been shown that vitamin D regulates gene expression of tyrosine hydroxylase, an essential enzyme involved in the synthesis of norepinephrine and dopamine. Both neurotransmitters are involved in mood regulation and depression.

Besides this, vitamin D has also found to be involved in stimulation of nerve growth factor and promotes neurogenesis. ^{37,38} Also, vitamin D regulates calcium homeostasis, membrane permeability and axonal conduction, it is thought to have an indirect role in the regulation of neurotransmission.

Further to this, we have also analysed the association of depressive symptom domains with level of vitamin D. Upon analysing we found that BDI II cognitive symptoms of depression particularly punishment feeling, suicidal ideation or wishes, worthlessness, self-criticism and pessimism were significantly related to vitamin D deficient and insufficient cases. Previous data by Kanel R et al, supports our finding.³⁹

Also, Grudet C et al, found significant lower levels of vitamin D among Suicide attempters than non-suicidal depressed patients and healthy controls. 40 In addition to this, concentration difficulty, tiredness, indecisiveness, crying and loss of energy were among the somatic-affective symptoms that were significantly higher among Vitamin D deficient and insufficient cases. All these symptoms can be correlated with the severity of depressive episode which was also found to be higher in vitamin D deficient and insufficient population as compared to vitamin D sufficient population.

Therefore, our study construed that deficient vitamin D level may require definite clinical attention in severely depressed patients. Even if this can be assumed, further studies are warranted to show that these depressive symptoms can certainly be lowered in this cohort group through intervention with Vitamin D supplementation along with the antidepressant treatment.

CONCLUSION

The inference from the study was that a significant inverse association was found between level of vitamin D and severity of depression. Also, there was a strong relationship found between deficient vitamin D level and cognitive symptom domain of depression. Therefore, it might be prudent to further study the effect of supplementation of Vitamin D in this cohort group for its effect in alleviating these symptoms.

Present study had several limitations. First, we have conducted this study at a single centre, there results couldn't be generalized. Secondly, we have used single rating scale for depression, the BDI II questionnaire, but more elusive Montgomery Asberg Depression Rating Scale and HADS could have yielded an additional information. Also, the study sample was small and more randomized are warranted. In addition, most of the patients were from low socioeconomic status and had poor nutritional diet. Further to it, important confounding factors like physical activity and sunlight exposure were not assessed.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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