VITAMIN D LEVELS IN DEPRESSIVE DISORDER

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ABSTRACT

BACKGROUND
There is a dearth of studies evaluating the role of vitamin D in depression in Kerala, which has a high prevalence rate of depressive disorder and suicide. In this study, we aimed to compare the levels of vitamin D of 50 depressed patients with that of 50 age matched controls.

MATERIALS AND METHODS
This is a case control study, conducted in a tertiary care teaching hospital in Kochi, Kerala between October 2012 and October 2014 (2 years). The vitamin D levels of 50 (cases) patients diagnosed to have depressive disorder as per the International Classification of Disease, 10th revision; Diagnostic Criteria for Research (ICD-10-DCR) were compared to 50 age matched controls. The vitamin D levels were estimated from the venous blood samples by using Abbot Architect i.

RESULTS
In this study, 58% (29) of the cases and 26% (13) of the controls had Vitamin D deficiency. The difference was statistically significant (p-value <0.001).

CONCLUSION
In this study, the serum vitamin D levels are significantly lower in cases than in the controls. Vitamin D deficiency is common and often unrecognized and yet may be an important contributor to depressive disorder. Further case control studies with larger random samples are needed to establish the association of vitamin D deficiency with depression.

KEYWORDS
Vitamin D, Depression, Vitamin D Deficiency.


BACKGROUND
Globally, depressive disorders are ranked as the single largest contributor to non-fatal health loss (7.5% of all Years Lived with Disability).¹ As per Nationa Mental 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 2015.² Kerala state had one of the highest suicide rate of 22.4 per lakh population in India (National suicide rate -10.6 per lakh) for the reporting year 2014.³

One can sort causes of major depressive disorder into biological causes, behavioural causes, relative risk factors and emotional reactions.⁴ While the mechanism involved in major depressive disorder is far from established, the neurobiological findings support a model of major depressive disorder as a dysfunction in the brain’s capacity for stress management.⁴ Vitamin D receptor and the vitamin D activating enzyme 1-alpha-hydroxylase are widely distributed in human brain, particularly hypothalamus, and it is speculated that 25 hydroxyvitamin D (25(OH)D) deficiency might increase the odds of suffering depression.⁵ Several mechanisms of action have been proposed to explain the association between vitamin D and depression. The role of Calcitriol the bioactive form of vitamin D, in brain tissue has been confirmed by the presence of vitamin D receptors (VDR) and hydroxylase in various brain regions.⁶,⁷ One area where vitamin D receptors and hydroxylase have been found is the amygdala, which is the center of the limbic system, where behaviour and emotions are regulated.⁸ Vitamin D has been reported to exert a neuro protective function through several mechanisms. Calcitriol regulates calcium concentrations intra- and extracellularly in neurons, consequently reducing toxicity caused by excess calcium.⁹,¹⁰ Active vitamin D enhances glutathione metabolism in neurons, therefore, promotes antioxidant activities that protect them from oxidative degenerative processes.¹¹,¹² Vitamin D also stimulates the expression of nerve growth factor and promotes neurogenesis.¹²,¹³ Moreover, 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.

Many studies indicate that low levels of 25(OH) D were associated to the presence of depressive disorder. A study has also showed that low levels of 25(OH) D were associated to the presence and severity of depressive disorder. A strong body of evidence has demonstrated the seasonality of mood, and vitamin D levels also vary seasonally with low values during the winter period because of the reduced sun light. Therefore, there is a hypothesis that vitamin D may be the link between seasonality of mood and seasonal change in photoperiod. But randomized clinical trials yielded mixed results about vitamin D supplementation on symptoms of depression.

The above-mentioned statistics shows the alarming rise in the rate of depression not only worldwide but also in India. Low levels of 25(OH) D are associated with presence of depressive disorder in previous studies. There is a dearth in studies related to vitamin D and depressive disorder in Kerala, which has a high prevalence rate of depressive disorder and suicide. In this study we have compared the levels of 25(OH) D of 50 depressed patients with that of 50 age matched controls.

MATERIALS AND METHODS
This is a case control study, conducted among patients attending the outpatient and inpatient wings of department of psychiatry of a tertiary care teaching hospital in Kochi, Kerala. The study was conducted over a period of 2 years from October 2012 to October 2014, as per the approval and guidelines of the Institutional Ethical Committee and with the informed, written consent of the participants. Based on the figures available in the literature on Vitamin D and depressive disorder with 95% confidence and 80% power, the calculated sample size was 40 cases and 40 controls. In this study 50 cases and 50 controls were included. The cases were patients aged between 15-80 years diagnosed to have depressive disorder (Depressive episode and Recurrent depressive disorder) as per the International Classification of Disease, 10th revision, Diagnostic Criteria for Research (ICD-10-DCR) by a psychiatrist. Patients with renal disease, liver disease, thyroid dysfunction and those on vitamin D therapy were excluded from the study. Fifty age matched healthy subjects were taken as control.

Procedure Methodology
The parameters used for this study were levels of 25(OH) D and it was estimated by using Abbot Architect i.

Sample Collection
The venous blood samples were obtained under aseptic precautions. Blood samples of patients meeting the above-mentioned criteria which were ordered in the biochemistry laboratory for the determination of vitamin D in the above time period was taken for this study. The blood samples were stored at -20°C, till we collected enough samples for the Vitamin D assay.

Test Method
Chemiluminescence Immunoassay.

Principle
The architect 25-OH vitamin D assay is a delayed one step immunoassay including a sample pre-treatment for the quantitative determination of vitamin D in human serum and plasma using CMIA Technology (Chemiluminescence immunoassay). Sample and pre-treatment reagent are combined with assay diluent and paramagnetic anti vitamin D Coated microparticles. After incubation a biotinylated vitamin D anti-biotin acridinium labelled conjugate complex is added to the reaction mixture and binds to un occupied binding sites of the antivitamin D coated microparticles. After washing, pretrigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light unites. An indirect relationship exists between the amount of vitamin D in the sample and the relative light unites detected by the ARCHITECT I system optics.

Reference Range
Vitamin D Deficiency = <20 ng/ml
Normal = >30 ng/ml

Statistical Analysis
Statistical analysis was done using IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, USA). For all the categorical variables data are as percentage or in frequency. Chi-square analysis was used for finding the association between two categorical variables. Odds Ratio was estimated for risk. Independent two sample t-test was applied to compare the mean age of the two groups. The p-value <0.05 were considered as statistically significant.

RESULTS
This case control study included 50 patients diagnosed to have depressive episode (Cases) and 50 age matched controls. The mean age of the cases was 37.68 ± 10.33 years and that of controls was 39.24±15.001 years, also among the 50 cases 60% were females and in the control group 42% were females, but the difference was not statistically significant (Table 1).
In this study 58% (29) of the cases and 26% (13) of the controls had Vitamin D deficiency. The difference was statistically significant. Also, the odds ratio shows that the cases had 3.930 times chance to develop Vitamin D deficiency than the controls. (Table 2).

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Vitamin D Deficiency &lt;20</th>
<th>OR</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>50</td>
<td>13</td>
<td>26%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Case</td>
<td>50</td>
<td>29</td>
<td>58%</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

In the present study we tried to find the association between low levels of 25(OH)D and depressive disorder. The mean age of the cases was 37.68 ± 10.33 years and that of controls was 39.24 ± 15.001 years, also the difference between the percentage of females, when the cases and controls were compared was not statistically significant (Table 1). So, the two groups were demographically comparable.

The results of this study show that 58% (29) of the patients diagnosed to have depressive episode, had Vitamin D deficiency and among the controls 26% (13) had the same. The difference was statistically significant (P value <0.001). The results of the cross-sectional studies conducted by MinhTu T. et al. 2011 and Hamidreza Jamilian et al. 2013 showed that vitamin D level in healthy participants was significantly higher than depressed patients.15,16 Ju SY et al. 2013 in a systematic review and meta-analysis aimed to summarize the current evidence from cross-sectional and prospective cohort studies that have evaluated the association between vitamin D levels and the risk of depression and the results indicated an inverse association between the same.17 A large population-based study by Hoogendijk, et al. 2008 shows an association of depression status and severity with decreased serum 25(OH)D levels.18 In this study the result is similar to those in the previous studies. Further case control studies with larger random samples are needed to establish the association between vitamin D deficiency and depression.

The limitations of this study were, the small sample size and as it includes people attending a tertiary care teaching hospital, it might not represent the general population. It is very difficult to establish that vitamin D deficiency causes depressive disorder, because the differences in levels of serum vitamin D might be due to true physiological differences or due to differences in characteristics of study population, nutritional status of study participants, and timing of the blood collection. Also, vitamin D deficiency in depressed patient may be because of reduced exposure to sun light secondary to their depressed mood and reduced activity.

**CONCLUSION**

In this study, the serum vitamin D levels are significantly lower in cases than in the controls. Vitamin D deficiency is common and is often unrecognized and yet may be an important contributor to depressive disorder. Perhaps this could contribute to the current knowledge about the pathogenesis of depressive disorder and might help in managing treatment resistant depressive disorders.

Further case control studies with larger random samples are required to establish the association between vitamin D deficiency and depression. It is said that “prevention is better than cure”. This is true for vitamin D deficiency which is easily preventable. Thus, the current recommendations of taking 1 to 1.5 gm of dietary calcium and 2000 IU of Vitamin D per day in the diet which should be adhered to, to avoid vitamin D deficiency in the Indian population.

**REFERENCES**


