

Investigation of vitamin D levels in obsessive-compulsive disorder

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ABSTRACT

Background: The impact of vitamin D on obsessive-compulsive disorder (OCD) remains unknown.

Aim: Studies suggest that vitamin D deficiency may be associated with neuropsychiatric diseases. The purpose of this study is to investigate vitamin D levels in those diagnosed with OCD. In addition, the relation between OCD symptom severity and serum vitamin D level is investigated.

Methods: About 174 patients newly diagnosed with OCD and 170 healthy volunteers were included in the study. Yale-Brown Obsessive Compulsive Scale (YBOCS) was used to assess the severity of OCD symptoms. Serum vitamin D levels of the two groups were compared.

Results: The serum vitamin D levels of the OCD group were found to be significantly lower than the control group. Serum vitamin D levels were negatively correlated with the obsession, compulsion, and total scale scores measured in YBOCS but there was no correlation between the serum vitamin D levels and illness duration of OCD patients.

Conclusions: To the best of our knowledge, this is one of the first studies to investigate vitamin D levels in newly diagnosed adult OCD patients without comorbidities. Although our findings suggest that vitamin D may play a role in the pathophysiology of OCD, further studies are needed to support our findings.

Key words: Biomarkers, central nervous system, obsessive-compulsive disorder, vitamin D

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a psychiatric disorder characterized by obsessions (intrusive thoughts, images, and urges) and/or compulsions (repetitive actions performed to reduce obsessional distress) and the lifetime prevalence of OCD in the adult population is 1.6–2.3%.^[1,2] OCD usually begins in childhood or adolescence and it is often found in such additional psychiatric disorders as anxiety disorder, major depression, somatoform disorder, and bipolar disorder in OCD patients.^[3]

Neurochemical, genetic, immunological, and structural factors are thought to play a role in the etiology of OCD.^[4] Some studies report neurotransmitters such as serotonin, dopamine, and glutamate play a role in the etiology of OCD.^[5-7] Use of selective serotonin reuptake inhibitors (SSRIs) as the first option for psychopharmacological treatment of OCD, and the addition of typical/atypical antipsychotics, clomipramine, and glutamatergic agents to treat treatment-resistant patients supports these studies.^[8-10]

Vitamin D is synthesized in the epidermis as vitamin D₃ (cholecalciferol) and converted to 25-OH D₃ by hydroxylation in the liver. 25-OH D₃ is hydroxylated again in the kidneys and the active form, 1,25 dihydroxy vitamin D₃,

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is formed.^[11] Vitamin D is an important molecule that plays a role in the regulation of calcium and phosphorus balance in the body, as well as in immunity, inflammatory response, and antioxidant processes.^[12] Vitamin D is essential for brain development and maintenance of normal brain function.^[13] It also plays an important role in cell proliferation and differentiation in the central nervous system (CNS).^[14,15] There are studies reporting that vitamin D deficiency may be associated with neuropsychiatric diseases such as major depression, schizophrenia, attention deficit hyperactivity disorder (ADHD), and autism.^[16-19]

Levels of tryptophan hydroxylase, a speed-limiting enzyme in serotonin synthesis, and tyrosine hydroxylase, a speed-limiting enzyme in dopamine, epinephrine, and norepinephrine synthesis, are regulated by 1,25 dihydroxy vitamin D₃. Therefore, vitamin D deficiency can be effective in the etiology of OCD by disrupting the synthesis of serotonin and catecholamine.^[20,21] However, vitamin D protects cells against neurotoxicity by inhibiting inducible nitrite oxide synthetase (iNOS), the enzyme responsible for the synthesis of nitrite oxide. Vitamin D deficiency can contribute to OCD development by causing decreased neuroprotectivity. Studies that reported increased levels of nitrite oxide in OCD support this view.^[22-24]

Currently, in the adult population, vitamin D insufficiency is defined as serum 25 (OH) D₃ levels between 20 and 30 ng/mL; vitamin D deficiency is defined as serum 25 (OH) D₃ levels of <20 ng/mL; and sufficient levels of serum 25 (OH) D₃ are 30 ng/mL and above.^[25]

There are a limited number of studies investigating the relation between OCD and vitamin D, and only one of these studies was conducted in a small sample of adult OCD patients.^[26-29] For these reasons, we believe that this issue is worth investigating. What was aimed in this study is to investigate vitamin D levels and related parameters such as calcium, phosphorus, alkaline phosphatase, thyroid-stimulating hormone (TSH), and parathyroid hormone (PTH) levels in adult OCD patients and to compare them with healthy controls. We also intended to determine the relation between vitamin D levels and the severity of OCD symptoms and the duration of the illness.

MATERIALS AND METHODS

Study Design

This study was conducted at the Ministry of Health, Kayseri City Hospital. The study was approved by the Ethical Committee of Kayseri City Hospital and written informed consent was obtained from all the participants.

Participants

About 307 patients between the age of 18 and 45 who were admitted to Kayseri City Education and Research Hospital

Psychiatry Outpatient Clinic between July 15 and September 15 in 2021 and newly diagnosed with OCD according to Diagnostic and Statistical Manual for Mental Disorders, fifth edition (DSM-V) criteria were included in the study.^[1] The healthy control group was selected among hospital staff or healthy volunteers with consideration of age and gender distribution of the OCD group. Exclusion criteria of the study: The patients with comorbid psychiatric diseases other than OCD, those diagnosed with mental retardation, those using calcium or vitamin D supplement in the past 6 months, those using corticosteroid drugs for any reason in the past 3 months, those having a history of alcohol or substance use, those having a chronic systemic disease such as hypothyroidism, hyperthyroidism, hypoparathyroidism, hyperparathyroidism, and diabetes, those having a clinically active infection, those with pathology detected in routine biochemical tests, and those who were pregnant or breastfeeding. Diagnoses were confirmed by applying The Structured Clinical Interview for DSM-V (SCID-V) to the patients.^[30] Thirty-eight patients with comorbid depression, 19 patients with comorbid generalized anxiety disorder, 12 patients with comorbid panic disorder, 3 patients with comorbid social anxiety disorder, 5 patients with comorbid bipolar disorder, 9 patients using calcium or vitamin D supplements in the last 6 months, 6 patients using corticosteroid medication for any reason in the last month, 7 patients with a history of alcohol or substance use in the last 6 months, 6 patients with hypothyroidism, 3 patients with hyperthyroidism, 4 patients with diabetes, 14 patients with pathology in routine biochemical tests (leukocytosis was found in 7 patients, anemia in 5 patients, and thrombocytopenia in 2 patients), 2 breastfeeding patients, and 2 pregnant patients were excluded from the study. Three patients did not want to participate in the study. A total of 174°CD and 170 healthy subjects were included in the study.

Biochemical measurements

Since plasma vitamin D concentrations have seasonal biologic variance, the blood of all the participants was only collected between July 15 and September 15. 10 mL of fasting venous blood was collected in the morning between the hours of 08.00 and 10.00 AM into K2-EDTA-containing serum separator tubes. Serum and plasma were centrifuged for 30 min after collection. Plasma total 25 (OH) D₃ concentrations were measured by using liquid chromatography (Shimadzu, HPLC Prominence LC-20A, Japan) coupled with tandem mass spectrometry (LC MS/MS) (AB Sciex Q TRAP 4500, Toronto, Canada), using an Immuchrom 25 OH Vitamin D₃/D₂ kit (Immuchrom GmbH, Germany). Serum calcium (Ca) and phosphorus (P) were measured by photometric methods, alkaline phosphatase (ALP) by colorimetric method, and thyroid-stimulating hormone (TSH) and parathyroid hormone (PTH) by sandwich immunoassay methods on, Roche Cobas c501 and 601 (Roche Diagnostics GmbH, Mannheim, Germany) autoanalyzers.

Data collection instruments

SCID-V Disorders, Clinician Version (SCID-V-CV): It is a clinical interview scale developed and structured to investigate DSM-V diagnoses.^[30] Validity and reliability tests of the Turkish version were performed by Elbir *et al.*^[31]

The Yale–Brown Obsessive Compulsive Scale (YBOCS): This scale was developed by Goodman *et al.*^[32] to evaluate the severity of obsession and compulsion symptoms. The scale consists of 19 items and 10 items are scored (5 obsessions and 5 compulsive items). Three different evaluation scores can be calculated from the scale: obsession, compulsion, and total. The total score of the scale changes between 0 and 40. Higher total scores indicate higher severity of OCD symptoms. Validity and reliability tests of the Turkish version were performed by Karamustafalıoğlu *et al.*^[33]

Statistical analyses

The data were evaluated in the statistical package program of IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). Shapiro–Wilk test was used to determine whether the parameters in the study showed normal distribution. The Chi-square test was used in the analysis of categorical expressions. Mann–Whitney *U* test was used for binary variables for parameters that did not show normal distribution. Spearman correlation analysis was used to determine the relationship between continuous measurements. The statistical significance level was taken as 0.05 in all tests.

RESULTS

The sociodemographic characteristics of the control group and the OCD group are presented in Table 1. There was no significant difference between the groups in terms of sociodemographic characteristics such as age, gender, marital status, profession, and educational status ($p > 0,05$).

Biochemical data of the control group and the OCD group are presented in Table 2. The serum 25OH-D₃ levels of the OCD group were found to be significantly lower than the control group ($p < 0.001$), but there was no significant difference between the two groups in terms of serum calcium, serum phosphate, ALP, PTH, and TSH levels ($p > 0,05$). The number of participants with vitamin D insufficient (20–30 ng/mL) and vitamin D deficiency (< 20 ng/mL) in the OCD group was statistically significantly higher than the control group ($p < 0,001$) and also the number of participants whose vitamin D levels were in the normal range (> 30 ng/mL) in the OCD group was statistically significantly lower than the control group ($p < 0,001$).

Table 1: Sociodemographic data of control group and OCD group

	Control Group <i>n</i> =170	OCD Group <i>n</i> =174	<i>P</i>
Age (years)	28 (CI: 24-30)	29 (CI: 27-32)	0,135 ^a
Gender <i>n</i> (%)			
Female	92 (54,1)	88 (50,6)	0,642 ^b
Male	78 (45,9)	86 (49,4)	
Education (years)	13 (CI: 11-13)	13 (CI: 12-13)	0,251 ^a
Marital status <i>n</i> (%)			
Single	68 (40)	60 (34,5)	0,339 ^b
Married	94 (55,3)	96 (55,2)	
Divorced	8 (4,7)	18 (10,3)	
Profession <i>n</i> (%)			
Not working	70 (41,2)	62 (35,6)	0,455 ^b
Working	100 (58,8)	112 (64,4)	

OCD: Obsessive-compulsive disorder; ^aMann–Whitney *U* test; ^bChi-square test

Table 2: Biochemical data of the control group and OCD group

	Control Group <i>n</i> =170	OCD Group <i>n</i> =174	<i>P</i>
25OH-D ₃ (ng/mL)	27,8 (CI: 25,8-29,1)	19,4 (CI: 18,3-20,9)	<0,001 ^a
Min-max (ng/mL)	9,4-37,3	13,6-43,8	
Sufficient (>30 ng/mL)	50 (29,4%)	21 (12,1%)	<0,001 ^b
Insufficient (20-30 ng/mL)	102 (60%)	55 (31,6%)	<0,001 ^b
Deficiency (<20 ng/mL)	18 (10,6%)	98 (56,3%)	<0,001 ^b
Phosphor (mg/dL)	3,73 (CI: 3,64-3,95)	3,76 (CI: 3,65-3,89)	0,870 ^a
TSH (mU/L)	2,68 (CI: 2,45-3,12)	2,64 (CI: 2,45-3,23)	0,814 ^a
PTH (pg/mL)	34,4 (CI: 30,8-36,4)	34,9 (CI: 30,2-37,8)	0,575 ^a
ALP (IU/L)	65 (CI: 58-72)	64 (CI: 58-72)	0,879 ^a

TSH: Thyroid-stimulating hormone; PTH: Parathyroid hormone; ALP: Alkaline phosphatase; ^aMann–Whitney *U* test; ^bChi-square test

In the OCD group, the YBOCS obsession score is 12 (CI: 11-13), the YBOCS compulsion score is 13 (CI: 12-14), and the YBOCS total score is 26 (CI: 24,5-27). The illness duration of OCD patients is 12 months.

Serum 25OH-D₃ levels were negatively correlated with the obsession ($r = -0,693$, $P < 0.001$), compulsion ($r = -0,633$, $P < 0.001$), and total scale scores measured in YBOCS ($r = -0,705$, $P < 0.001$). No correlation was found between the serum 25OH-D₃ levels and illness duration of OCD patients ($p > 0,05$).

DISCUSSION

In this study, we purposed to investigate vitamin D levels and related parameters such as calcium, phosphorus, ALP, TSH, and PTH levels in OCD patients and to compare them with healthy controls. We also investigated the relation of vitamin D levels with the severity of OCD symptoms and the duration of the illness. The results of the study showed that OCD may be associated with vitamin D deficiency and there is a moderately negative correlation between serum vitamin D levels and OCD symptom severity. According to this, as vitamin D levels decrease, YBOCS scores increase.

The idea that vitamin D deficiency may play a role in various psychiatric disorders is getting stronger day by day. In recent studies, it has been shown that vitamin D levels in patients with depression and anxiety disorders are lower than in healthy controls.^[34-36] Depression and anxiety disorders have a similar etiology to OCD and serotonin plays an important role in this etiology.^[37] Low levels of vitamin D can increase the severity of OCD symptoms as they decrease the amount of serotonin by decreasing tryptophan hydroxylase synthesis. We found that there was no significant correlation between disease duration and serum vitamin D levels. This may be because vitamin D levels fluctuate seasonally as it is affected by sunlight.

As far as we know, there are only four studies that investigate the association between OCD and vitamin D. In addition, three of these studies were conducted on pediatric and adolescent OCD patients.^[26-28] There is only one study conducted on adult OCD patients.^[29] Our study is the first to investigate vitamin D levels and related parameters such as calcium, phosphorus, ALP, TSH, and PTH levels in adult OCD patients without comorbid psychiatric conditions.

In a study conducted in 2016, vitamin D levels were found to be lower in patients diagnosed with OCD and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) compared to healthy controls but it was not statistically significant.^[26] In this study, increased oxidative stress due to autoimmune disease may have affected vitamin D levels in patients. Therefore, it is not clear whether low vitamin D levels are due to OCD or autoimmune processes. In our study, the participants did not have acute or chronic systemic diseases that may affect vitamin D levels, such as hypothyroidism, hyperthyroidism, hypoparathyroidism, hyperparathyroidism, diabetes, and clinically active infection.

A study published in 2017 by Esnafoğlu and Yaman reported lower vitamin D levels in children and adolescents with OCD compared to healthy controls.^[27] There are some important differences between Esnafoğlu and Yaman's study and ours in terms of methodology and limitations: First, vitamin D deficiency is known to be associated with depression or anxiety disorder.^[38] Since the patients in this study had depression and other anxiety disorders comorbid with OCD, it is unclear whether low vitamin D levels in the OCD group are associated with comorbidities of depression or anxiety disorder. Secondly, the authors did not provide information about the previous or current use of psychotropic drugs by the patients. In our study, the patients did not have any comorbid psychiatric disease other than OCD and patients had not been using any drug for at least 3 months. Thirdly, since vitamin D levels are affected by sunlight, blood samples must all be collected during the same season. For this reason in our study, blood was only collected between July 15 and September 15 but it is not clearly stated what

time of year the blood collection occurred in the study of Esnafoğlu and Yaman.

In the study of Yazıcı *et al.*,^[28] serum vitamin D levels were found to be lower in children and adolescent OCD patients compared to healthy controls, but this finding was not statistically significant. These findings support our findings.

Finally, Marazziti *et al.*^[29] in their study reported that serum vitamin D levels in 50 adult OCD patients were statistically significantly lower than in the control group. Although this study was conducted in adult OCD patients, it has some important methodological differences from our study. First, the comorbidity with different psychiatric disorders was quite common. Thirty-eight of 50 patients had at least one psychiatric disorder comorbid with OCD. Therefore, low vitamin D levels in OCD patients may be affected by comorbidity. Secondly, 34 of 50 patients were taking at least one or more psychotropic drugs such as antidepressants, mood stabilizers, antipsychotics, and benzodiazepines. Psychotropic drugs can affect both OCD severity and vitamin D levels. It may also mask other psychiatric disorders in patients. Therefore, the OCD group in our study consisted of patients who did not use any psychotropic drugs for at least 3 months. Thirdly, vitamin D-related parameters such as calcium, phosphorus, ALP, TSH, and PTH levels have not been investigated. Lastly, since their sample is relatively small, it may not represent all patients diagnosed with OCD in the community, and there was no control group in the study, a comparison of vitamin D was made between patients and normative values.

Limitations of the study

This study must be considered with its limitations. We collected blood samples between July 15 and September 15, when sunlight is the most intense in our country. This may have influenced vitamin D levels in both groups. Also, no data were collected regarding the duration of sunlight exposure. OCD patients have great tendency to spend their time in the home due to their obsessions. Therefore, they may be less exposed to sunlight. It may have affected vitamin D levels in the OCD group.

CONCLUSION

The study demonstrated that newly diagnosed OCD patients have lower vitamin D levels than healthy controls. Vitamin D may play a role in the pathophysiology of OCD and may be related to the severity of the disorder. Since vitamin D is affected by sunlight, further studies are needed in different seasons in different parts of the world to support or disprove our findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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