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Study of Serum Vitamin D Level and its Relationship with Depression in Patients Visiting the Department of Psychiatry and Mental Health of Tertiary Care Hospital, Nepal: A Case-Control Study

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Abstract

***Background & Aims*:** An estimated 350 million individuals worldwide suffer from depression, making it a widespread ailment. The mapping of vitamin D receptors in the brain suggests that vitamin D plays a function in psychosomatic illnesses like depression. Limited information exists on vitamin D status and depression in the Nepalese population. The present study aimed to determine the level of vitamin D in patients with depression and compare it with normal individuals. Similarly, it aimed to find out how the level of vitamin D varies with the severity of depression.

Materials & Methods: The case-control study was conducted at Tribhuvan University Teaching Hospital (TUTH), in Kathmandu, Nepal. In this study, 85 depressive patients and 85 age-sex-matched healthy controls were enrolled. Vitamin D was assessed in the Department of Biochemistry with the Electro-Chemiluminescent Immune Assay (E-CLIA) method. The data were entered into the Microsoft Excel program. Statistical analyses were performed with SPSS software 17.0 version. The mean comparison, group association, and correlation were determined by using t-test, Chi-square test, and Pearson's correlation, respectively. A probability of < 0.05 was accepted as significant.

Results: The level of vitamin D in patients with depression was found to be significantly lower than that in healthy controls. Likewise, the level of vitamin D was found to vary with the severity of depression; with severe depression, the level of vitamin D was the lowest and the result was found to be statistically significant ($P < 0.05$). Similarly, the level of vitamin D was found to be significantly lower in subjects having suicidal tendencies ($P < 0.05$).

Conclusion: The cause-and-effect link between depression and vitamin D deficiency is unclear, but their coexistence in the Nepalese community raises public health concerns. Recognizing those at risk and taking early action is crucial, as severe depression is a potential risk factor for suicidal thoughts.

***Keywords*:** Case-Control Study, Depression, Suicidal Tendencies, Nepal, Vitamin D

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Introduction

Depression is a common psychiatric disorder that is characterized by sadness, loss of interest, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. It is a major cause of morbidity worldwide (1-4). Globally, 350 million individuals are thought to be affected by depression, which is a widespread ailment (5). Long-term or recurrent depression can significantly affect a person's capacity to perform at work or school or cope with day-to-day activities. Suicide can result from depression at its worst. People with mild depression can be cured without medication, while those with moderate or severe depression may require both medication and professional treatment (6, 7). Its effects on daily life and well-being have been compared to those of long-term illnesses like diabetes (5, 8, 9). Exactly what causes depression is still unknown, but a huge number of risk variables have been found. Individuals are at a higher risk if they are female, have a family history of alcoholism or depression, experienced trauma as children, or are going through tough life circumstances (10-13). Biological evidence suggests that differences in brain structure, changes in hormone production, and malfunctions of the biological feedback mechanisms that regulate neurotransmitter activity are involved in the development of depression (14, 15).

Apart from these triggering factors of depression, recent studies have shown some relation between vitamin D and depression (16). The active form of vitamin D, calcitriol, is a secosteroid with potent endocrine, paracrine, and autocrine effects (17, 18). Like other hormones with nuclear receptors, it affects the gene expression of a multitude of target genes that are involved in calcium and phosphorus balance (19, 20). The role of calcitriol extends beyond this with the involvement in Central Nervous System (CNS) function (21, 22). It has been shown that it activates the expression of the tyrosine hydroxylase gene, a key enzyme in the synthesis of catechol amines, particularly dopamine (23). It may enhance cholinergic function, both by increasing the activity of choline acetyltransferase and by decreasing the activity of acetylcholine esterase (24). Dopamine, noradrenaline, and acetylcholine are well-known actors in the pathophysiology of mood disorders and attention deficit (25-27).

The presence of the vitamin D Receptor (VDR) in the CNS was discovered in 1982 (28, 29). VDR has been identified in multiple areas of the human brain, such as the prefrontal cortex, hippocampus, cingulated gyrus, thalamus, hypothalamus, and substantia nigra, some of which have been implicated in the pathophysiology of depression (15, 30). Similarly, calcitriol is a potent enhancer of Nerve Growth Factor (NGF) and Glial-Derived Neurotrophic Factor (GDNF) (31-33). It increases neurotrophin-3 (NT-3) and decreases neurotrophin-4 (NT-4) activity (34). Recent research has shown that NGF, NT-3, and GDNF may also be involved in both depression and schizophrenia, which underscores the role of vitamin D in depression (35-39).

To our knowledge, there are limited reports regarding the level of vitamin D in patients with depression in the Nepalese population. The present study aimed to determine the level of vitamin D in patients with depression and to compare it with that of a normal individual. Similarly, this study aimed to find out how the level of vitamin D varies with the severity of depression.

Material & Methods

This is a hospital-based analytical case-control study conducted at the Department of Biochemistry and Department of Psychiatry and Mental Health, Institute of Medicine (IOM), TUTH, Kathmandu, Nepal. In total, 85 patients with depressive illness visiting the Department of Psychiatry and Mental Health were included in the study. In accordance with National Ethical Guidelines for Health Research (NHRC) in Nepal, the study was approved by the Institutional Review Board (IRB), IOM, TUTH with reference number $22(6\text{-}11\text{-}E)^2/070/071$. Informed and written consent was obtained from all the patients. An equal number of age -and sex-matched healthy

individuals without having any acute or chronic illnesses were used as control.

Depression was diagnosed using the International Classification of Disease-10- Diagnostic Criteria for Research (ICD-10 DCR) guidelines by a Consultant Psychiatrist. The level of depression among the patients and the presence of any suicidal tendencies were found using ICD-10 DCR and American Psychiatric Association (APA) guidelines by attending Consultant Psychiatrist. Venous blood was drawn after overnight fasting. Serum samples were separated, within half an hour of blood collection. Serum vitamin D was measured on the same day of sample collection at the Department of Biochemistry with the E-CLIA method. The remaining sample was stored at -20°C. Laboratory standard operating procedures were maintained for all laboratory analyses. Internal quality control sera, both normal and pathological, were also run for each lot, for the validation of the results. The data were entered into the Microsoft Excel program. Statistical analyses were done by SPSS 17.0 version. The mean comparison was done by t-test, group association was determined using the Chi-square test, and the correlation was determined by Pearson's correlation.

Results

In total, 170 individuals were enrolled in this study. Among them, 85 were individuals with depression (cases) as shown in Figure 1 (A), and 85 were age-sex-matched healthy control. About 40 (47%) of the cases were male, and the remaining 45 (53%) were female. The mean age of depression in males was 43.65 years, while that of females was 35.91 years.

The depression status of 85 cases is shown in Figure 1 (B). Out of 85 cases, 16 (19%) cases had mild depression where 6 (7%) were male, and 10 (12%) were female, 56 (66%) of cases had moderate depression where 26 (31%) were male, and 30 (35%) were female, and the remaining 13 (15%) subjects had severe depression where 8 (9%) were male, and 5 (6%) were female. However, we found a higher prevalence of mild and moderate depression among the female compared to the male.

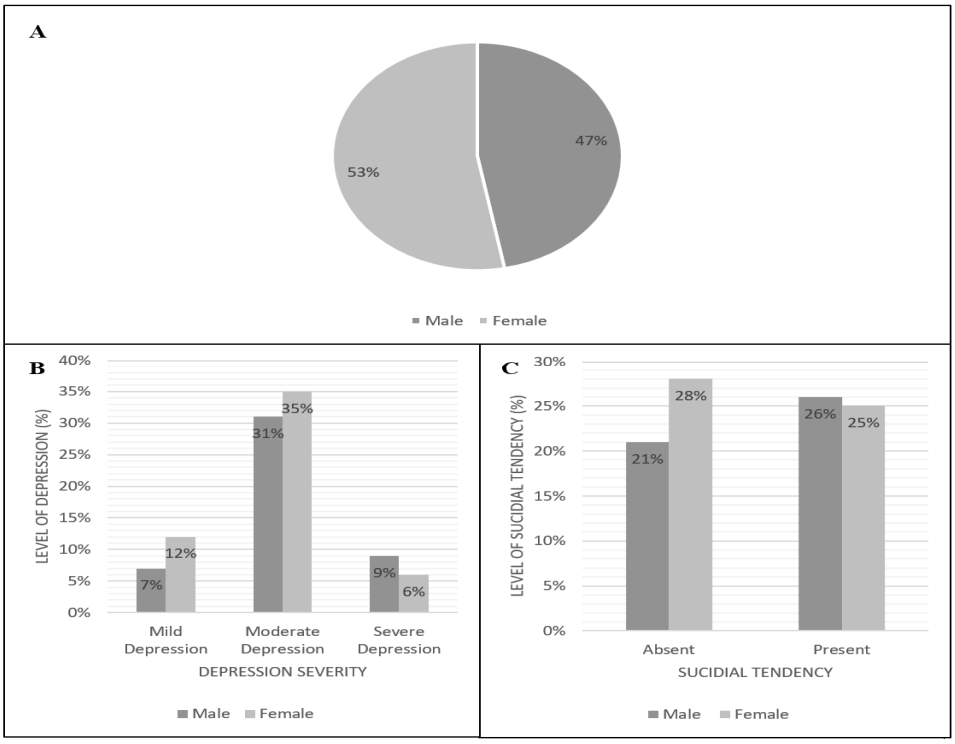

Fig. 1. A) Demographic characteristics of cases. B) Depression status in cases. C) Suicidal tendency in cases.

Suicidal tendencies of 85 cases are shown in Figure 1 (C). Out of 85 cases, 43 (51%) of cases showed the presence of suicide behavior, among them 22 (26%) were male and 21 (25%) were female. Absence of suicide behavior was seen in 42 (49%) of cases, among them 18 (21%) were male and 24 (28%) were female.

As shown in Table 1, the vitamin D level of cases was compared to that of the control group. The mean level in the cases was found to be significantly lower than that of the control group. It was 18.50 ng/ml ± 7.14 vs 25.8 ng/ml ± 7.59 in cases and control, respectively. The reference range of vitamin D was 30-100ng/ml. The result was found to be statistically significant with a P-value of < 0.05.

Table 1. Vitamin D level in cases and control group.

	Case (n = 85)	Control group (n = 85)	P-value
Vitamin D	18.5 ng/ml ± 7.14	25.8 ng/ml ± 7.59	< 0.05

Similarly, in Table 2, the level of vitamin D in cases with the presence of suicidal tendencies was found to be significantly lower as compared to those without suicidal tendencies. It was 13.6 ng/ml ± 4.0 vs 23.52 ng/ml ± 6.0, respectively. The result was statistically significant with a P-value of < 0.05.

Table 2. Vitamin D level and suicidal tendencies in cases.

	In suicidal tendency	Without suicidal tendency	P-value
Vitamin D	13.6 ng/ml ± 4.0	23.52 ng/ml ± 6.0	< 0.05

Likewise, in Table 3, cases with severe depression were found to have the lowest vitamin D level as compared to those with moderate and mild depression. It was 11.79 ng/ml ± 2.97, 18.56 ng/ml ± 7.19, and 23.75 ng/ml ± 4.51 in cases with severe, moderate, and mild depression, respectively. The result was found to be statistically significant with a P-value of < 0.05.

Table 3. Vitamin D level and depression severity.

	Mild Depression	Moderate Depression	Severe Depression	P-value
Vitamin D	23.75 ng/ml ± 4.51	18.56 ng/ml ± 7.19	11.79 ng/ml ± 2.97	< 0.05

Discussion

This small-scale study was conducted to compare the level of vitamin D in patients with depression to that of healthy controls. Our study found that the level of vitamin D was significantly lower in patients with depression as compared to healthy controls. Likewise, the level of vitamin D in patients with severe depression was lowest compared to those with moderate and mild depression, respectively. Our study found that in spite of being healthy and not having any diseases, the level of vitamin D in the control population was sub-optimal. In our view, the sub-optimal level of vitamin D in the control group could be due to their lower socioeconomic status which caused undernourishment. Similarly, Nepalese people are less likely to seek and are less aware of nutritional supplementation which ultimately leads to vitamin D insufficiency, and the skin pigment is probably a major factor in the very low vitamin D levels seen in the Indian subcontinent, despite abundant sunshine (40-42). Due to the paucity of information, the exact prevalence of vitamin D insufficiency in the Nepalese population could not be obtained. However, studies suggest a higher prevalence of vitamin D deficiency and insufficiency in South Asia, including the Nepalese population (43-46).

As stated above, the level of vitamin D in depression cases was found to be significantly lower compared to the control group, and the level of vitamin D decreased with the severity of depression. Several

studies from abroad have similar results, such as those by Gangi et al. (47), Maria et al. (48), Stewart et al. (49), and Khattri et al. (50).

In our study, we found a significantly higher prevalence of mild and moderate depression among females compared to men. This was in agreement with a study conducted by Sherchand et al. (46) in Nepal where moderate depression was seen to be more common among working women than working men.

Similarly, this study found that vitamin D level is lower in subjects with suicidal tendency than those without suicidal tendencies, which shows an agreement with a study conducted by Tariq et al. which showed the association of vitamin D deficiency with multiple suicide risk factors (51). Another study conducted by Grudet et al. (52) also concluded that suicide attempters in the study were deficient in vitamin D (52). This also suggests that vitamin D deficiency could be a contributing factor to the elevated pro-inflammatory cytokines previously reported in suicidal patients.

Although, it is not clearly understood how vitamin D plays a role in mental health, but some theories have been forwarded that support the role of vitamin D in neuroprotective effects. Studies have demonstrated that vitamin D can act on cells of the nervous system by modulating the production of neurotrophins which is correlated with neuroprotective effects (53, 54). Likewise, vitamin D could mediate its neuroprotective effects via modulation of neuronal calcium ion (Ca^{2+}) homeostasis (55). Vitamin D has also been reported to inhibit the synthesis of Inducible Nitric Oxide Synthase (iNOS), enzyme induced in CNS neurons and non-neuronal cells during various insults or diseases, such as ischemia, Alzheimer's disease, Parkinson's disease, etc. (56, 57). Similarly studies have shown that vitamin D is involved in brain development, and its deficiency results in altered morphology and behavior in adulthood (58, 59). Moreover, it has been shown that vitamin D regulates the gene expression of tyrosine hydroxylase which is an essential enzyme involved in the synthesis of norepinephrine and dopamine (60). Both neurotransmitters are involved in mood regulation and depression. On the other hand, vitamin D regulates calcium homeostasis, membrane permeability, and axonal conduction; it is thought to have an indirect role in the regulation of neurotransmission. All of these can be the reason for the risk of the development of depression in patients with low vitamin D levels (61, 62).

Conclusion

The likelihood of having depression in vitamin D-deficient persons is significantly higher. Due to the case-control nature of this study, the results should not be viewed in terms of cause-and-effect relationships. It is not known whether vitamin D deficiency leads to depression or depression leads to vitamin D deficiency. Although the direction of the cause-and-effect relationship between depression and vitamin D deficiency is not known clearly at this time, from a public health perspective, the coexistence of vitamin D and depression in the Nepalese population at large is a concern. It is important to identify persons who are at risk for vitamin D deficiency and/or depression and to intervene early because these two conditions have enormous negative consequences on long-term health. Cases with suicidal tendencies were mostly with severe depression. Severe depression is a potential risk factor for suicidal tendencies. More studies describing the relation between low vitamin D levels and suicidal tendencies could not be obtained. So that it might be a topic of interest for further study.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Data Availability

The raw data supporting the conclusions of this article are available from the authors upon reasonable request.

Ethical statement

In accordance with National Ethical Guidelines for Health Research (NHRC) in Nepal, the study was approved by the Institutional Review Board (IRB), IOM, TUTH with reference number 22(6-11-E)2/070/071. Informed and written consent was obtained from all the patients.

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