CORRELATION STUDY OF VITAMIN D DEFICIENCY IN DEPRESSION PATIENTS: A STUDY FROM A TERTIARY CARE HOSPITAL IN EASTERN ODISHA

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ABSTRACT: INTRODUCTION:
Depression is a mood disorder which is characterized by hopelessness towards life, lack of interest in daily activities, pessimism and sense of inadequacy. According to estimation of World Health Organization (WHO), more than 4 percent of the world’s population deals with depression, and women, youth and the elderly are the most prone to its disabling effects. Numerous vitamin D receptors have been situated in various parts of the brain like the neuroglia, prefrontal cortex, substantia nigra. Vitamin D plays an important role in the transcriptional activation of serotonin (an important neurotransmitter), which influences various brain functions including mood, sleep, appetite. As a unique neurosteroid hormone, vitamin D seems to play an important role in the improvement of depression. Thus, insufficient vitamin D may invariably result in depression. Also, it has been shown in several studies that patients with depression can have low vitamin D levels.

OBJECTIVES: The study was taken up to measure the levels of vitamin D in depression patients and to find out any correlation between vitamin D and depression.

METHODOLOGY: 50 diagnosed cases of depression and 50 age and gender matched controls were studied over a period of 2 years in IMS & SUM Hospital, psychiatry OPD. Biochemical parameters were assayed in the Central laboratory of Department of Biochemistry. RESULTS: Serum Vitamin D was found to be statistically significantly higher in the control group i.e they have higher vitamin D levels than case group (p=0.033).

CONCLUSION: In this study it was found that depression disorder shows a negative correlation with serum vitamin D level, indicating the intricate mechanism of vitamin D deficiency and depression.

Keywords: Vitamin D, Mental health, Vitamin D deficiency, Sunshine vitamin, Serotonin, Counselling, Awareness, Vitamin D receptors
I. BACKGROUND

Depression has emerged as a leading cause of disability with around 264 million people affected. Depression is quiet distinct from usual mood fluctuations and short-lived responses to the day to day challenges in life. Depression is a common, yet serious, mental disorder with symptoms that can have detrimental effects on daily activities of living, especially in the work environment as well as family life.

Depression can turn out to be a serious health condition when it is long-lasting or of moderate to severe intensity. It impoverishes the performance of the person concerned. Depression can lead to suicide in the worst scenario. It has become a silent killer engulfing lives worldwide. Over the years, many researchers have studied various aspects of depression.

Still, there is social stigma surrounding depression. Increased awareness and seeking out professional help can reduce the disabilities caused due to depression.

Depression engulfs the lives of nearly 800,000 people, due to suicide. Suicide has been the second leading cause of death between age group 15-29 years. Majority of the suicides can be attributed to depression.

Depression is mostly common in ages between 18 and 25 (10.9 per cent) and in individuals belonging to two or more races (10.5 percent). Women are at a double risk than men, according to the NIMH and the World Health Organization (WHO) Trusted Source. From 2013 to 2016, 10.4 percent of women was found to be suffering from depression, compared with 5.5 percent of men, which is almost half, according to the CDC Trusted Source2.

According to the WHO, around 300 million people worldwide suffer from depression and is one of the world’s leading causes of disability2.

Depression can be defined as a common mental disorder, characterized by persistence of sadness and a loss of interest in daily activities that one normally enjoyed, along with an inability to perform daily activities, for at least two weeks3.

People with depression generally have several of the following symptoms: a loss of energy to do daily activities; a change of appetite; change of sleep pattern; increased anxiety; lack of concentration; indecisiveness; restlessness; feelings of guilt, or hopelessness; and at the worst, thoughts of self-harm or suicide3.

Depression is treated with counselling or antidepressant medications or a combination of both of them3.

Based on symptoms, depression can be classified into mild, moderate and severe depression. The art of listening helps in the diagnosis, proper history taking from the patient or a family member or observation by friends or family members, as objective assessments are not available yet. While detection of severe forms can be done easily, mild and moderate forms of depression, especially with co-morbid conditions, can go undetected often.

Depending on the severity of disease, social & cultural factors and age, depression can manifest differently, with varied presentations like children usually present depression as sadness, irritability, tantrums, lack of concentration in activities, physical complaints (headache, stomach ache), separation anxiety as well as poor academic performance and disturbed family relations. Whereas in adults, it is usually manifested as a difficulty or change in the functioning level or can even be accompanied with suicidal thoughts and behaviour. Depression, in late life, is often presented with marked psycho-motor agitation or irritability. Individuals may frequently report somatic complaints, poor appetite and with psychotic features sometimes.

Thus, due to these varied presentations, the recognition of mild to moderate depression by family members or close associate/friends at an early stage, is quiet challenging2.

Classification: Depression is broadly classified into Major Depression, Chronic depression, Bipolar disorder, Seasonal Affective Disorder, Psychotic Depression, Post-partum Depression, Substance Induced Disorder.
More types include Double depression, Secondary depression, masked depression, Seasonal depression (Winter/Summer)4,5.

Although, vitamin D is mostly known to play an important role in calcium homeostasis and bone development, vitamin D receptors have been found mostly in all the tissues of our body. Vitamin D can also have a neuroprotective role.

Various studies have reported that vitamin D has a role in cognitive function and in maintaining mental health6.

Many studies have shown a link between patients suffering from depression and low serum vitamin D levels.

Position: Numerous vitamin D receptors have been located in various parts of the brain like the neuroglia, prefrontal cortex, substantia nigra7. Vitamin D acts as a factor for the transcriptional activation of serotonin. Vitamin D activates the enzyme tryptophan hydroxylase which catalyzes the conversion of tryptophan to serotonin. Vitamin D hormone (calcitriol), then activates the transcription of the serotonin-synthesizing gene which is tryptophan hydroxylase 2 (TPH2) in the brain at a Vitamin D Response Element (VDRE)8. Serotonin acts as a neurotransmitter which influences mood; regulates appetite, sleep and other brain functions.

Reference levels: Vitamin D deficiency is considered as serum levels of 25(OH)D less than 20 ng/mL, insufficiency as 20–29 ng/mL and sufficiency as ≥30 ng/mL.

Vitamin D deficiency is prevalent in 70%–100% in the general population of the Indian subcontinent. The commonly consumed food items in India, such as dairy products are not usually fortified with vitamin D. The social, cultural and religious practices of India do not provide adequate exposure to the sun, thus potential benefits of plentiful sunshine are prevented from being utilized. Consequently, sub-clinical vitamin D deficiency is commonly prevalent in urban as well as rural areas, and across all geographic, social & economical strata9.

Though various aspects of depression have been studied earlier, very few studies have been conducted in India regarding this topic. This study has been undertaken to establish the co-relation between vitamin D and depression.

II. MATERIALS AND METHODS

The study was carried out over a period of 2 years from April 2016 to July 2017. 50 patients of depression were selected from the OPD of Department Of Psychiatry and 50 age and gender matched apparently normal subjects (who came for routine check up/ patient’s attendants/ hospital staffs) were selected as controls. Patients aged between 18-60 years who were newly/old diagnosed of depression by ICD-10 (International classification of Diseases, tenth revision) diagnostic criteria by the psychiatrist were included as cases. Pregnant women, patients on Vitamin D supplementation or with diseases like osteoporosis were excluded. It was a Cross sectional case-control study.

Sample collection and requirements: Venous blood (5 ml) was collected from the subjects under sterile conditions. Blood sample was collected in fluoride vial for fasting blood sugar after overnight fasting. Plain vials for Vitamin D, urea and creatinine. For vitamin D analysis, no such preparations like overnight fasting are needed. The samples were stored in 2-8 °c. The analysis was done in Central Lab, Department of Biochemistry. Vitamin D was done in Autoanalyser-cobas e 411 using ECLIA method, FBS, RFT (urea and creatinine ) were done using Autoanalyser cobas Integra 400. Patients were selected as per the Performa with detailed history. Physical parameters like Pulse, Blood pressure, BMI were measured.

HAM D score was used to assess the degree of depression. (mild/moderate/severe). Family history and treatment history (if any) were taken into account. Statistical Analysis was done using SPSS version 20.0.

III. RESULT AND DISCUSSION

In the current study, a total of 100 subjects were included. Among them 50 were suffering from depression called as case group and 50 of them were apparently healthy individuals called as control group.

Vitamin D level was higher in control group (20.88 ± 9.46) as compared to the mean Vitamin D level in cases group (16.88 ± 9.88). This difference was found to be statistically significant (p value= 0.033) (Table 2).
The correlation between the HAM-D score and vitamin D level was found to be inversely proportional. It was seen that as the HAM-D score increases the vitamin level decreases. The correlation coefficient \( r = -0.358 \) and this negative correlation was statistically significant (p value = 0.011) (fig:1).

On applying Chi-square test, strong association between was found between vitamin D and depression. Chi –square value is 3.852 and the significant p value is 0.0041 (Table:3).

Vitamin D level was higher in control group (20.88 ± 9.46) as compared to the mean Vitamin D level in cases group (16.88 ± 9.88). This difference was statistically significant (p value= 0.033) (Table 2).

In the present study it was found that patients suffering from depression had lower vitamin D levels as compared to the healthy controls.

No statistical significance was found in the physical parameters and routine parameters in between the case and control groups. The difference of Vitamin D levels between cases and control was statistically significant. (p value= 0.033).

It is another such case of “Hen first or egg first” where we may be baffled to explain whether vitamin D deficiency was due to depression as patients were restricting their outdoor movements or depression was caused due to deficiency of vitamin D as they had less outdoor movements earlier.

Biosynthesis of Vitamin D3 is majorly dependent on sunlight exposure and 15 minutes to one-hour exposure to sunlight is sufficient for generating 10,000-50,000 IU vitamin D synthesis within 24 hours of exposure10 .

Studies have shown that the noontime around 11 AM to 1PM is the best time to get vitamin D as the sun is at its highest point and our body may produce it most efficiently around that time of day11.

In this geographical area average day length is 13 hours between sunrise and sunset and an average of 5-7kWh/m²/day sunlight exposure is there which is adequate for vitamin D synthesis12.

Vitamin D is responsible for the transcriptional activation of serotonin which is a potent neurotransmitter affecting and regulating sleep, appetite and mood13. Thus low vitamin D level can cause low serotonin levels leading to mood changes and ultimately depression.

The sedentary lifestyle along with excessive pressure and competition at school/work/household have decreased the level of outdoor activities and have increased the stress of the younger generation. Little to no outdoor activity diminishes the exposure to sun and can be related to diminished synthesis of vitamin D on skin. Due to lesser vitamin D synthesis, there is deficiency of serotonin as well. Thus, low vitamin D levels can result in depression.

Alone, inadequate sunlight exposure cannot be attributed to depression.

Factors or events like sudden death of close ones or loss of employment etc can trigger onset of depression in individuals. Certain drugs, such as isotretinoin (used for treating acne), the antiviral drug interferon-alpha, and corticosteroids, can increase the risk of depression. Family history of depression is also a crucial factor. Nearly 30% of people with substance abuse problems also have major or clinical depression. Even if drugs or alcohol temporarily can make you feel better, they ultimately will aggravate depression. Some researchers have noted differences in the brains of people who have a clinical depression as compared to normal people. For instance, the hippocampus, a small part of the brain which is vital for the storage of memories, appears to be smaller in some depression patients than in those who have no history of depression. A smaller hippocampus has fewer number of serotonin receptors than normal14.

Studies can be done to specify the duration between any tragic event and onset of depression in a group of individuals. Many people experience an acute phase of depression which can pass off with taking therapy or counselling. On the other hand, others can find it difficult to cope up and develop moderate to severe depression which requires drug treatment.
People suffering from chronic illnesses like diabetes, heart disease, AIDS, lupus, multiple sclerosis etc are likely to get depressed as these diseases can cause disturbance in sleep-wake cycle, can diminish ability to exercise and productivity in work. These diseases can overall decrease the performance of a person and the person can isolate himself and get depressed. Hence it becomes a vicious cycle of vitamin D deficiency and outdoor activity decline.

Most of the studies done on the subjects go by questionnaires and qualitatively assayed. This study further plans to extend it by measuring the stress markers, such as ROS, serotonin, cortisol quantitatively and studying the correlation which would further reinforce the association between Vitamin D deficiency and stress markers15,16,17

With passing years, the attitude of people towards mental illness have changed. Counselling and proper medication are helping people to get back to optimizing function. Various workshops, seminars and ‘webinars’ are being conducted to create awareness and to encourage people come out of their ‘cocoons’ and seek counselling/treatment. Also, 2020 had been a worse year due to the corona virus (COVID-19) pandemic. People had been ‘locked up’ in their homes to prevent exposure to the nCoV-19. Though there is ongoing vaccination in 2021, still the number of cases are on the rise. It is very important to stay connected with family and friends specially in these difficult times and the stigma around mental illness should be eradicated. People should be encouraged to seek counselling or therapy during such difficult times.

However, more studies with larger case group are needed to establish the fact that low vitamin D levels can actually cause depression concretely.

### IV. SUMMARY AND CONCLUSION

In this study it was found that depression disorder shows a negative correlation with serum vitamin D level, indicating the intricate mechanism of deficiency of vitamin D and depression. The study being comprised of a small number of cases though a conclusive statement can’t be drawn, there is a scope for further research on the same. A vitamin D supplementation along with outdoor activities may benefit the depression patients. Thus it can be advised that people should add a pinch of sunshine in their daily routine to keep depression at bay.

### REFERENCES

Table 1: Comparison of laboratory parameters in between the groups.

<table>
<thead>
<tr>
<th>Parameters (mg/dl)</th>
<th>Cases (Mean ± SD)</th>
<th>Control (Mean ± SD)</th>
<th>Mann Whitney (U value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS</td>
<td>88.05 ± 12.14</td>
<td>94.67 ± 17.98</td>
<td>1123.0</td>
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<tr>
<td>Urea</td>
<td>23.89 ± 6.97</td>
<td>23.94 ± 6.39</td>
<td>494.0</td>
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<tr>
<td>Creatinine</td>
<td>0.86 ± 0.322</td>
<td>0.91± 0.164</td>
<td>432</td>
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</tbody>
</table>

*p value not significant

Table 2: Comparison of vitamin D levels in between the groups

<table>
<thead>
<tr>
<th>Parameters (ng/ml)</th>
<th>Cases (Mean ± SD)</th>
<th>Control (Mean ± SD)</th>
<th>Mann Whitney (U value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>16.88 ± 9.88</td>
<td>20.88 ± 9.46</td>
<td>1559.0</td>
</tr>
</tbody>
</table>

*p value < 0.05 (significant)

Figure 1: Correlation between Vitamin level and HAM-D scores

Table 3: Association of Vitamin D with depression

<table>
<thead>
<tr>
<th>Vitamin D level</th>
<th>Depression Absent (HAM D &lt; 7) N(%)</th>
<th>Depression present (HAM D ≥ 7) N(%)</th>
<th>Chi squared value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 ng/ml</td>
<td>33 (57.9)</td>
<td>24 (42.1)</td>
<td>3.852</td>
</tr>
<tr>
<td>≥20 ng/ml</td>
<td>17 (39.5)</td>
<td>26 (60.5)</td>
<td></td>
</tr>
</tbody>
</table>

*p value < 0.05 (significant)