ACH Med J
(2023) 3: 231-236
ISSN:2822-5872
Doi : 10.5505/achmedj.2023.28247

RESEARCH ARTICLE

Investigating the Relationship of Vitamin D Deficiency and Certain Biochemical Parameters with Depression

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Article Info

Received Date: 28.08.2023
Accepted Date: 12.09.2023

Keywords:

Depression, Vitamin D, Beck's Depression Inventory

Abstract

Introductıon: Depression is the most common psychiatric disorder in the general population and is the most common mental health condition in primary care patients. Although theories involving biological, psychological, and environmental factors have been put forth, the underlying pathophysiology of depression is unknown, as several different mechanisms are likely involved. Identification of vitamin D receptors in brain regions active in depression has strengthened the link between vitamin D and depression. The aim of this study was to examine the relationship of depression with vitamin D and certain biochemical parameters. **Methods:** Patients who were admitted to Şanlıurfa Mehmet Akif İnan Training and Research Hospital Internal Medicine outpatient clinic who had no chronic diseases and whose vitamin D, ferritin, hemoglobin (Hb), thyroid stimulant hormone (Tsh), free thyroxine (T4), folate, magnesium and B12 levels were recorded were included in the study. Beck's Depression Inventory was presented to the patients to examine the relationship of depression with the selected parameters. **Results:** A total of 352 cases were included in the study. Of the cases, 246 (69.9%) were female and 106 (30.1%) were male. There was no significant correlation between Beck's Depression Inventory scores and magnesium, hemoglobin, ferritin, B12, Tsh and T4 levels ($p>0.05$). A significant correlation was found only between folate levels and Beck's Depression Inventory scores ($p=0.046$). There was not a significant correlation between vitamin D levels and Beck's Depression Inventory scores ($p=0.727$), although a weak negative correlation was discovered between them ($r= -0.019$). There was no significant correlation between vitamin D levels and depression severity ($p=0.650$). None of the patients who had normal vitamin D levels were found to have severe depression. **Conclusion:** Depression is a common psychiatric disease and its pathophysiology has not been fully elucidated. Further studies are need to better understand the relationship between biochemical parameters and depression. The evidence-based results of these studies should be used to prevent and treat depression, which is an important health problem.

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Introduction

Depression is the most widespread psychiatric disorder in the general population and is also the most common mental health condition in primary care patients.[1] It is characterized by a despondent mood or loss of interest or pleasure in almost all activities for a period of at least two weeks. Symptoms of depression include changes in sleep patterns, appetite and psychomotor function, irritability, feelings of worthlessness, guilt and hopelessness, suicidal thoughts or attempts, and decreased energy. Major depressive disorder, which is more common in females (10-25%) than in males (5-12%), significantly affects everyday activities and social relationships. The average age of onset of depression is the mid-twenties, and in 50-60% of those who experience a single depressive episode, depression recurs and is often associated with anxiety.[2]

Although theories involving biological, psychological, and environmental factors have been developed, the underlying pathophysiology of depression is unknown and several different mechanisms are reportedly involved. Vitamin D, a neurosteroid hormone, has been shown to affect the pathology of depression. Receptors for vitamin D are found in neurons and glia in many regions of the brain, including the cingulate cortex and hippocampus, which are involved in the pathophysiology of depression.[3] Vitamin D plays a part in numerous brain processes such as neuroimmunomodulation, regulation of neurotrophic factors, neuroprotection, neuroplasticity, and brain development, which makes it biologically plausible that this vitamin may be associated with depression and that its supplementation may factor into the treatment of depression.[4]

Recent studies have reported that vitamin D is significant in the prevention and treatment of many chronic diseases.[5] Identification of vitamin D receptors in brain regions involved in depression strengthened the link between vitamin D and depression. Prior human and animal studies showed that vitamin D receptors and the 1-α-hydroxylase enzyme are found in the brain and vitamin D has a role in central nervous system functions.[6,7] The aim of this study was to examine the relationship of depression with vitamin D and a few specific biochemical parameters.

Material and Methods

Ethics approval was obtained from the institutional review board prior to initiation of the study. Those included in the study were patients who were admitted to Şanlıurfa Mehmet Akif İnan Training and Research Hospital Internal Medicine outpatient clinic who had no chronic diseases and whose vitamin D, ferritin, hemoglobin (Hb), thyroid cytimulan hormone (Tsh), free thyroxine (T4), folate, magnesium and B12 levels were recorded. Beck's Depression Inventory (BDI) was given to the patients to examine the relationship of depression with the selected parameters. BDI was developed by Beck et al. in 1961 to measure behavioral findings of depression in adolescents and adults.[8] In 1978, the whole scale was revised, duplications of statements defining severity were removed and the questions were reorganized to examine the status of the patients during the prior week, including the day they on which they completed the test. Regarding severity, scores are interpreted as 0-9 = Minimal, 10-16 = Mild, 17-29 = Moderate, and 30-63 = Severe.[9] This scale is open-access. Patients with active malignancy, liver failure, renal failure, chronic diseases and those under 18 years of age were excluded from the study.

Statistical Analysis

Descriptive statistics were used to explain the data of the study. Quantitative variables were described using means and standard deviation ($x \pm SD$) and qualitative variables were described using numbers (n) and percentages (%). Differences between groups regarding quantitative variables were evaluated with Independent Sample T Test or One-Way Analysis of Variance (ANOVA). Differences between groups regarding qualitative variables were analyzed with the Chi-Square Test. Pearson's Correlation Analysis was used to examine the relationships between quantitative variables. A significance level of $p<0.05$ was considered statistically significant. Statistical software was used for calculations (IBM SPSS Statistics 22, SPSS inc., an IBM Co., Somers, NY)

Results

A total of 352 Cases were included in the study. Of the cases, 246 (69.9%) were female and 106 (30.1%) were male. The ages of the patients ranged between 18 and 74 years, with a mean age of 33.32±11.86 years (Table 2). Of these patients, 212 (60.2%) were between the ages of 18-34 years, 136 (38.6%) were between the ages of 35-64 years, and 4 (1.1%) were over the age of 65 years. There were 115 (32.7%) primary school graduates, 18 (5.1%) secondary school graduates, 97 (27.6%) high school graduates, and 102 (29%) with a bachelor's or master's degrees. While 143 (40.6%) of the patients were employed, 209 (59.4%) were not. 64 (18.2%) of the patients were smokers and 288 (81.8%) were non-smokers. Only 2.8% of the cases (n=10) consumed alcohol (Table 1).

Table 1: Distribution of Qualitative Characteristics (n=352)

		n	%
Age	18-34	212	60.2
	35-64	136	38.6
	65+	4	1.1
Gender	Female	246	69.9
	Male	106	30.1
Education	No	20	5.7
	Primary school	115	32.7
	Secondary school	18	5.1
	High school	97	27.6
	Bachelor or Master	102	29.0
Employment	Employed	143	40.6
	Unemployed	209	59.4
Smoking	No	288	81.8
	Yes	64	18.2
Alcohol Use	No	342	97.20
	Yes	10	2.80
BDI	Minimal Depression	76	21.60
	Mild Depression	92	26.10
	Moderate Depression	151	42.90
	Severe Depression	33	9.40
Vitamin D	Severe Deficiency	304	86.40
	Deficiency	39	11.10
	Normal	9	2.60

Table 2. Distribution of Quantitative Characteristics (n=352)

	Mean	Standard Deviation	Median	Minimum	Maximum
Age	33.32	11.86	31.00	18.00	74.00
BDI	17.68	8.92	17.00	0.00	49.00
Mg	2.01	0.14	2.01	1.20	2.47
Hb	13.19	2.14	13.00	7.10	18.00
Ferritin	49.58	66.69	25.00	1.57	442.90
Vitamin D (Ng/ml)	12.05	7.05	10.12	0.85	63.00
B12	316.46	125.49	292.00	50.00	890.30
Folate	6.57	4.36	5.60	1.31	58.00
Tsh	2.23	1.72	1.78	0.01	16.13
T4	15.23	2.76	15.00	6.40	42.63

Patients' BDI scores varied between 0 and 49. The mean BDI score was 17.68±8.92 (Table 2). Of the patients, 76 (21.6%) had minimal depression, 92 (26.1%) had mild depression, 151 (42.9%) had moderate depression, and 33 (9.4%) had severe depression (Table 1).

Vitamin D levels of the patients ranged between 0.85 ng/ml and 63 ng/ml with a mean of 12.05±7.05 ng/ml (Table 2). A severe vitamin D deficiency was found in 304 of the patients (86.4%), while 39 (11.1%) had less severe vitamin D deficiency, and 9 (2.6%) had normal vitamin D levels (Table 1).

Magnesium values of the patients ranged between 1.2 and 2.47 mg/dl with a mean value of 2.01±0.14 mg/dl. Their hemoglobin (Hg) values ranged between 7.1 and 18 g/dl and the mean value was 13.19±2.14 g/dl. Ferritin levels ranged between 1.57 and 442.9 ng/ml with a mean value of 49.58±66.69 ng/ml. Vitamin B12 levels varied between 50 and 890.3 pg/ml, with a mean of 316.46±125.49 pg/ml. Folic acid levels of the patients had a range between 1.31 and 58 ng/ml with the mean value being 6.57±4.36 ng/ml. Tsh levels varied between 0.01 and 16.13mIU/L with a mean value of 2.23±1.72mIU/L. Free T4 levels ranged between 6.4 and 42.63 mIU/L with a mean value of 15.23±2.76 mIU/L (Table 2).

No significant correlation was found between BDI scores and age, gender, educational status, employment status, smoking and alcohol use (p=0.880, p=0.762, p=0.380, p=0.397, p=0.105, p=0.337, respectively).

There was also no significant correlation between BDI scores and magnesium, hemoglobin, ferritin, B12, Tsh, or Free T4 levels (p=0.923, p=0.740, p=0.313, p=0.818, p=0.109, p=0.810, respectively). BDI scores only had a significant correlation with folate levels (p=0.046). A negative correlation was found between BDI scores and ferritin, folate and Tsh levels (r=-0.054, r=-0.106, r=-0.086, respectively). There was a positive correlation between BDI scores and magnesium, hemoglobin, B12 and free T4 levels and (r=0.005, r=0.018, r=0.012, r=0.013, respectively) (Table 3).

There was no significant correlation between vitamin D levels and BDI scores (p=0.727), although there was a weak negative correlation between them (r= -0.019). There was no significant correlation between vitamin D levels and depression severity (p=0.650). None of the patients who had normal vitamin D levels were found to have severe depression (Table 4).

Table 3. Relationship Between Quantitative Characteristics and BDI Scores (n=352)

		BDI
Mg	r	0.005
	p	0.923
Hb	r	0.018
	p	0.740
Ferritin	r	-0.054
	p	0.313
B12	r	0.012
	p	0.818
Folate	r	-0.106
	p	0.046*
Tsh	r	-0.086
	p	0.109
T4	r	0.013
	p	0.810
Vitamin D (Ng/ml)	r	-0.019
	p	0.727

r: Pearson's Correlation Coefficient
* A p value of 0.05 was considered significant.

Interpretation:
r<0.4 is considered a weak correlation.
r=0.4-0.6 is considered a moderate correlation.
r> 0.6 is considered a strong correlation.

Table 4. Relationship Between Vitamin D Levels and Depression Severity (n=352)

		Vitamin D			p
		Severe Deficiency	Deficiency	Normal	
BDI	Minimal Depression	64(84.2)	9(11.8)	3(3.9)	0.653
	Mild Depression	80(87.0)	8(8.7)	4(4.3)	
	Moderate Depression	131(86.8)	18(11.9)	2(1.3)	
	Severe Depression	29(87.9)	4(12.1)	-	

Data is presented as n (%).
p: Chi-Square Test, * A p value of 0.05 was considered significant.

No significant correlation between vitamin D levels and age was found (p=0.202). Vitamin D levels of females (mean of 11.12±7.49 ng/ml) were significantly lower than those of males (mean of 14.22±5.34 ng/ml) (p<0.001). There was no statistically significant correlation between educational status and vitamin D levels (p=0.101). Vitamin D levels of employed patients were significantly higher than those of unemployed patients (p=0.003). No statistically significant correlation was found between smoking and alcohol use and vitamin D levels (p=0.773 and p=0.137, respectively).

Discussion

Prior studies examining the relationship between vitamin D levels and depression have conflicting results. Studies have suggested that vitamin D deficiency triggers depression through different mechanisms. Saji Parel et al. argued that vitamin D deficiency may lead to depression by affecting gene expressions, some neurotransmitters and various brain functions.[10-11]

In a study by Lars Libuda et al. involving approximately 322,000 participants, no relationship was found between vitamin D levels and depression symptoms and severity.[12]

Leila Kamalzadeh et al. investigated the relationship between vitamin D deficiency and depression in 174 obese patients, and found that vitamin D deficiency was significantly more common in depressive patients (p<0.05).[13]

In Menon et al.'s review of a total of 61 articles, including 46 original articles, 13 review/meta-analysis articles and two commentaries, it was found that depressive subjects had significantly lower vitamin D levels compared to controls and those with the lowest vitamin D levels had the greatest risk of depression .[14]

The results of studies suggesting a relationship between vitamin D deficiency and depression do not answer the question of whether vitamin D deficiency is a cause or a consequence of depression. This is because introversion and decreased interest in daily activities, which are common in individuals with depression, affect time spent outdoors, and therefore, time spent under the sun. Consequently, vitamin D levels in these people naturally decrease over time.

In our study, no significant correlation between vitamin D levels and Beck's Depression Inventory scores was found (p=0.727), though a weak negative correlation was detected (r= -0.019). There was also no significant correlation between vitamin D levels and depression severity (p=0.650). In addition, none of the patients who had normal vitamin D levels were found to have severe depression.

The fact that the number of patients with normal vitamin D levels was low (n=9) is a limitation of this study. In addition, lower levels of vitamin D in females may be related to the fact that females in Turkey dress more conservatively and are less exposed to the sun than males.

In the current study, a weak negative correlation was found between folate levels and BDI scores. As folate levels decreased, BDI scores increased significantly (p=0.046). This result was consistent with the results of previous studies.

Numerous studies have found associations between low folate levels and increased risk of depression,[15-16] more severe depressive symptoms,[17] increased risk of recurrence of depressive symptoms,[18] and prolonged depressive episodes.[19]

In a meta-analysis of 43 studies that included a total of 8,519 participants with depression and 27,282 participants without depression, it was found that depressive individuals had significantly lower serum folate levels compared to individuals without depression ($p < 0.001$).[20]

The results of studies on the relationship between B12 deficiency and depression are inconsistent. The results of one study suggested that vitamin B12 deficiency may play a role in the pathology of depression through its effects on the adrenergic, glutaminergic, serotonin, and dopamine systems.[21] In a 6-year study conducted with elderly patients by Elstgeest et al., no relationship was found between serum vitamin B12 levels and depression symptoms.[22] Yet another study has found no relationship between vitamin B12 levels and depression.[23]

The results of the present study also indicated no significant relationship between B12 levels and BDI scores (p=0.818).

In a study conducted with 60 depressed individuals with hypomagnesemia, a significant improvement in serum magnesium levels and depression symptoms was found in the experimental group after being given 500 mg magnesium oxide for 8 weeks .[24]

The results of another study showed a relationship between serum magnesium levels and depression symptoms, and suggested that magnesium supplementation may improve depressive symptoms in individuals with low serum magnesium levels.[25]

In our study, no statistically significant relationship was found between Mg levels and BDI scores (p=0.923). Since the extracellular concentration of magnesium ions may not reflect intracellular concentrations, none of the available assessment methods for magnesium levels are considered satisfactory.[26] This may explain the inconsistency between the results of the present study and prior research.

In a study conducted with 11,876 Japanese participants, which included 1,000 individuals with a history of depression, iron deficiency anemia was found to be associated with depression. In addition, self-reported lifetime history of iron-deficiency anemia was found to be associated with higher psychological distress ($p<0.01$).[27]

However, the results of the current study indicated no significant relationship between BDI scores and Hg and ferritin levels (p=0.740, p=0.313, respectively). The fact that our study objectively evaluated anemia diagnoses can be highlighted as a strength of this research.

In their study that included 2,142 participants, Ittermann et al. found that untreated hypothyroidism was associated with a higher BDI scores and more severe anxiety. In addition, untreated hyperthyroidism has been linked to a higher risk of major depressive disorder.[28]

In contrast, no statistically significant correlation was found between BDI scores and TSH and ST4 levels in the present study (p=0.109, p=0.810, respectively).

Conclusion

Depression is an important public health problem all over the world. Further studies are need to better understand the relationship between biochemical parameters and depression. The evidence-based results of these studies should be used among efforts to prevent and treat depression.

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