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Co-Relation between Vitamin D Levels and Hamilton Depression Scores in Patients with Depression

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ABSTRACT
Mood disorders have been described as one of the most common illnesses of humankind for last 2500 years. The vitamin D receptors are present on various areas of the human brain. There are various biological mechanisms that may explain the relationship between vitamin D deficiency and the risk of depression. The vitamin D receptors are present on various areas of the human brain (ie. prefrontal cortex, hippocampus, cingulated gyrus, thalamus, hypothalamus, and substantia nigra), that are important in pathophysiology of depression. 50 cases of major depression were randomly selected from psychiatry OPD and an equal number of controls with matched age, sex, religion and socioeconomic background were also recruited for the study. Hamilton Depression rating was done and their Vitamin D level was checked. It was found that Severity of depression has indirect relationship with vitamin D levels in depressed patients.
Keywords: *Depression, Hamilton, Vitamin D.*

INTRODUCTION

Mood disorders have been described as one of the most common illnesses of humankind for last 2500 years. Major depressive disorder is reported to be the most common mood disorder. It may manifest as a single episode or as recurrent episodes. In India prevalence of depression have varied from 1.7 to 74 per thousand population [(1,2)]. In spite of that much global burden, the pathophysiology of depression is not completely understood[(3)]. If current trends continue, it will become the leading cause of disease burden by the year 2030[(4,5)]. It is hypothesized as a second leading cause of death by year 2020 [(6)].

There are various biological mechanisms that may explain the relationship between vitamin D deficiency and the risk of depression. Serum 25 (OH) D is the main circulatory form and its level are indicative of vitamin D insufficiency or sufficiency. The circulating 1, 25 (OH) 2D is generally not a good indicator of vitamin D, and its level remain in range until the deficiency is severe. [(7, 8)]

The vitamin D receptors are present on various areas of the human brain (ie. prefrontal cortex, hippocampus, cingulated gyrus, thalamus, hypothalamus, and substantia nigra), that are important in pathophysiology of depression [(9)].

Annweiler C et al [10] suggested that Vitamin D possibly helps in the regulation of neurotran-smission, neuroprotection, neuroimmumodulation, and nerve growth factor synthesis.

1,25 (OH)2D the active molecule of vitamin D has been shown to increase the production of tyrosine hydroxylase, an enzyme which is important in synthesis of norepinephrine, potentially involved in depression [11].

Ganji V et al [12] conducted a cross sectional study including 7970 US residents ageing 15-39 yrs. The study reported that persons with current depression had higher prevalence of vitamin D deficiency compared to the counterparts.

Hoogendijk *et al* [13] conducted a cross sectional study on population-based cohort of 1,282 community residents between the age of 65 and 95 years old in the Netherlands. The study reported that Levels of 25 (OH) D were 14% lower in both minor depression and major depressive disorder compared with levels in 1087 control individuals ($P < .001$). The severity of Depression was significantly associated with decreased serum 25(OH) D levels ($P = .03$).

Zhao G *et al* [14] evaluated the relationship between serum vitamin D status and depression in the United States adults. There were 3,916 participants older than 20 years of age. PHQ-9(Patient Health Questionnaire-9) was used to assess the symptoms of depression. The study reported that there is NO statistically significant association between serum vitamin D and Depression.

Dean AJ et al [15] in a randomized controlled trial on healthy adults using 50,000 IU of Vitamin D daily or placebo for 6 weeks reported that Vitamin D supplementation doesn't affect cognitive or emotional functioning.

In summary, there is no clear established relationship between Vitamin D and depression. Also, most of these studies were conducted outside India. Vitamin D level depends upon the environmental and the social factors, so the result of study from other country may not be applicable to Indian population. Therefore, we plan to study the relationship between serum vitamin D (25-hydroxycholecalciferol) level and depression.

MATERIAL AND METHODS

50 cases of major depression were randomly selected from psychiatry OPD and equal number of age, sex, religion and socioeconomically matched controls were also recruited for the study. Diagnosis of major depression was made according to DSM-5 criteria for major depression.

DSM 5 criteria for major depressive disorder:

Five (or more) of the following symptoms have been present during the same 2- week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure

Depressed mood most of the day, nearly every day, as indicated by either subjective report or observation made by others. Note: In children and adolescents, can be irritable mood.

Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.

Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day.

Insomnia or hypersomnia nearly every day.

Psychomotor agitation or retardation nearly every day.

Fatigue or loss of energy nearly every day.

Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day.

Diminished ability to think or concentrate, or indecisiveness, nearly every day.

Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

The symptoms are not due to the direct physiological effects of a substance (e.g., a drug

of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

Inclusion criteria:

- Age between 18 and 60 year.
- Diagnosis of depression according to DSM -5.
- Consent for the study.

Exclusion criteria

- Acutely suicidal and homicidal patient.
- Patient having other co morbid psychiatric disorder.
- Patient having other general medical illness.
- Patient taking any calcium or vitamin D supplements.
- Patient taking any drug which may influence the level of vitamin D.
- Patient taking or used any antidepressants in last 6 weeks.

Following investigations were done in all study participants to confirm absence of any co-existing medical condition.

- Total leukocyte count
- Differential Leukocyte Count
- Erythrocyte Sedimentation Rate
- Hemoglobin Percentage
- Blood Urea
- Serum Creatinine
- Blood Sugar
- Serum Bilirubin
- SGOT
- SGPT
- Serum Alkaline Phosphatase
- X Ray Chest
- Electrocardiogram

After making diagnosis of depression, the severity of depression was rated by "The Hamilton rating scale for depression (HAM-D)". This scale was developed by Max Hamilton and published in 1960. The HAM- D has been devised for use only on already diagnosed patients.

It is used to quantify the problem and, it is also of great use for monitoring treatment of depression [(16)].

The Hamilton scale has 21 items but the scoring is based on first 17 items only. Eight items are scored on a 5-point scale, ranging from 0 = not present to 4 = severe. Nine are scored from 0-2.Total score are obtained by adding scores from first 17 items. The total score is graded as:

0 - 7 ⇔ Normal
8 - 13 ⇔ Mild
14 - 18 ⇔ Moderate
19 - 22 ⇔ Severe
> = 23 ⇔ Very severe

Diurnal variation, derealisation, paranoid symptoms, obsessional symptoms are the last four items which are not included in scoring because the diurnal variation doesn't tell about severity but only of type and other three occur very infrequently.

Non fasting blood samples were collected for vitamin D estimation. Body vitamin D status was assessed by measuring 25-hydroxyvitamin D (25 hydroxycholecalciferol). The laboratory used LIAISON 25 OH Vitamin D TOTAL assay for estimation of Vitamin D levels. The assay uses a direct competitive chemiluminescence immuno-assay technique for the quantitative determination of 25-hydroxyvitamin D in human serum. The procedure takes around 20 minutes. During 1st incubation, 25OH vitamin D is dissociated from its binding protein and bind to specific antibody on the solid phase. After 10 minutes the tracer is added. Subsequently, the starter reagent are added which initiate a flash chemiluminescent reaction. The light signal is measured and is inversely proportional to the concentration of 25OH vitamin D in sample (diasorin product mini CD). The detection limit of this assay is 4ng/ml and the range which it can measure is 4ng/ml to 150ng/ml. The vitamin D status was categorised as [(17,18,19)] given in Table 1

STATISTICAL ANALYSIS

All statistical data was analyzed using SPSS software version 21 Statistical package for window. For comparing continuous variables between two groups with normal distribution two

sample independent t test was used. Chi- square test was used to compare qualitative data. Pearson correlation test was test to look for correlation between vitamin D level and depression severity. All p- values were two tailed and values of $p < 0.05$ were considered statistically significant. All confidence interval were calculated at 95% level.

RESULT

Refer Table 2.

The minimum BDI score was 15 and maximum score was 40. The mean BDI score was 27.92(std. dev- 7.494). The below pie chart is showing the severity of depression according to BDI II scale. 10(20%) of cases were having mild depression, 15(30%) moderate depression, 25(50%) very severe depression.

The mean vitamin D level is 15.36ng/ml (SD- 8.595) and 27.60ng/ml (SD -4.721) in cases and control group respectively. Independent sample t test was applied. There is significant difference between two groups (p value < 0.000). The vitamin D is significantly lower in depression group. In cases 3(6%) were vitamin D sufficient, 16(32%) insufficient, 15(30%) deficient and 16(32%) severely deficient. In controls 18(36%) were vitamin D sufficient, 25(50%) insufficient 3(6%) deficient and 4(8%) were severely deficient.

The relation of vitamin D level and depression severity was assessed by using Pearson's correlation. The correlation coefficient between HAMD score and vitamin D level was found to be – 0.468 i.e. there is an inverse relation between vitamin D level and HAMD score. It was found to be significant (p value – 0.001).

Table: 1

Vitamin D status	25 (OH) D Level in ng/ml
Severe vitamin D deficiency	<10
Vitamin D deficiency	10-19
Vitamin D insufficiency	20–29
Vitamin D sufficiency	D >30

Table 2

		HAM D SCORE	VITAMIN D LEVEL
HAM D SCORE	Pearson Correlation	1	-0.468
	Sig. (2-tailed)		0.001
	N	50	50
VITAMIN D LEVEL	Pearson Correlation	-0.468	1
	Sig. (2-tailed)	0.001	
	N	50	50

DISCUSSION

The vitamin D in the depression group has a mean of 15.36 (st. dev- 8.595) while in control group the vitamin D has a mean of 27.60(st. dev -4.721). The vitamin D is lower in depression group and the difference is found to be significant (p value - < 0.000). This finding is similar to the other studies who have found that low vitamin D level in serum is associated with depression [10,13,20, 21, 22, 23].

We have found a negative correlation between serum vitamin D level and severity of depression. The correlation coefficient was – 0.468 with HAMD score. The serum vitamin D level is decreasing with increasing the score of HAMD. It means that serum vitamin D level is low in more severe depression as compared to less severe. The correlation was found to be statistically significant with p value of 0.001.

The finding is similar to other studies. Hoogendijk et al [13] reported in a cross sectional study of 1284 subjects that severity of depression was significantly associated with a low level of vitamin D (p value <0.001).

CONCLUSION

Our study has shown that vitamin D level is significantly low in patients of major depression.

There is negative correlation between vitamin D levels and severity of depression. Age, sex, marital status, locality, family type, occupation and religion were matched in the patient population and control population. We would like to suggest larger studies with more participants. We will also like to suggest similar studies on depressed patients of Bipolar Disorders and also patients of dysthymia.

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