Original Research Article

Role of vitamin D in management of depression

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Abstract

Background: Major depressive disorder (MDD) is a common psychiatric disorder leading to severe dysfunction in multiple spheres of life. Etiopathogenesis of MDD is multifactorial with multiple inconclusive theories including putative role for vitamin D so it has been investigated as a potential strategy for the prevention and/or treatment of depressive symptoms. **Method:** A longitudinal study in patients of Major Depressive Disorder as per DSM-5 attending the psychiatry outpatient department (OPD), from March 2018 - June 2019 of a tertiary care center was planned. Sociodemographic data was collected .Level of vitamin D was assessed at 0 and 12 weeks. . Patients were divided into 2 groups i.e. cases (patients with low vitamin D) and controls (patients with normal vitamin D). Cases were further divided into 2 groups, out of which one group was supplemented with vitamin D(60k/week) and the other group was not supplemented with vitamin D. All the above groups were given antidepressant (Sertraline) with benzodiazepines (Lorazepam) according to clinical assessment. Severity of the disease was assessed using MADRS and HAM-A at 0,4,8,and 12 weeks. **Result:** Out of 78 patients who were enrolled in the study, low vitamin D level was seen in 76.9% of the patients. At 0 week out of 60 cases, 30% had mild depression, 70% had moderate depression, while none of the cases had severe depression and 8.33% had mild anxiety ,55.00% patients had moderate anxiety, 36.66% had severe anxiety. Analysis of mean MADRS and HAM-A scores was done by taking into consideration all the three groups i.e. cases with vitamin D supplementation, cases without vitamin D supplementation and controls using ANOVA test at 0 and 12th week through which it could be seen that there was significant difference between all the three groups at 0 week but not at 12 week. **Conclusion:** Patients with low vitamin D levels are more likely to have depression than general population but there appears to be no beneficial effect of vitamin D supplementation in management of depression.

Key words: Major depressive disorder, Vitamin D, MADRS, HAM-A.

Introduction

Major depressive disorder (MDD) is a commonly encountered psychiatric disorder. The report on Global Burden of Disease estimates the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women, and the one-year prevalence has been estimated to be 5.8% for men and 9.5% for women .As per National Medical Health Survey (2015-16) in India, one in 20 (5.25%) people over 18 years of age have ever suffered (at least once in their lifetime) from depression amounting to a total of over 45 million persons with depression in 2015[1].Pathophysiology of MDD is complex, several mechanisms namely impairment in neurotrophic support and neurogenesis, neuroinflammation, disruption of bioenergetic signaling, oxidative stress, and excitotoxicity have been postulated to exert a key role in the development of the depressive symptoms.All these alterations can be triggered by chronic stress, that may cause the activation of the peripheral macrophages and central microglia, dysfunction of the hypothalamus–pituitary–adrenal (HPA) axis, hypercortisolemia, and a consequent impairment of synaptic plasticity, dendritic spine growth, and synaptic communication[2,3,4]. Considering that vitamin D plays a role in neuroimmunomodulation and neuroplasticity and may reduce oxidative stress[5] it has been investigated as a potential strategy for the prevention and/or treatment of depressive symptoms.

It has been shown that one of the actions of vitamin D is to induce the expression of the serotonin-synthesizing gene tryptophan hydroxylase 2 while repressing the expression of tryptophan hydroxylase 1. Both tryptophan hydroxylase 1 and tryptophan hydroxylase 2 play a role in serotonin synthesis. Vitamin D may thus prevent depression by maintaining normal serotonin levels[6].

Nutritional deficiency, especially of Vitamin D, is highly prevalent and potentially modifiable. Vitamin D deficiency is pandemic[7], globally about 1 billion people have Vitamin D deficiency

There is high prevalence of depression as well as vitamin D deficiency in general population, potential impact of vitamin D deficiency on treatment and outcome of depression so the present study was aimed to assess Vitamin D status in patients with depression, its association with time to remission, and role of Vitamin D supplementation in the outcome of patients with depressive disorders.

Aim

To study role of vitamin D_3 in depression.

Material and Methods

This was a longtitudinal study conducted in psychiatry department of government medical college in north India. The patients diagnosed as case of MDD were included in the study after taking written consent. At the first visit serum calcium, liver function test (serum bil T/D/I,SGOT/SGPT), kidney function test (serum urea/creatinine) and thyroid profile(T3 ,T4,TSH) was done to exclude any condition needing medical attention. Vitamin D levels were done at 0 and 12 weeks. Depression severity was assessed on Montgomery–A˚ sberg Depression Rating Scale (MADRS)[8], Hamiton anxiety Scale(HAM –A)[9] at interval of 0, 4, 8, and 12 weeks. Patients were divided into 2 groups i.e. cases and controls. Cases included patients with low vitamin D levels and controls included patients with normal vitamin D levels. Cases were further divided into 2 groups, out of which one group was supplemented with vitamin D(60k/week) and the other group was not supplemented with vitamin D. All the above groups were given antidepressant (Sertraline) with benzodiazepiens (Lorazepam) according to clinical assessment. The correlation between vitamin D_3 depressive symptoms and anxiety symptoms was done using student-t and ANOVA test.

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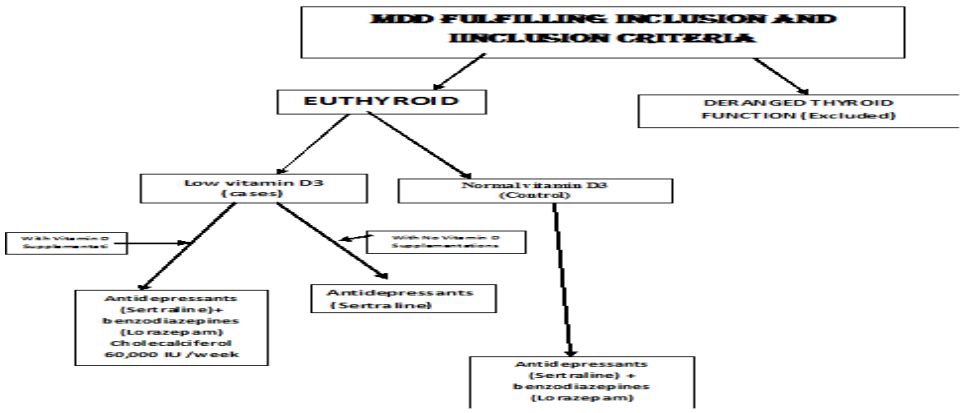
Inclusion criteria

1. Patients who gave written informed consent
2. Patients diagnosed as case of major depressive disorder (MDD) without Psychotic symptoms according to DSM V
3. Euthyroid patients within age group of 18-40 years

Exclusion criteria

1. Patients with deranged liver function and kidney function test.
2. Patients taking antiepileptic medications
3. Patients on medications for tuberculosis.
4. Patient taking antidepressants.
5. Patients with chronic illness.
6. Pregnant or lactating females.
7. Patients taking calcium supplementation.



Result

Out of 78 patients who were enrolled in the study low vitamin D levels was seen in majority, with 76.9% of participants (60 Patients) having levels in either the deficient range or the insufficient range. 7 (8.97%) patients were lost to follow up. Mean duration of present illness in patients with low vitamin D levels was 6.10 months with standard deviation of 2.90. Relatively, the mean duration of present illness in patients with normal vitamin D levels was 6.39 months with a standard deviation of 2.03. However there was no significant difference between the two groups (p value>0.05). At 0 week it was seen that out of 60 cases, 30% had mild depression; 70% had moderate depression; while none of the cases had severe depression. Out of 18 controls, 55.5% had mild depression; 38.88% had moderate depression & none of the controls had severe depression (Table no 1).Comparison of mean values of MADRS scores of cases and controls at baseline further revealed that there was significant difference between the two groups (p value<0.05). At 0 week out of 60 cases 8.33% had mild anxiety, 55.00% patients had moderate anxiety, 36.66% had severe anxiety. Out of 18 controls 22.2% had mild anxiety, 77.78% patients had moderate anxiety, and none of the controls had severe anxiety (table no 2).Comparison of mean values of HAM-A scores of cases and controls at 0 week revealed significant difference (p value<0.05). On subsequent visits at 4^{th} ,8^{th} and 12 weeks mean values of MADRS and HAM -A scores were compared using student t test between cases with vitamin D supplementation and without vitamin D supplementation which showed that there was no significant difference between the two groups Comparisons were carried out between MADRS scores of cases with vitamin D supplementation and controls at 0 and 12 weeks which revealed significant difference (p value<0.05) at 0 week and non significant difference at 12 weeks.(p value>0.05). Comparison between HAM-A scores of cases with vitamin D supplementation and controls at 0 and 12 weeks also revealed significant difference at 0 week (p value<0.05) and non significant difference at 12 weeks(p value>0.05). More detailed analysis of mean MADRS and HAM-A scores was done by taking into consideration all the three groups i.e. cases with vitamin D supplementation, cases without vitamin D supplementation and controls using ANOVA test at 0 and 12^{th} week through which it could be seen that there was significant difference between all the three groups at 0 week but not at 12 week (Table no 3 & 4)

MADRS values at 0 week

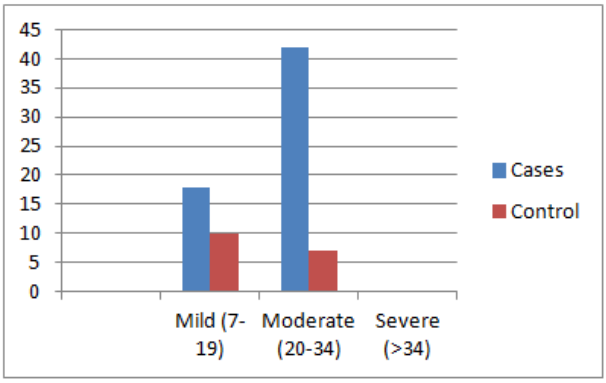


Fig 1:MADRS values at 0 week

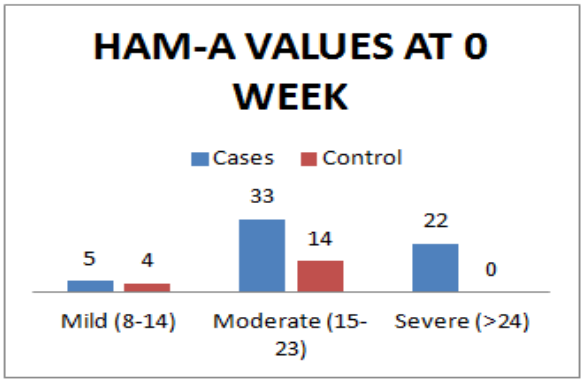


Fig **2:HAM-A values at 0 week**

Table 1:Comparison of mean MADRS values b/w cases with VIT d supplementation at 0 & 12 week, no VIT d supplementation at at 0 & 12 week and controls at 0 & 12 weeks

	0 week			12 weeks		
	N	Mean	SD	N	Mean	SD
Cases with vitamin D supplementation	30	20.93	1.83	27	12.00	3.98
Cases with no vitamin D supplementation	30	21.87	3.95	28	13.21	3.18
Controls	16	19.31	1.40	16	10.88	1.15
F-value	4.314			2.773		
p-value	0.017			0.070		
Critical difference (CD)	1.56					

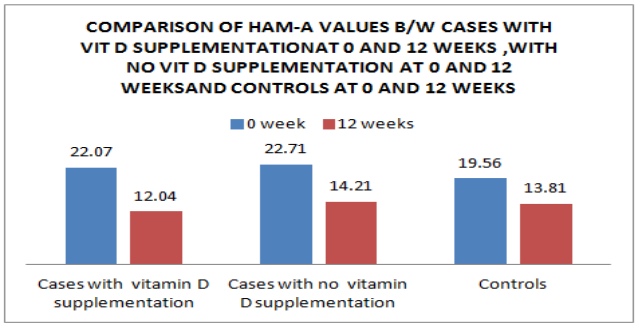


Fig 3: Comparison of HAM-A values b/w cases with VIT D supplementation at 0 and 12 weeks, with no VIT D supplementation at 0 and 12 weeks and controls at 0 and 12 weeks

Discussion

After following the set inclusion and exclusion criteria, 65% of the total patients diagnosed as case of Major Depressive Disorder had low vitamin D levels at their first visit It was seen that socio demographic factors did not contribute to vitamin D deficiency. . This is in contrast with findings of study conducted by Nebhinan *et al* which showed that sociodemographic factors were predictors of vitamin D deficiency as it was seen more in unemployed or homemaker, females, patients with smaller height, and from nuclear family[10]. According to study conducted at Kanchipuram district of Tamil Nadu by John Mechenro ***et al*** demographic variables that were significantly associated with vitamin D status included the educational status of the individual, the occupational profile of the individual, the socioeconomic class, and birth in a rural or urban area whereas gender, marital status, age, community, and religion did not show significant associations with vitamin D status[11].There was no significant difference between mean duration of present illness in patients with low vitamin D & normal vitamin D the two groups (p value>0.05). This is in contrast with Milaneschi *et al*. who reported greater duration of depressive symptoms, compared to patients with normal vitamin D levels[12]. Most of the patients with low vitamin D levels had severe depression and severe anxiety as compared to patients with normal vitamin D levels (table 1&2) as there was significant difference between their mean MADRS and HAM-A scores at 0 week thus it seems that vitamin D deficiency has some association in pathophysiology of depression and anxiety . These findings are consistent with study of Marie Kjærgaard *et al.* who concluded that the participants with low vitamin D levels had significantly higher HADS(Hospital Anxiety and Depression Scale) & MADRS score[13]. These findings can be further supported by results of the study conducted by M. bičíková et al which revealed that the levels of vitamin d were significantly lower both in the group of depressive and anxiety patients in comparison to the group of healthy controls[14]. Results of study conducted by MinhTu T. Hoang *et al* also reveal that higher vitamin D levels were associated with a significantly decreased risk of current depression[15]. Witte J. G. Hoogendijk et al also stand with the above finding that depression severity was significantly associated with decreased serum vitamin D levels and increased serum PTH level[16]. Collin *et al* also reported lower probability of recurrent depressive symptoms with ≥10 ng/mL level of vitamin D[17]. At 4th, 8th & 12 week there was no significant difference between mean values of MADRS and HAM-A scores of cases with vitamin D supplementation and without vitamin D supplementation. Thus it can be said that vitamin D supplementation

did not show any significant improvement in MADRS and HAM-A scores. Support of this finding can be given by study carried out by Maria A. Choukri *et al*. which showed that there were no statistically significant differences between the vitamin D and placebo groups in any of the outcome measures – depression, anxiety, flourishing, or positive and negative mood, controlling for the baseline measures and the covariates[18]. Comparison between mean MADRS and HAM–A scores of cases with vitamin D supplementation and cases with no vitamin D supplementation showed significant difference at 0 week but no showed significant difference at 12 weeks Through this we can conclude that though vitamin D may play a role in pathophysiology of depression and anxiety symptoms, there appears to be no beneficial effect of vitamin D supplementation in management of depression. This is consistent with findings of Marie Kjærgaard *et al.* who did not find a significant effect of vitamin D supplementation[13]. Vieth et al presented a two-step study where participants were randomised to either 600 or 4000 IU vitamin D per day for 6 months, there was no difference between the two groups[19].Detailed analysis of mean MADRS and HAM-A scores by taking into consideration all the three groups i.e. cases with vitamin D supplementation, cases without vitamin D supplementation and controls using ANOVA test at 0 and 12th week revealed that there was significant difference between all the three groups at 0 week but not at 12 week(table no 3&4)which further supports the previous finding that vitamin D supplementation has no significant role in management of depressive symptoms. Kerrie M. Sanders *et al*. support this finding by their study which concluded that no significant differences between the vitamin D and placebo groups were detected in any of the measured outcomes of mental health[20]. But this finding is against the findings of study done by Naresh Nebhinan *et al.* which signified the importance of treating hypovitaminosis D for effective management of depression, to avoid delay in response, and incomplete remission by observing that majority of patients who had Vitamin D deficiency, took a longer time to remission and reported improvement with Vitamin D supplementation.

Conclusion

We found that 65% of the total patients were diagnosed as case of Major Depressive Disorder had low vitamin D levels at their first visit. Most of the patients with low vitamin D levels had severe depression and severe anxiety as compared to patients with normal vitamin D levels as there was significant difference between their mean MADRS and HAM-A scores at 0 week thus it seems that vitamin D deficiency has some association in pathophysiology of depression and anxiety. No significant difference was found at 12 week between mean MADRS and HAM–A scores of cases with vitamin D supplementation and cases with no vitamin D supplementation .Through this we can conclude that though vitamin D may play a role in pathophysiology of depression and anxiety symptoms, there appears to be no beneficial effect of vitamin D supplementation in management of depression

Limitations of study

1. A relatively small sample of outpatients
2. Smaller sample size for patients with normal Vitamin D status
3. Short follow-up of the patient
4. Lack of detailed exploration of nutritional status, physical activity, dietary patterns, sun exposure and indigenous medicines

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