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Comparison of Serum Vitamin D Levels in Depressed and Healthy Individuals at the Zahedan Psychiatric Clinic

Mansour Karajibani*[1], Farzaneh Montazerifar[2], Fatemeh Sadat Tabatabei[3], Ahmad Bolouri[4], Maryam Lashkaripour[5], Mahdieh Sheikhi[1]

1. Health Promotion Research Center, Department of Nutrition, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.
2. Department of Nutrition, Pregnancy Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.
3. General Medicine, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.
4. Department of Cardiology, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.
5. Department of Psychiatric, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.

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ABSTRACT

Introduction: Recent research has highlighted the potential role of vitamin D in brain function and development, including its influence on cognitive function and mental health. However, evidence regarding the association between vitamin D levels and depression remains inconsistent.

Objective: This study aimed to compare serum vitamin D levels between individuals with depression and healthy controls referred to the psychiatric clinic in Zahedan.

Methods: A case-control study was conducted involving 54 individuals with depressive symptoms and 45 healthy controls. Serum vitamin D levels were measured using the ELISA immunoassay. Statistical analyses were performed using SPSS version 21.0.

Results: The mean serum vitamin D levels in the case and control groups were 24.2 ± 13.3 ng/ml and 30 ± 14.4 ng/ml, respectively (P = 0.04). No significant differences in demographic characteristics were observed between the two groups. Serum vitamin D levels were significantly lower in depressed patients compared to healthy controls (P = 0.04). The analysis revealed that 36 (66.7%) depressed patients and 19 (42.2%) controls had vitamin D deficiency, while 18 (33.3%) and 26 (57.8%) participants in the case and control groups had normal or higher serum vitamin D levels, respectively. Furthermore, the frequency of vitamin D insufficiency was significantly higher in the depressed group compared to controls (P = 0.01).

Conclusions: This study demonstrated that vitamin D deficiency was more prevalent in individuals with depression, suggesting increased vulnerability in this population. Further diagnostic investigations and educational programs focusing on the prevention, detection, and treatment of vitamin D deficiency are warranted.

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Introduction

Depression is a common mental health disorder that affects individuals across all ages, genders, and ethnicities, making a substantial contribution to the global burden of psychological illness (1). In addition, depression is a multifactorial condition characterized by complex interactions among genetic, environmental, and biochemical factors (2). Among the biological contributors, vitamin D has garnered attention for its potential roles beyond traditional functions like bone health and calcium metabolism (3). Vitamin D deficiency not only adversely affects skeletal health but also has significant implications for the immune system, potentially contributing to the development of autoimmune disorders (4).

Emerging evidence suggests a potential association between vitamin D deficiency and various mental health conditions, including depression, anxiety, and mood disorders, particularly in individuals with conditions such as fibromyalgia (5, 6). Despite increasing interest, the relationship between vitamin D and mental health remains controversial and inconclusive (7, 8). While the impact of vitamin D deficiency on bone health is well-established, its

* *Corresponding author:* Mansour Karajibani, Professor, Department of Nutrition, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran. Phone: +989153414358 E-mail: mkarajibani@gmail.com.

influence on mental health requires further exploration, especially as studies have yielded mixed results regarding its role in cognitive function and psychological well-being (9).

Research has shown that patients with depression and schizophrenia often exhibit lower serum levels of vitamin D3 compared to healthy individuals. These differences are believed to be influenced by socioeconomic and nutritional factors (10). Furthermore, individuals with seasonal affective disorder (SAD) may experience worsened vitamin D deficiency during months with reduced sunlight exposure, although this association requires further validation (11). Seasonal variations, which can elevate serum vitamin D levels during summer months, may confound assessments and underestimate the true prevalence of vitamin D deficiency during other times of the year (12).

Studies have demonstrated that vitamin D receptors and activating enzymes are widely distributed throughout the human brain, suggesting a significant role in neurological processes (13). Experimental research in animal models, such as studies on maternal vitamin D deficiency in rats, has revealed that offspring exhibit altered brain structures, increased mitotic cell numbers, reduced nerve growth factor levels, and diminished expression of neurotrophin receptors, highlighting a potential relationship between vitamin D and brain development (14). In humans, vitamin D metabolites are thought to support neuronal integrity by upregulating neurotrophic factors within the hippocampus and neocortex (15). Additionally, vitamin D's role in modulating pro-inflammatory and anti-inflammatory pathways through vitamin D receptor (VDR)-mediated gene transcription underscores its potential connection to depression (16).

Although numerous studies suggest that individuals at risk for mood disorders and cognitive dysfunction often exhibit lower vitamin D levels, a significant gap remains in the literature regarding this relationship within specific populations, such as those in regions like Zahedan. The unique geographical and sociocultural characteristics of Zahedan may affect sunlight exposure and, consequently, the vitamin D status of its residents. Given the limited research in this area, the present study seeks to address this gap by evaluating and comparing serum 25-hydroxyvitamin D levels in depressed and healthy individuals referred to the Zahedan psychiatric clinic.

Material and Methods

Subjects

This case-control study was conducted in 2020 and included 54 patients presenting with depressive symptoms referred to the Psychiatric Clinic of Baharan Hospital, Zahedan, Iran, along with 45 healthy individuals as the control group. Depressive symptoms in patients were identified using the Beck Depression Inventory (BDI), and inclusion was confirmed by a clinical psychiatrist following standardized criteria. Healthy participants were matched to the case group and similarly assessed by a clinical psychiatrist to confirm the absence of psychiatric disorders. Baharan Hospital, as a central psychiatric treatment facility in Zahedan, regularly monitors patients with mental health conditions, ensuring a consistent and reliable source for study recruitment. The limited number of patients available for enrollment at this facility facilitated controlled sampling.

The sample size was determined using findings from a study by Jamilian et al. (17). The sample size formula for comparing means of serum vitamin D levels was applied, considering a standard deviation of 11.3 mg/dl for subjects with depressive symptoms and 10.4 mg/dl for the control group. A 95% confidence interval was used for the calculation (18).

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (S_1^2 + S_2^2)}{(\mu_1 - \mu_2)^2}$$

Participation in the study was voluntary, and informed consent was obtained from all participants. Convenience sampling was utilized, which is recognized as a potential limitation that may impact the generalizability of the findings. To minimize bias, measures such as rigorous screening and matching of participants were implemented. All collected data were coded, kept strictly confidential, and analyzed in compliance with ethical standards.

Inclusion and Exclusion Criteria

Inclusion criteria required participants to be aged between 20 and 60 years, exhibit depressive symptoms persisting for at least two weeks prior to assessment, and have no psychiatric conditions other than depression. Exclusion criteria included the absence of

depression, a history of chronic kidney failure or parathyroid disorders, use of calcium, phosphorus, vitamin D, or parathyroid hormone supplements within the past three months, and refusal to provide consent for participation.

The control group underwent rigorous screening to confirm the absence of depressive symptoms:

Absence of Depression: Participants were assessed using the Beck Depression Inventory (BDI), with only those scoring below 10 included in the study.

Clinical Evaluation: A clinical psychiatrist further verified the absence of any psychiatric conditions.

Additionally, participants with chronic conditions such as liver disease, renal disease, or malabsorption syndromes—factors known to affect vitamin D levels—were excluded

General Characteristics and Laboratory Measurements

The case group consisted of patients referred to the psychiatric clinic with complaints of depressive symptoms. After obtaining informed consent and with guidance from a clinical psychiatrist, these individuals were asked to complete the Beck Depression Inventory (BDI). Participants scoring 11 or higher on the questionnaire were included in the study. The control group was selected from healthy individuals with no reported depressive symptoms. These participants also completed the BDI, and those scoring below 10 were included in the control group. All procedures were conducted under the supervision of a clinical psychiatrist. For both groups, demographic information—including age, occupation, educational level, and body mass index (BMI)—was collected using a structured questionnaire. Subsequently, 3 ml of fasting blood was drawn from each participant under equal conditions. The blood samples were centrifuged, and the serum was separated and stored in coded microtubes for further testing. Samples were preserved at -20°C. Serum 25(OH) vitamin D levels were measured using a commercial kit (Lot No: 9900, Pishtazteb Company, Iran) at the laboratory of Imam Ali Hospital in Zahedan. The analysis was performed by a laboratory expert in the hormone department using an ELISA device. Informed consent was obtained from all participants, including both patients and healthy individuals.

Statistical Analysis

Data were analyzed using SPSS Version 21.0. Descriptive statistics, including percentages, means, standard deviations, and variable ranges, were utilized to summarize the data. An independent t-test was applied to compare intergroup differences, while the chi-square test was used to examine relationships between various qualitative variables. A statistical significance level of $P < 0.05$ was considered.

Results

Fifty-four patients aged 23–60 years and 45 healthy individuals aged 22–51 years were included in the case and control groups, respectively. The mean ages of the case and control groups were 39.8 ± 10.8 years and 37.4 ± 7.8 years, respectively ($p = 0.24$). No significant differences were observed between the two groups in terms of age, gender, occupation, educational level, or BMI ($P > 0.05$). Serum vitamin D levels in patients with depression were significantly lower than in the control group ($p = 0.04$).

The results revealed that 36 (66.7%) participants in the case group and 19 (42.2%) in the control group had vitamin D deficiency. Additionally, 18 (33.3%) and 26 (57.8%) participants in the case and control groups, respectively, had normal or higher vitamin D levels ($X^2 = 5.94$, $P = 0.11$).

The findings revealed that the mean serum vitamin D levels in the case and control groups were 24.2 ± 13.13 ng/ml (range: 3–70) and 30 ± 14.4 ng/ml (range: 4–76), respectively ($P = 0.04$) (Figure 1). A significant difference was observed between the two groups regarding the different degrees of vitamin D deficiency, including mild, moderate, and severe deficiencies ($P = 0.004$) (Table 1). Additionally, there was a significant difference in the mean serum vitamin D levels (≥ 20 ng/ml) between the two groups (Table 2). The classification of vitamin D deficiency is based on reference guidelines (19, 20).

The results further demonstrated that 47 (87.1%) participants in the case group and 26 (57.7%) in the control group had serum vitamin D levels below 30 ng/ml. Conversely, 7 (12.9%) and 19 (42.2%) participants in the case and control groups, respectively, had serum vitamin D levels above 30 ng/ml ($X^2 = 10.85$, $P = 0.001$).

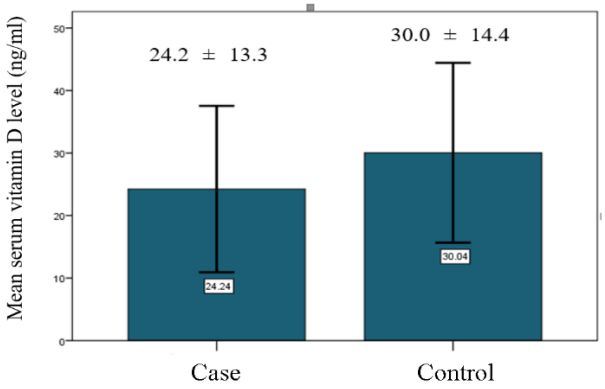

Figure 1. Comparison of mean serum vitamin D levels in two groups

Table 1. Frequency distribution of serum vitamin D levels (ng/ml) in the studied groups*

Vit D. serum	Case (N%)	Control (N%)	P-Value
Severe deficiency (< 10 ng/ml)	1(1.85%)	1 (2.2%)	
Moderate deficiency (10-30 ng/ml)	46 (85.19%)	24 (53.33%)	X^2=10.86, df=2
Natural and more (≥ 30 ng/ml)	7 (12.96%)	20 (44.22%)	P=0.004
Total	54(100.0%)	45 (100.0 %)	

*It should be noted that the above classification is based on the following reference (19).

Table 2. Frequency distribution of serum vitamin D levels (ng/ml) in the studied groups*

Vit D. serum	Case (N%)	Control (N%)	P-Value
< 20 ng/ml	22 (40.7%)	11 (24.4%)	X^2= 2.93, df=1
≥ 20 ng/ml	32 (59.2%)	34 (75.5%)	P= 0.09
Total	54(100.0%)	45 (100.0 %)	

*It should be noted that the above classification is based on the following reference (20).

Discussion

The findings indicated that the mean serum vitamin D level in patients with depression was significantly lower than that of the healthy group. Furthermore, severe vitamin D deficiency was significantly more prevalent among depressed patients compared to healthy individuals.

The prevalence of vitamin D levels equal to or greater than 30 ng/ml was 13.0% in the case group and 44.2% in the control group (P = 0.004). This result highlights the clear vulnerability of depressed patients to vitamin D deficiency. However, further studies with larger sample sizes are necessary to validate these findings.

Previous research has reported a high prevalence of vitamin D deficiency across various regions of Iran (21). Similarly, the status of vitamin D deficiency in other cities, including Yazd, has been described as concerning (22). Several factors contribute to this widespread deficiency, including geographical location, cultural practices such as clothing choices, skin pigmentation, dietary habits, and avoidance of sunlight exposure (23).

A high prevalence of vitamin D deficiency has been observed among depressed patients, similar to other groups, highlighting the need for further investigation into its causes and the potential impact of vitamin D deficiency on depression. According to the findings of this study, the serum level of 25-hydroxyvitamin D showed no significant relationship with the Beck Depression Inventory (BDI) score. Previous studies have reported conflicting results regarding the relationship between vitamin D status and depression. These discrepancies may be attributed to differences in sample size, study methodologies, confounding factors, or the inclusion of specific target groups, such as patients with Alzheimer's disease, secondary hyperparathyroidism, or alcohol dependence (24, 25). Nonetheless, reductions in vitamin D levels have been linked to metabolic alterations that may adversely affect brain function. Such complications include reduced insulin sensitivity, impaired insulin signaling, elevated

blood glucose levels, diabetes, low high-density lipoprotein cholesterol, hypertriglyceridemia, obesity, and metabolic syndrome (26).

Furthermore, no significant relationship between age and vitamin D levels was observed in our study. However, findings from a previous study indicated that vitamin D deficiency is a risk factor for the development of depressive symptoms in elderly women (27).

Consistent with the results of the present study, it has been reported that individuals with vitamin D deficiency exhibit more depressive symptoms compared to those with normal vitamin D levels. Additionally, vitamin D deficiency has been associated with both severe and mild forms of depression (28).

In another study, no significant correlation was observed between depression and vitamin D concentration in elderly and middle-aged individuals (29). Similarly, consistent with the present study, no significant relationship was found between demographic characteristics and serum vitamin D levels, indicating the need for further investigation. Additionally, in another study, after adjusting for confounding factors such as age, leisure time, and smoking, no significant relationship was observed between serum vitamin D levels and severe, mild, or moderate depression (30).

Although in this study, the decrease in the severity of depression was associated with an increase in vitamin D levels, the relationship was not statistically significant. Among the factors influencing the role of vitamin D in depression are the presence of vitamin D receptors (1,25-DHCC), the enzyme that activates this vitamin (1-alpha hydroxylase), and cytochrome P450 in various regions of the central nervous system. Vitamin D also regulates the expression of critical factors involved in neurotransmission and synaptic plasticity (31). Additionally, vitamin D has been reported to play a neuroprotective role by synthesizing specific calcium-binding proteins and exhibiting antioxidant properties (32). Furthermore, it regulates the gene expression of tyrosine hydroxylase, an essential enzyme for the production of dopamine and norepinephrine, which are critical neurotransmitters in the regulation of mood and the pathophysiology of depression (33).

The results revealed a significant difference in the degrees of vitamin D deficiency between the two groups (P=0.004). This finding highlights the vulnerability of the studied patients, particularly in cases of mild and moderate vitamin D deficiency, which could potentially progress to severe nutritional deficiencies and their associated complications within the studied population.

Furthermore, considering the region's conditions and prevalent food insecurity, a substantial proportion of vulnerable groups in the studied population are likely to suffer from vitamin D deficiency (34). studies with a larger sample size are necessary to provide a more accurate assessment of vitamin D levels in this population.

Conclusion

The findings of this study revealed that over 60% of participants in the case group and 40% in the control group had vitamin D deficiency, potentially increasing the vulnerability of the population to depression. This prevalence may be attributed to regional vitamin D deficiency. Long-term hypovitaminosis D (HVD) has been reported to contribute to the development of several conditions, including changes in mood and cognition. However, the findings regarding this association remain inconclusive, as cognitive and mental disorders may take years to manifest fully (26).

Nevertheless, further research is recommended to better understand the association. It is also advisable to conduct and review screening studies on vitamin D deficiency and implement treatment programs that include educational initiatives and the prescription of supplements to prevent and address this issue.

A limitation of this study was the lack of evaluation of vitamin D status in the studied population considering other potential confounding factors, such as genetic and hormonal characteristics, economic and social status, and family history of depression among patients.

Studies with larger sample sizes, including both healthy and depressed individuals, as well as screening studies on vitamin D deficiency in this region, are recommended. Clinical trials investigating the effectiveness of different doses of vitamin D supplements in patients prone to depression are also suggested. Additionally, monitoring serum vitamin D levels and conducting supplementary tests related to vitamin D deficiency, such as calcium,

phosphorus, and alkaline phosphatase levels in depressed patients, are advised. Educational and support programs promoting the consumption of vitamin D-rich food sources in this population are also necessary. Due to the cross-sectional, case-control design of this study, it is challenging to establish a causal relationship. However, while this design limits the ability to draw fundamental conclusions, it provides valuable insights into the potential role of vitamin D in the pathophysiology of depression compared to healthy controls. These findings underscore the need for further studies aimed at elucidating the precise mechanisms underlying this relationship.

Declarations

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Conflict of Interest

The authors declare no conflict of interest.

Authors' Contributions

K M contributed and designed the research, drafted and finally revised the manuscript; TFS and L M performed experiments and prepared tools facility for field study; M F, B A and S M performed statically analysis, drafted and final revised the manuscript. All author read and approved the final draft of the manuscript.

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