e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(4); 742-746

Original Research Article

Interrelationship of Vitamin D and Cortisol with Depression: A Cross-Sectional Study Conducted in a Tertiary Care Hospital of Odisha

Sudeshna Ray[1], Manas Talukdar[2], Subhashree Ray[3], Rati Ranjan Sethy[4], Viyatprajna Acharya[5], Subrat Kumar Tripathy[6]

[1]Demonstrator, Department of Biochemistry, College of Medicine & Sagore Dutta Hospital, Kamarhati, Kolkata

[2]Assistant Professor, Department of Biochemistry, Shri Guru Ram Rai Institute of Medical & Health Sciences, Dehradun

[3]Professor & Head, Department of Biochemistry, IMS & SUM Hospital, Bhubaneswar

[4]Assistant Professor, Department of Psychiatry, SCB Medical College & Hospital, Cuttack

[5]Professor, Department of Biochemistry, Kalinga Institute of Medical Sciences, Bhubaneswar

[6]Professor, Department of Biochemistry, IMS & SUM Hospital, Bhubaneswar

Received: 25-01-2024 / Revised: 23-02-2024 / Accepted: 26-03-2024

Corresponding Author: Dr. Sudeshna Ray

Conflict of interest: Nil

Abstract:

Background: According to WHO, an estimated 3.8% of the population affected, including 5.0% among adults and 5.7% among adults older than 60 years. Approximately 280 million people in the world have depression. Numerous vitamin D receptors are present in the brain (neuroglia, prefrontal cortex, substantia nigra etc). Vitamin D helps in the transcriptional activation of serotonin (an important neurotransmitter influencing mood, sleep, appetite and other brain functions). Thus, low vitamin D levels can be related to depression.

Methodology: 50 diagnosed cases of depression and 50 age and gender matched controls were included in the study over a period of 1 1.5 years in IMS & SUM Hospital, Department of psychiatry OPD. Biochemical parameters were assayed in the Central laboratory, Department of Biochemistry.

Results: Serum Vitamin D was statistically significantly lower (p=0.033) in the case group with no significant alteration in the serum cortisol in both groups. Family history showed strong association with depression with p value = 0.019.

Conclusion: In this study, depression disorder showed a negative correlation with serum vitamin D level with non-significant alteration of serum cortisol level, indicating the involvement of vitamin D deficiency with depression.

Keywords: Depression, Vitamin D, sunshine, serotonin, role of vitamin D, cortisol, family history.

Introduction

Dr. Dan Chisholm, WHO's Department of Mental Health and Substance Abuse commented that "Depression is the single largest contributor to years lived with disability. So, it's the top cause of disability in the world today." [1]. Depression is emerging as a major health problem worldwide including India.

Mmore than 4 percent of the world's population are living with depression, and women, youth and the elderly are the most prone to its disabling effects, according to World Health Organization (WHO), [1]. Mental health conditions were exacerbated during the COVID 19 pandemic. Depressive symptoms grew from about 193 million people worldwide to 246 million, which is about 28%. Those aged 18-29 have the highest prevalence of depression at 30.6%.[2] Vitamin D plays a role in a wide range of ailments such as osteoporosis, cancer, cardiovascular diseases, and diabetes[3]. Recently, a role for vitamin D in cognitive function and mental health has been reported [4]. Many studies have shown a link between patients suffering from depression and low serum vitamin D levels.

Numerous vitamin D receptors are located in the brain (neuroglia, prefrontal cortex, substantia nigra etc) [5]. Vitamin D plays a crucial role in the transcriptional activation of serotonin. Vitamin D activates the enzyme tryptophan hydroxylase which converts tryptophan to serotonin. Vitamin D hormone (calcitriol) activates the transcription of the serotonin-synthesizing gene tryptophan hydroxylase 2 (TPH2) in the brain at a Vitamin D Response Element (VDRE) [6]. Serotonin plays a

significant role as a neurotransmitter influencing mood, sleep, appetite and other brain functions. Thus, low vitamin D levels can lead to low serotonin levels resulting in depression. There are also several studies showing that patients suffering from depression have high serum cortisol levels.

During stress, the hypothalamus stimulates the pituitary gland to secrete Adreno-corticotropic Hormone (ACTH) which in turn stimulates the adrenal gland to release cortisol. This can explain that depression is related to stressful conditions. Some animal studies have found that high cortisol levels interfere with transport of vitamin D in intestinal mucosa. Light therapy has been shown to improve the depression in adjunction with antidepressants, which may be in part due to improved vitamin D synthesis associated with light therapy [7] .

Very few studies have been conducted in India linking depression with Vitamin D and cortisol. Hence, this study has been undertaken to establish any relationship among vitamin D, depression and cortisol, if present.

Materials and methods

The study was conducted in IMS & SUM Hospital (IMS & SH), Bhubaneswar over a period of 2 years. 50 cases of newly or old diagnosed depression (diagnosed by ICD-10 criteria) between the age of 18-60 years were selected from the OPD of Dept of Psychiatry, IMS & SH. 50 age and gender matched apparently healthy controls(who came for routine check-up/ hospital staffs) were selected for this study. Pregnant women, those taking Vitamin D supplementation. Or having Diabetes Mellitus (DM) or hypertension was excluded from the study.

Study Design: Cross Sectional case-control study.

Venous blood (5 mL) was collected from the subjects under sterile conditions. Apart from Vitamin D and cortisol, Fasting Blood Sugar (FBS), urea and creatinine were also analyzed. Blood sample was collected in fluoride vial for FBS after overnight fasting and in plain vials for Vitamin D, Cortisol, urea and creatinine. The samples were stored in 2-8 °c and the analysis was done in Central Laboratory, Dept of Biochemistry, IMS & SH, Bhubaneswar, and Odisha. After selection of cases and controls, a thorough clinical examination was done to rule out the exclusion criteria. The analysis of Vitamin D and cortisol were done in Autoanalyser-Cobas e411 using Electrochemiluminescence Immunoassay (ECLIA), FBS, urea and creatinine was done using Autoanalyser Cobas Integra 400. Patients were selected as per the proforma with detailed history.

A detailed clinical examination (monitoring of pulse, Blood Pressure and Body Mass Index) were done and family history along with treatment history were taken into account.

The Hamilton Depression Rating Scale (HAM-D) [8] was used in determining the patients' level of depression. Although the HAM-D form lists a total of 21 items, the scoring is based on the first 17 items.

- 0-7 = Normal
- 08-13 = Mild Depression
- 14-18 = Moderate Depression
- 19-22 = Severe Depression
- ≥ 23 = Very Severe Depression
- Statistical analysis was done using SPSS version 20.0.

Written consent was taken from the study subjects (cases and controls). The option of opting out of the study was kept open without any clause. The data collected is strictly confidential. Ethical clearance was obtained for the study.

Results and Discussions

Total 100 subjects were included in this study of which 50 were cases of depression and 50 were apparently healthy individuals taken as controls. The comparison of age and gender between two groups did not show any statistical significance. However, there was a higher preponderance of females in the case group.

There was also no statistical significance of BMI, Systolic and Diastolic Blood pressure and pulse rate between the two groups. In the laboratory parameters, the FBS, urea and creatinine levels were not statistically significant.

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 1 shows the comparison of vitamin D level in both the groups.

Table 1: Comparison of vitamin D levels in between the cases and controls

Parameters	Cases (Mean ± SD)	Control (Mean ± SD)	Mann Whitney U value	P value*
Vitamin D	16.88 ± 9.88	20.88 ± 9.46	1559.0	**0.033**

*Mann-Whitney U test was used. Cortisol level was higher in control group (10.67 ± 3.44) as compared to the mean cortisol level in cases group (10.34 ± 2.96). Although, this difference was not statistically significant (p value= 0.811). Table 2 shows the comparison of cortisol level in both the groups.

Table 2: Comparison of cortisol levels in between the groups

Parameters	Cases (Mean ± SD)	Control (Mean ± SD)	t-value	P value*
Cortisol level	10.34 ± 2.96	10.67 ± 3.44	-0.242	0.811

Figure 1 shows the correlation between the HAM-D score and vitamin D level. 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).

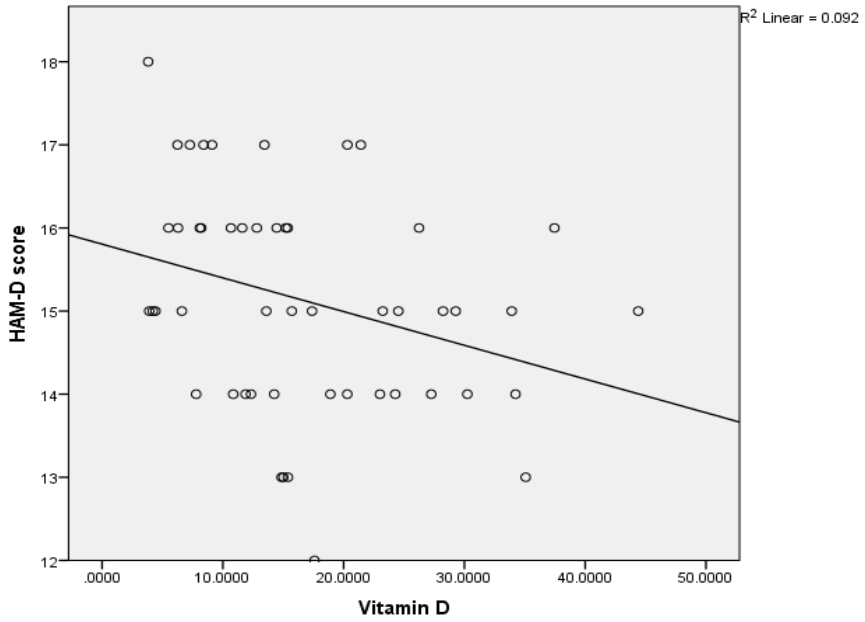

Figure 1: Correlation between Vitamin level and HAM-D scores

Table 3 shows the correlation between Vitamin D and cortisol levels in cases and control group respectively. In cases group, there was a positive correlation between Vitamin D & cortisol with correlation coefficient (r) 0.104 but this correlation was not statistically significant (p value= 0.734). In the control group, a negative correlation between Vitamin D & cortisol was found with correlation coefficient (r) - 0.009 and this correlation was also not statistically significant (p value= 0.980).

Table 3: Correlation between Vitamin D with Cortisol level in cases and control groups

Statistical parameters	Cases	Control
Vitamin D vs cortisol Correlation coefficient (r)	0.104	- 0.009
P value	0.734	0.980

Table 4 shows the association of family history with depression. On applying Chi-square test it was found that family history was strongly associated with depression. Chi –square value is 5.482 and the significant p value is 0.019.

Table 4: Association of family history with depression

Family History	Depression Absent (HAM D < 7) N (%)	Depression present (HAM D ≥ 7) N (%)	Chi squared value	P value
Present	7 (29.2)	17 (70.8)	5.482	**0.019**
Absent	43 (56.6)	33 (43.4)		

Table 5 shows the association of vitamin D with depression. On applying Chi-square test, it was found that vitamin D was strongly associated with depression. Chi –square value is 3.852 and the significant p value is 0.0041.

Table 5: Association of Vitamin D with depression

Vitamin D level	Depression Absent (HAM D < 7) N (%)	Depression present (HAM D ≥ 7) N (%)	Chi squared value	P value
< 20 ng	33 (57.9)	24 (42.1)	3.852	**0.041**
≥20 ng	17 (39.5)	26 (60.5)		

Table 6 shows the association of cortisol with depression. In this study, the association was not statistically significant.

Table 6: Association of Cortisol with depression

Cortisol level	Depression Absent (HAM D < 7) N (%)	Depression present (HAM D ≥ 7) N (%)	Chi squared value	P value
< 20 mcg	3 (60.0)	2 (40.0)	0.0312	0.859
≥ 20 mcg	10 (55.5)	8 (44.5)		

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 1) In a study by Eskandari et al [9], which had premenopausal women with depression as study subjects, the difference between mean vitamin D levels between cases and healthy controls was clinically significant.

This finding is in concordance with the present study.

A study by Minhtu et al [10,11] examined the association of low vitamin D level and depression in a large sample with a higher mean age. The results demonstrated that individuals with higher vitamin D levels were at lower risk for depressive symptoms and that lower vitamin D levels were associated with depressive symptoms, particularly among individuals with a history of depression.

Inadequate exposure to sunlight and diminished outdoor activity could lead to low vitamin D levels and depression in the cases. As vitamin D is responsible for the transcriptional activation of serotonin which is a neurotransmitter affecting sleep, appetite and mood, vitamin D deficiency can cause low serotonin levels which can ultimately lead to depression.

However, more studies are required to establish the fact that low vitamin D levels can actually cause depression concretely.

In the present study, Cortisol level was higher in control group (10.67 ± 3.44) as compared to the mean cortisol level in cases group (10.34 ± 2.96). The difference was not statistically significant. (Table 2) In a meta-analysis carried by Burke et al [12], they included seven studies. They found that there was no significant effect of depression on baseline cortisol levels. Since cortisol levels are typically highest in the morning and lowest in the afternoon, we reasoned that the time of day of each study might be a significant source of this variability.

In the present study, the serum cortisol was measured around noon time when they visited the OPD. The findings of Strickland et al [13,14] suggest that some patients (those reporting recent severe life events) with depression do hypersecrete cortisol. However elevated cortisol levels after life events are not necessarily associated with development of depression [14].

People suffering from depression exhibit abnormal brain 5-Hydroxytryptamine (serotonin) function. Decreased tryptophan availability is one possibility. Increased cortisol secretion increases tryptophan 2,3 dioxygenase, the main metabolizing enzyme of tryptophan. Elevated cortisol levels can therefore explain lowered tryptophan levels in patients with recent life event [14]. As serotonin is formed from tryptophan, lower levels of serotonin may lead to depression. However, more studies with a larger population is required to understand the reason clearly.

In the present study, 34% of the cases had family history. Strong association was found between family history and depression in my study subjects (p=0.019) (Table 6). Family history is a very important and crucial aspect of history taking in mental illness.

In a previous study, researchers interviewed a longitudinal retrospective cohort study sample of 251 grandchildren. Biological children of parents with depression had significantly higher risk for major depressive disorder [15].

The increased risk of psychiatric disorders in the offspring of depressed parents is well known. Whether this risk is transmitted beyond two generations is lesser known. This information is important for detecting individuals who may benefit from early intervention and may be candidates for biological marker studies [15].

If someone has a parent or sibling with major depression, that person probably has a 2 or 3 times greater risk of developing depression compared with the average person (or around 20-30% instead of 10%).

The situation is a little different if the parent or sibling has had depression more than once ("recurrent depression"), and if the depression started relatively early in life (childhood, teens or twenties). This form of depression is less common, it is probably around 3-5%. But the siblings and children of people with this form of depression probably develop it at a rate that is 4 or 5 times greater than the average person [16]. People with a first-degree family member who has experienced depression are 2.8 – 10 times more likely to develop depression. [17]

However, the positive family history participants with recent major life stress may not as yet be sufficiently sensitized to become depressed with the relative absence of major stress (i.e., they still

require major stress to trigger an episode) [18,19]. The world recently experienced a devastating pandemic having diverse effects on the mental health. People need to be more aware of the mental health problems associated with pandemic conditions and need to seek help for betterment of life.

Thus, we can say that family history can be a strong risk factor for depression. Further studies are required to validate the findings of the present study.

Summary and Conclusion

Depression disorder showed a negative correlation with serum vitamin D level in this study. Also there was a non-significant alteration of serum cortisol level. This might indicate the involved mechanism of vitamin D deficiency and depression. As the study comprised of a small number of case population, a conclusive statement could not be drawn, there is a definite scope for further research on the same involving larger study population and longer time frame. A vitamin D supplementation might be beneficial for the patients suffering from depression.

Limitations of the study

The study was conducted in a small study group, also the duration of the study could have been longer.

References

1. Depression and other common mental disorders: Global health estimates, Geneva: WHO; 2017. Available from: https://apps.who.int/iris/handle/10665/254610
2. Mental health statistics. Forbes Health; September 4, 2023. Available from : https:// https://www.forbes.com/health/mind/mental-health-statistics/
3. Holick M: Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr 2004, 80(Suppl 6):1678-1688.
4. Oudshoorn C, Mattace-Raso FU, van der Velde N, Colin EM, van der Cammen TJ: Higher serum vitamin D3 levels are associated with better cognitive test performance in patients with Alzheimer's disease. Dement Geriatr Cogn Disord 2008, 25:539-543.
5. Eyles D, Brown J, Mackay-Sim A, McGrath J, Feron F. Vitamin D_3 and brain development. Neuroscience. 2003; 118:641–653.
6. Patrick RP, Ames BN. Vitamin D hormone regulates serotonin synthesis. Part 1: Relevance for autism. FASEB Journal. 2014; 28(6):2398–413.
7. Martiny K, Lunde M, Unden M, Dam H, Bech P: Adjunctive bright light innon-seasonal major depression: results from clinician-rated depression scales. Acta Psychiatr Scand 2005; 112:117-125.
8. Gloth FM, Alam W, Hollis B. Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder. Journal of Nutrition, Health, & Aging. 1999; 3(1):5–7.
9. Eskandari F, Martinez PE, Torvik S, Phillips TM, Sternberg EM, Mistry S, et al. Low bone mass in premenopausal women with depression. Arch Intern Med 2007; 167: 2329–36.
10. Lapid, M.I., Cha, S.S., Takahashi, P.Y., 2013 a. Vitamin D and depression in geriatric primary carepatients. Clin. Interv. Aging 8, 509–514.
11. Kwasky AN, Groh CJ. Vitamin D, Depression and Coping Self-Efficacy in Young Women: Longitudinal Study. Archives of Psychiatric Nursing [Internet]. Elsevier Inc.; 2014; 28(6):362–7.
12. Burke HM, Davis MC, Otte C, Mohr DC. Depression and cortisol responses to psychological stress: A meta-analysis. Psycho neuroendocrinology. 2005; 30(9):846–56.
13. Penckofer S, Kouba J, Byrn M, Ferrans CE. Vitamin D and Depression: Where is all the Sunshine? Issues Ment Health Nurs. 2010 Jun; 31(6): 385–393.
14. Cowen PJ. Cortisol, serotonin and depression: All stressed out? British Journal of Psychiatry. 2002; 180(FEB.): 99–100.
15. Weissman MM, et al. JAMA Psychiatry. 2016; doi:10.1001/ Jama psychiatry. 2016. 1586. Family history of depression doubles risk for depression
16. Major depression and Genetics. Stanford: Stanford Medicine. Available from: http:// depressiongenet-ics.stanford.edu/mddandgenes.html
17. Wallace J, Schneider T, McGuffin P. Genetics of depression. In: Gotlib IH, Hammen CL, editors. Handbook of depression. New York: The Guilford Press; 2002; 169–191.
18. Monroe SM, Harkness KL. Life stress, the 'Kindling' Hypothesis, and the recurrence of depression: Considerations from a life stress perspective. Psychological Review.2005; 112: 417–445.
19. Monroe SM, Slavich GM, Gotlib IH. Life Stress and Family History for Depression: The Moderating Role of Past Depressive Episodes.