Assessment of Vitamin D level in Depression and its association with severity of depression

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Abstract

Background

Depression is a mental health condition which in severe conditions may lead to suicide and increase risk of mortality. Some biological markers have been identified as reliable indicators of depression. The aim of this study was to assess the level of depression in treatment naïve patients and compare the level of Vitamin D among treatment naïve cases of depression.

Methods

The study was a cross-sectional single hospital-based study conducted in treatment naïve patients diagnosed as depression by consultant psychiatrist as per ICD-10 in inpatient and outpatient department of Psychiatry, Patan Academy of Health Sciences, Lagankhel, from March 2021 to March 2022. 55 samples (treatment naïve cases of depression) were selected purposively. Information on age and gender were collected in the proforma and Serum Vitamin D level was also measured. Descriptive and inferential analysis was done using EZR software. Frequency, percentage, Fisher test and Kruskal Wallis test were used in the analyses.

Results

40% of the patients had moderate depression, 32.7% had mild depression and 27.3% had severe depression. 58.2% had optimal serum Vitamin D level, 25.4% had insufficient and 16.4% had deficient Vitamin D level. A significant association ($p<0.001$) was identified between severity of depression and Vitamin D level category. A significant difference ($p<0.01$) in the median serum Vitamin D level among all the categories of the severity of depression was also identified.

Conclusion

Serum Vitamin D level is different in different severity of depression with low level of Vitamin D significantly associated with severity of depression.

Keywords

cross-sectional, depression, ICD-10, Nepal, serum Vitamin D level, treatment naïve

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INTRODUCTION

Depression is a mental health condition which in its severe form can lead to suicide and increased risk of mortality. Depression, with an estimated 3.8% of affected population (280 million), is a common illness worldwide.[1] In Nepal, Major Depressive Disorder (MDD) is common among both adults and children (for 13 to 17 years: current 0.7% and past 1.8%; for 18 years and above: current 3.4% and past 4.4%).[2]

Besides the diagnostic criteria for depression, many tool, inventory and scale have been developed to assess depression in an individual. Some of these tools are used to assess depression across lifespan[3,4,5,6,7,8] some among children and adolescents[9,10,11,12] some among older adults[13,14] and others among general adult population.[15,16,17,18,19,20,21] The biological markers related to metabolism, neuroendocrine, neurotransmission, inflammatory process, kynurenine pathway, oxidative stress have been reliable indicator of depression..[22] Vitamin D a fat soluble vitamin primarily obtained from sunlight and has been long recognized for its role in abone health. Substantial observational and animal experimental studies over past decade have confirmed a broader role of Vitamin D in health and disease, including mental health given its involvement in brain functions, mood regulation and inflammatory process.[23,24] Literature, primarily from Western nations, has shown a negative association between Vitamin D deficiency and severity of depression, direction of causality remains unclear. However, the evidence is variable. Some suggest that depression may lead to lower Vitamin D levels due to

decreased outdoor activity, while others propose that Vitamin D deficiency itself may contribute to onset or severity of depression.[28] Vitamin D deficiency was significantly associated with increased odds of clinically significant depression in a study in Nepal, however the confounding variables were not addressed..[25] There are studies that favor and do not favor supplementation of Vitamin D to manage depression.[26,27] Some studies, however, have highlighted the importance of using Vitamin D level as objective screening tool to identify people at risk of depression.[28,29]. This study aims to check whether these findings will be replicated in a different hospital setting or not.

Still there are significant gaps in understanding the relationship between Vitamin D and depression. Most studies focus on medicated patients or those with comorbidities, complicating the interpretation of findings[29]. This study targets treatment-naïve patients offering a clearer view of the potential role of Vitamin D, free from the influence of medication. The study uses objective laboratory measures of serum Vitamin D avoiding the confounding factors present in previous studies. The objective of the study was to assess the level of vitamin D in depression and assess association between serum Vitamin D level and severity of depression in treatment naïve patients.

METHOD

The study was a cross-sectional single hospital-based study conducted in treatment naïve patients diagnosed as depression by consultant psychiatrist as per ICD-10 in the inpatient department (IPD) and outpatient department (OPD) of Psychiatry, Patan Hospital, Patan Academy of Health Sciences (PAHS), Lagankhel, Nepal from March 2021 to March 2022. Treatment naïve patient of any sex with age greater than or equal to 18 years, willing to perform Vitamin D level examination, able to converse and read in Nepali and willing to participate in the study were included in the study and were well informed about the nature and objectives of the study. Informed consent was obtained before participation. Participation was voluntary and patients had right to withdraw at any time without giving justification. Importantly, treatment was not affected by their decision to participate or withdraw. Patients with established Bipolar Depression and other comorbid psychiatric illness, uncooperative patients, patients with known cases of Vitamin D deficiency or with co-morbid illness affecting calcium level, chronic liver/ kidney disease, eating disorders and current use of oral corticosteroids, anticonvulsants, and bisphosphonates were excluded from the study. Approval for the study was obtained from the Institutional Review Committee (IRC) of Patan Academy of Health Sciences (PAHS) [Ref: PMS2103301511].

The sample size for the study after taking the prevalence of depression in Nepal i.e. 3.4%,8 as the prevalence (p), margin of error as 5%, and Z as 1.96, in the formula Minimum Sample Size= Z2 x p (1-p) / (0.05)2, the minimum sample size was calculated to be 51 cases. 55 samples (treatment naïve cases of depression) were selected purposively.

Information on age and gender of the patients were collected in the proforma by the investigator. The ICD-10 Classification of Mental and Behavioral Disorders was used to diagnose and classify depression category (Mild, Moderate and Severe). Hamilton rating scale for Depression (HAM-D), a clinician rated 21 items scale with good reliability (0.82 to 0.98) and validity,30 and Beck's Depression Inventory (BDI), a client rated 21 self-report items scale were also used for assessment of depression severity. Vitamin D level was sent at the same assessment (1stvisit) as a routine test in all newly diagnosed depression cases at the hospital and the reports were collected in follow up (2nd visit) for outpatients. In inpatients, HAM-D and BDI was applied at the time of admission and Vitamin D was sent at the same time i.e., at the 1st visit/time of admission before starting medication. A serum Vitamin D level of 30 ng/ml and above was considered normal, 21- 29 ng/ml as insufficient, and less than or equal to 20 ng/ml as deficient.

The ethical considerations like voluntary participation, informed consent, anonymity, and non- maleficence were maintained throughout the study. Names were not recorded and obtained records were kept within the department locker and all the electronic copy of the information were kept in the department's computer that was password protected. Data entry was done in Epi-Info 7 and imported to MS Excel for cleaning. The cleaned file was then imported to the EZR software for further analysis. Frequency and percentage of each categorical variable was calculated, and two-way tables developed between two categorical variables. Fisher exact tests were used to identify association among depression and Vitamin D level category and Kruskal Wallis test with Steel Dwass post-hoc

test was used to test difference in median serum Vitamin D level among patients with different depression category.

RESULT

A total of fifty-five patients with treatment-naïve depression diagnosed through ICD-10 with 56.4% females and 43.6% males. The Mean ± SD age of the patients was 36.1±16.3 years and the Mean ± SD Serum Vitamin D level of the patients was 34.1±15.1 ng/ml. Most of the patients (40%) belonged to the twenty-one to thirty years age group category. Two-fifth of the patients (40%) had moderate depression, followed by mild depression (32.7%) and severe depression (27.3%). More than half of the patients (58.2%) had optimal serum Vitamin D level, followed by insufficient (25.4%) and deficient (16.4%) levels.

The study revealed that males (70.8%) had optimal Vitamin D level than females, whereas females (25.8%) had deficient Vitamin D level than males (4.2%) (Table 1). Optimal level of Vitamin D was high (83.3%) among patients of age group 18-20 years and deficient level of Vitamin D was high (50.0%) among patients above 70 years of age (Table 2). All the patients with mild depression had optimal vitamin D level while 60.0% of patients with severe depression had deficient Vitamin D level (Table 3).

Table1: Sex and Vitamin D level Category among treatment naïve patients with depression

Sex	Vitamin D category			
	Optimal (%)	Insufficient (%)	Deficient (%)	Total (%)
Female	15(48.4%)	8(25.8%)	8(25.8%)	31(100.0%)
Male	17(70.8%)	6(25.0%)	1(4.2%)	24(100.0%)

Table2: Age group and Vitamin D level Category among treatment naïve patients with depression

Age group	Vitamin D category			
	Optimal (%)	Insufficient (%)	Deficient (%)	Total (%)
18-20years	5(83.3%)	1(16.7%)	0(0.0%)	6(100.0%)
21-30years	12(54.5%)	5(22.7%)	5(22.7%)	22(100.0%)
31-40years	7(70.0%)	3(30.0%)	0(0.0%)	10(100.0%)
41-50years	4(66.7%)	1(16.7%)	1(16.7%)	6(100.0%)
51-60years	2(50.0%)	1(25.0%)	1(25.0%)	4(100.0%)
61-70years	2(40.0%)	2(40.0%)	1(20.0%)	5(100.0%)
Above70years	0(0.0%)	1(50.0%)	1(50.0%)	2(100.0%)

Table3: Depression Category and Vitamin D level Category among treatment naïve patients with depression

Severity of depression	Vitamin D category			
	Optimal (%)	Insufficient (%)	Deficient (%)	Total (%)
Mild	18(100.0%)	0(0.0%)	0(0.0%)	18(100.0%)
Moderate	14(63.6%)	8(36.4%)	0(0.0%)	22(100.0%)
Severe	0(0.0%)	6(40.0%)	9(60.0%)	15(100.0%)

On Fisher's exact test, the study showed that there is significant association (p<0.001) between severity of depression and Vitamin D level category (Table 4).

Table 4: Association between Depression Category and Vitamin D level category

Depression category	Optimal (%)	Insufficient (%)	Deficient (%)	Fisher's p-exact
Mild	18(56.2%)	0(0.0%)	0(0.0%)	X2 (4) = 45.11;
Moderate	14(43.8%)	8(57.1%)	0(0.0%)	p=<0.001
Severe	0(0.0%)	6(42.9%)	9(100.0%)	
Total	32(100.0%)	14(100.0%)	9(100.0%)	

Table 5: Relation between Depression Category and Serum Vitamin D level

Depression Category	Minimum	Q1	Median	Q3	Maximum	Kruskal Wallis test
Mild	30.0	35.9	48.7	55.2	91.3	H (2) =37.64;
Moderate	22.7	28.4	32.2	37.8	46.7	p= <0.001
Severe	7.5	16.0	20.1	22.3	27.3	

Patients with mild depression had a median serum Vitamin D level of 48.7 ng/ml (IQR: 55.2-35.9 ng/ml), those with moderate depression had median serum vitamin D level of 32.2 ng/ml (IQR: 37.8-28.4 ng/ml) and those with severe depression had a median serum Vitamin D level of 20.1 ng/ml (IQR: 22.3-16.0 ng/ml) (Table 5). After testing for the difference in the median of serum Vitamin D level among patients with different severity of depression using Kruskal Wallis test, a significant difference (p<0.001) was identified in median serum Vitamin D level in any one of the categories of depression (Table 5). Steel Dwass post-hoc test identified that there was significant difference in the median serum Vitamin D level among all the categories of the severity of depression, i.e., Mild to Moderate p<0.01, Mild to Severe p<0.001, and Moderate to Severe p<0.001 (Table 6).

Table 6: Steel Dwass post-hoc test (t and p-values)

Depression category	T	p-value
Mild: Moderate	3.53	<0.01
Mild: Severe	4.88	<0.001
Moderate: Severe	4.89	<0.001

DISCUSSION

More females (56.4%) were diagnosed with depression (treatment-naïve) through ICD-10 in this study. Our finding is similar to other studies conducted in Nepal which have shown higher prevalence of depression in females than males[2,31] which could be due to hormonal changes mainly in level of oestrogen occurring at various life stages such as menarche, menstrual cycle pregnancy and menopause and this hormone has been shown to affect neurotransmitter, neuroendocrine and circadian system which has been implicated in mood disorders.[32] Socialization differences in social roles may also lead to sense of devaluation in the society. Furthermore, women tend to use a more emotion focused, ruminative coping style –mulling their problems over in their minds which may be the cause of increased stress and increased prevalence of depression in female. Prevalence of depression is identified to be higher in females than in males, regionally and globally.[33,34]

In this study majority of the treatment-naïve depression patients were below 60 years of age with 40% belonging to the 21 to 30 years age-group. However, studies with information collected on mental disorders before COVID-19 show higher prevalence of mental disorders and depression among older agedpopulation.[33,31] Study conducted in United States in 2019, National Health Interview Survey, showed depression to be highest among age group 18-29 (21%), followed by age group 45-64 (18.4%) and18.4% (D2 = 51) in age group 65 years and above. The higher prevalence of depression among younger population in this study may be due to the COVID-19 situationand limitation in the physical and social activities of those population. Furthermore, the fear of COVID itself and the ongoing turmoil regarding physical casualty and the lack of employment itself could have been the cause of the finding.[35]

In this study, 32.7% of the patients were diagnosed with mild depression, 40% of the patients with moderate depression and 27.3% had severe depression. A study conducted in a tertiary hospital of Nepal, in which patients were diagnosed asperICD-10 criteria for depression, showed higher prevalence of moderate depression (49.5%), followed by mild depression (29.7%) and then by severe depression (20.9%).[36]

Majority of the patients, 14.1% had sub clinical hypothyroidism, 3.1% had overt hypothyroidism which could be a reason for more number of patients having moderate depression further supported by findings of Chhetry et al, which also showed association of thyroid dysfunction with mood disorders.[37] A data brief from National Health Interview Survey of United States has shown the prevalence of mild depression to be greater than moderate depression, and the prevalence of moderate depression to be greater than severe depression.[35] Higher prevalence of moderate depression in this study may be because the patients were experiencing and understanding depressive symptoms and thereby visiting hospitals for treatment. Furthermore, in our study majority of the patients were enrolled from the OPD which could have contributed to more cases of moderate depression than severe depression. In this study 16.4% of the treatment-naïve depression patients had deficient serum Vitamin D level. A study in a teaching hospital of Nepal has identified similar prevalence (15.1%) of deficient serum Vitamin D level among patients with depression.[38] In this study more females (25.8%) were identified to have deficient Vitamin D level than males (4.2%). A study conducted among university students in 39 countries has also found out high prevalence of deficient Vitamin D level in females than in males.[39] On average subcutaneous fat is more in female than in male and Vitamin D being a fat soluble vitamin gets stored in the subcutaneous fat after being produced from skin which could lead to lower Vitamin D in female.[40] Furthermore a study by Jassen et al, showed that Vitamin D concentration was significantly and positively corelated to testosterone level,[41] and negatively associated with body estradiol concentration in healthy postmenopausal women.[42] This study also showed that with the increase in age there is decrease in optimal level of Vitamin D among the treatment-naïve depression patients.

Elderly age has been identified to be a common factor for both increased severity of depression and reduced serum Vitamin D level.[43] With increasing age the concentration of 7 – dehydrocholesterol in epidermis is decreased and also there is reduced response to UV light which results in 50% decrease in formation of pre vitamin D3 and hence decreased Vitamin D level.[44] Besides with increasing age increased probability of increasing comorbidities, declining health, increasing disability, various life events increase probability of depression with age.

This study identified that 60.0% of patients with severe depression had deficient Vitamin D level. The patients with

deficient Vitamin D level had higher BDI and HAM-D scores. This study also identified that the mean serum Vitamin D level among the patient decreased with increase in the severity of depression. A high prevalence of low Vitamin D level in depressed patients have been identified in studies done in Nepal,[38] and elsewhere as in Kouider DAR et al.[39] Although research regarding Vitamin D deficiency and depression is growing however it is not clear whether Vitamin D deficiency is the cause or effect of depression. Patients with depression are more likely to develop low Vitamin D because of lower outdoor activity or due to decreased appetite which can lead to nutritional deficiency. Conversely, presence of Vitamin D receptors in areas of brain which are associated in development of depression also strengthens the plausibility of a relationship between Vitamin D and depression.

The study showed a significant association($p<0.001$) between severity of depression and Vitamin D level category. All patients with mild depression had optimal Vitamin D levels whereas most with severe depression had deficient Vitamin D level, median Vitamin D levels decreased progressively with greater severity of depression and a significant difference in the median serum Vitamin D level among all the categories of the severity of depression, i.e., Mild to Moderate $p<0.01$, Mild to Severe $p<0.001$, and Moderate to Severe $p<0.001$ was found. The findings add evidence that Vitamin D deficiency is not only prevalent but also found to decrease with more severe depressive symptoms. Thus, a study under controlled setting (randomized control trial), prospective cohort study or an analysis negating the effect of all the co - variates (multivariate analysis) addressing the confounders like anaemia, dyselectrolytemia, thyroid levels, vitamin b12 levels which were not addressed in this study may be supportive to identify the cause-effect relationship of serum Vitamin D level and depression

Association and relation between depression and Vitamin D deficiency have been identified in studies done in Nepal[25,38] and elsewhere.[39,45,46] similar to the results of this study. Ameta-analysis has identified increased odds ratio of depression for the lowest to highest vitamin D categories in the cross-sectional studies (OR=1.31,95%CI1.0–1.71) and a significantly increased hazard ratio of depression for the lowest to highest vitamin D categories (HR= 2.21, 95% CI 1.40–3.49) in the cohort studies.47. Vitamin D receptors in brain regions involved in mood regulation support a biological plausibility for the association. Vitamin D deficiency may contribute to depression via inflammatory pathways, neurotransmitter dysregulation, or neurotrophic effects. Alternatively, depression itself could reduce sunlight exposure and appetite, leading to Vitamin D deficiency[22,23].

The study included purposive sampling from one hospital which may not represent general population, was reliant on self-report BDI score which could introduce subjectivity and residual confounding could occur with factors like nutrition, comorbidities, or socioeconomic status which were not fully adjusted. Key strengths of this study include the exclusive focus on treatment naïve patients, minimizing medication related confounding, use of validated scales (ICD – 10, HAM – D, BDI) alongside laboratory-based Vitamin D measurement. However, as the study was a cross-sectional study conducted in a hospital setting which precludes causal inference, modest sample size, single center recruitment and lack of adjustment for factors like diet, BMI, sunlight exposure and the sample being non-randomized sample so the results of the study cannot be applied to general population.

The study strengthens the case that Vitamin D deficiency is not just a comorbidity, but closely linked to the severity of depressive symptoms. It highlights objective biomarkers (Vitamin D levels) may be integrated into screening or risk assessment for depression in clinical practice. Thus, screening Vitamin D levels in patients with depression could help identify high-risk patients and addressing Vitamin D deficiency through diet, supplementation, or safe sun exposure may become an adjunctive strategy in managing depression and nutritional/biochemical assessments can be integrated into holistic mental health care. Future research should use longitudinal or randomized controlled designs with larger, multicenter samples to clarify causality and explore interactions with other biomarkers. This would help establish whether correcting Vitamin D deficiency can improve depression outcomes and improve public health strategies in Nepal.

CONCLUSION

This study shows relationship between Vitamin D deficiency and symptoms of depression and low level of Vitamin D was associated with severity of depression but is unclear if low Vitamin D levels are the cause or the effect of depression. Thus, a study under controlled setting (randomized control

trial), prospective cohort study or an analysis negating the effect of all the covariates (multivariate analysis) addressing the confounders like anaemia, dyselectrolytemia, thyroid levels, vitamin b12 levels which were not addressed in this study may be supportive to identify the cause-effect relationship of serum Vitamin D level and depression.

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CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTION

The authors confirm contribution to the paper as follows: Study conception and design: Nabin Lekhak, Sulochana Joshi and Rabi Shakya; data collection, analysis, and interpretation of results: Nabin Lekhak; draft manuscript preparation: Nabin Lekhak. All authors reviewed the results and approved the final version of the manuscript.

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