



# Evaluation of Vitamin B12, Folic Acid, Ferritin and Vitamin D Levels in Obsessive Compulsive Disorder

## Obsesif Kompulsif Bozuklukta B12 Vitamini, Folik Asit, Ferritin ve D Vitamini Düzeylerinin Değerlendirilmesi

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### Abstract

**Aim:** Obsessive compulsive disorder (OCD) is a heterogeneous disorder characterized by obsessions and compulsions. Despite the studies, etiopathogenesis is not fully understood. Pharmacological and psychosocial interventions in OCD may be insufficient due to limited knowledge of etiopathogenesis. Therefore, it is important to find inexpensive and easily determined biochemical parameters related to etiopathogenesis. In this study, the relationship between OCD and vitamin B12 (VitB12), folic acid (FA), vitamin D (VitD) and ferritin was investigated.

**Material and Method:** 50 patients with OCD (12 female, 38 male) and 50 healthy controls (HC) (13 female, 37 male) were included in this retrospective study. Serum VitB12, FA, ferritin and 25-OH VitD levels of both groups were compared.

**Results:** VitB12 ( $p < 0.001$ ), FA ( $p = 0.004$ ) and 25-(OH)VitD ( $p = 0.001$ ) serum levels were significantly lower in the OCD group than in the HC group. There was no significant difference between the two groups in terms of ferritin values.

**Conclusion:** Our study shows that serum VitB12, FA and VitD deficiency can contribute to etiopathogenesis in OCD patients. This study may lead to research to find new pathways related to etiopathogenesis. For this, prospective studies, including the post-treatment phase, are needed.

**Keywords:** Obsession, vitamin B12, folic acid, ferritin and vitamin D

### Öz

**Amaç:** Obsesif kompulsif bozukluk (OKB), obsesyon ve kompulsiyonlarla karakterize heterojen bir bozukluktur. Yapılan çalışmalara rağmen etiopatogenezi tam olarak anlaşılamamıştır. OKB'de farmakolojik ve psikososyal müdahaleler, sınırlı etiopatogenez bilgisi nedeniyle yetersiz olabilir. Bu nedenle etiopatogenez ile ilgili ucuz ve kolay saptanabilen biyokimyasal parametrelerin bulunması önemlidir. Bu çalışmada OKB ile B12 vitamini (VitB12), folik asit (FA), D vitamini (VitD) ve ferritin ilişkisi araştırıldı.

**Gereç ve Yöntem:** Bu retrospektif çalışmaya 50 OKB hastası (12 kadın, 38 erkek) ve 50 sağlıklı kontrol (SK) (13 kadın, 37 erkek) dahil edildi. Her iki grubun serum VitB12, FA, ferritin ve 25-OH VitD düzeyleri karşılaştırıldı.

**Bulgular:** VitB12 ( $p < 0.001$ ), FA ( $p = 0.004$ ) ve VitD ( $p = 0.001$ ) serum düzeyleri OKB grubunda HC grubuna göre anlamlı olarak düşüktü. Ferritin değerleri açısından iki grup arasında anlamlı fark yoktu.

**Sonuç:** Çalışmamız OKB hastalarında serum VitB12, FA ve VitD eksikliğinin etiopatogenez ile ilişkili olabileceğini göstermektedir. Bu çalışma, etiopatogenez ile ilgili yeni araştırmalara öncülük edebilir. Bunun için tedavi sonrası dönemi de içeren prospektif çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** Obsesyon, B12 vitamini, folik asit, ferritin ve D vitamini



## INTRODUCTION

Obsessive compulsive disorder (OCD) is a highly heterogeneous disorder characterized by obsessions and compulsions. Obsessions are unwanted and disturbing thoughts and images. Compulsions, on the other hand, are repetitive thoughts and behaviors done to eliminate or relax these disturbing thoughts.<sup>[1]</sup> OCD reduces the quality of life. It is one of the major causes of disability. It causes the loss of many social and occupational functions.<sup>[2,3]</sup> Its prevalence is around 1.6-2.3%.<sup>[4]</sup> In some epidemiological studies, the lifetime prevalence of OCD has been reported to be between 1.3-3%.<sup>[5,6]</sup> Despite the studies, it is a disorder whose etiopathogenesis is not fully understood.<sup>[7]</sup> Neurochemical, immunological and genetic factors are thought to play a role in the etiopathogenesis of OCD.<sup>[8]</sup> Due to limited information on etiopathogenesis, pharmacological and psychosocial interventions may be insufficient in OCD.<sup>[9]</sup> Therefore, it is important to find inexpensive and easily detectable biochemical parameters related to etiopathogenesis. On the other hand, it is known that levels of VitB12, FA, VitD and ferritin affect brain functions.<sup>[10-13]</sup> These vitamins and ferritin protein are necessary for various biochemical functions in our body. S-adenosylmethionine synthesis is decreased in vitamin B12 and FA deficiency. S-adenosylmethionine (SAM) deficiency is associated with many psychiatric diseases.<sup>[14]</sup> In addition, homocysteine levels increase in VitB12 and FA deficiency.<sup>[15,16]</sup> Increasing homocysteine may cause mitochondrial damage and oxidative stress, leading to various psychiatric disorders.<sup>[17]</sup> Homocysteine acts as an agonist for N-methyl-D-aspartate receptors. With the stimulation of these receptors, the intracellular secondary messenger Ca ion increases. It is thought that increasing Ca ion induces cell damage and prepares the ground for various psychiatric disorders.<sup>[18]</sup> In addition, high homocysteine may cause neurotoxicity in brain tissue by changing GABAergic and glutamatergic levels.<sup>[19]</sup> Homocysteine cannot be reconverted to methionine and SAM due to FA and VitB12 deficiency. SAM synthesis is also decreased with the increase of neurotoxic homocysteine. SAM deficiency causes hypomethylation. Hypomethylation can lead to disruption in the synthesis of neurotransmitters necessary for the structural integrity of the brain.<sup>[20]</sup> In addition, it is thought that VitB12 and FA may be effective in the treatment of OCD due to their relationship with neurotransmitters.

VitD was previously known to act only on calcium and phosphorus metabolism. With increasing technology, VitD is known to affect nearly 2000 gene regions on DNA today. For this reason, many studies are being conducted on VitD. These researches range from the antioxidant properties of VitD, its relationship with cardiovascular diseases, to cancer, and even to the fact that it is the most effective Vitamin against COVID-19. For all these reasons, VitD may be associated with psychiatric disorders.<sup>[21-24]</sup>

Iron is essential for life but too much iron is toxic. For this reason an iron storage protein is needed to regulate tissue and body iron homeostasis. Ferritin is one of the iron-storing proteins. In recent studies, it has been revealed that ferritin is not only an intracellular iron storage protein, but also has an important role in protecting brain cells against oxidative stress damage by binding excess iron.<sup>[25]</sup> The relationship between OCD and oxidative stress has been proven in many studies.<sup>[26]</sup> Therefore, there may be a relationship between OCD and ferritin. There are few studies investigating the relationship between OCD and serum VitB12, FA, VitD and ferritin. The results of these studies are different from each other.

Based on the aforementioned literature, our main aim in this study is to compare serum levels of VitB12, FA, VitD and ferritin between individuals with OCD and healthy control group and to investigate the relationship of these biochemical parameters with OCD.

## MATERIAL AND METHOD

The study was carried out with the permission of Karamanoglu Mehmetbey University Clinical Researches Ethics Committee (Date: 01.06.2023, Decision No: 5-17). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this retrospective study, the patient group was selected from the patients who applied to the Training and Research Hospital Psychiatry Clinic between January 1, 2017 and January 1, 2022. This study included a total of 50 treatment-naive patients who were diagnosed with OCD (study group). The patients with OCD were diagnosed by a psychiatrist, according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria.

The control group was composed of people who donated to the hospital blood bank according to age and gender. The age range of the OCD and healthy control (HC) groups was between 18 and 65 years. The control group consisted of a total of 50 healthy individuals (male 37, female 13). None of the control groups were using any medication or vitamin supplements. After obtaining the necessary permissions, a retrospective file search was performed in the hospital archive.

The levels of serum VitB12, FA, ferritin, and 25(OH)VitD were measured using commercially available kits based on routine methods on Maglumi X3/X8 System (Snipe Diagnostic, Shenzhen, P.R. China).

### Statistical Analysis

The data were analyzed using the IBM SPSS 16.0 packet data software, with 95% confidence limits ( $p=0.05$ ). In the statistical evaluation of biochemical tests, The Mann-Whitney U test was used. Data were given as mean values  $\pm$  standard deviation (SD), as well as confidence interval values.

## RESULTS

When the patient and control groups were compared in terms of age and gender, no statistically significant difference was found (data were not shown). The patient group consisted of 38 men and 12 women. In the patient group, in addition to the diagnosis of OCD, 3 patients had major depressive disorder and 2 patients had anxiety disorder. The age range of the patient group was 18-48. OCD onset age was 21±6.5 years. The duration of the disease was 16±3.2 months. The age range of the control group was 18-47 years (**Table 1**). Serum levels of VitB12 (p<0.001), FA (p=0.004) and VitD (p=0.001) were found to be lower in the OCD group than in the healthy control group. There was no significant difference between OCD and HC in terms of ferritin values (p=0.164), (**Table 2**). In the OCD group, VitB12 was below the normal limit in 12 patients, FA in 2 patients, and VitD in 32 patients (**Table 3**). Although it was higher in the control group than in the OCD group, VitD was below normal values in 14 patients (**Table 3**). In terms of ferritin, both groups were within the normal range, there was no deficiency or excess.

**Table 1: Comparison of demographic values in obsessive compulsive disorder and healthy control groups.**

Parameters	OCD (n= 50)	HC (n= 50)
	mean±SD / CI	mean±SD / CI
Age (years)	27.7±8.1 / 25.4-30.2	27.7±5.9 / 26.1-29.4
Gender (M/F)	37 / 13	38 / 12
BMI (kg/m2)	28.7	27.2
Age of onset	21±6.5	-
Duration (month)	16±3.2	-

OCD: obsessive compulsive disorder, HC: healthy control groups, BMI: Body Mass Index

**Table 2: Comparison of vitamin B12, folic acid, Vitamin D and ferritin levels in obsessive compulsive disorder and healthy control groups.**

Parameters	OCD (n= 50)	HC (n= 50)	p values
	mean±SD / CI	mean±SD / CI	
Vitamin B12 (pg/ml)	285±81.5 / 262-308	398±120 / 364-432	<0.001
Folic acid (ng/ml)	7.98±3.22 / 7.06-8.89	9.50±3.31 / 8.55-10.4	=0.004
Ferritin (ng/ml)	27.5±26.8 / 19.9-35,1	34.3±26.7 / 26.7-41.9	0.164
Vitamin D (ng/ml)	10.4±4.57 / 9.11-11.7	13.6±4.79 / 12.3-15.0	=0.001

Note: CI: Lower and upper values at 95% confidence interval for the mean. Mann-Whitney test. OCD: obsessive compulsive disorder, HC: healthy control groups, SD: standard deviation, CI: confidence interval

**Table 3: Vitamin B12, folic acid, Vitamin D deficiency in obsessive compulsive disorder and healthy control group**

Parameters	OCD (n= 50)	HC (n= 50)
Vitamin B12 (<210 pg/ml)	12	0
Folic acid (<3.1 ng/ml)	2	0
Vitamin D (<10 ng/ml)	32	14

OCD: obsessive compulsive disorder, HC: healthy control groups,

## DISCUSSION

In this retrospective study, VitB12, FA, ferritin, and VitD levels were evaluated in the OCD group compared to the HC group. The low levels of VitB12 in the OCD group in our study are consistent with the literature. In the two most recent meta-analyses, the level of VitB12 was found to be somewhat lower

than the healthy control groups of OCD.<sup>[27,28]</sup> In our study, the FA level was found to be significantly low in OCD studies.

In terms of FA, there are different results in the literature. While some specific OCD groups had higher FA levels than the healthy control group,<sup>[29]</sup> no difference was found between a study OCD and HC groups.<sup>[30]</sup> Consistent with our study, several studies have reported lower FA levels in the OCD group.<sup>[31]</sup> In the studies in the literature, the small number of patients in the groups and the fact that FA was affected by nutrition may have led to conflicting results.<sup>[32]</sup> In a study in the literature, it was reported that the addition of FA to the treatment-resistant OCD treatment was not beneficial.<sup>[33]</sup> This situation can be clarified with prospective studies with larger participation.

In our study, VitD levels were found to be significantly lower in the OCD group compared to the HC group. There are few studies in the literature investigating the relationship between OCD and VitD levels. Most of the studies were conducted in children and adolescent groups. In some studies, no significant difference was found in serum VitD in OCD patients compared to the HC group.<sup>[23,34]</sup> In a few studies, the VitD level was found to be significantly lower in the group with OCD, consistent with our study.<sup>[35-37]</sup> This difference between study results may be due to the fact that Vit D metabolism is affected by many factors. The relationship between OCD and serotonin, norepinephrine and dopamine has been demonstrated in various studies.<sup>[38-40]</sup> The active form of VitD, 1,25 dihydroxy vitamin D3, has a regulatory role for tryptophan hydroxylase and triosine hydroxylase enzymes. These two enzymes act as rate limiters in the synthesis of serotonin, dopamine norepinephrine and epinephrine. VitD can also act as an antioxidant by inhibiting inducible nitric oxide synthase.<sup>[41]</sup> VitD deficiency may play a role in OCD by both causing impaired neuroprotection and affecting serotonin and catecholamine synthesis. In some studies, it has been reported that VitD supplementation is beneficial for resistant OCD patients.<sup>[42]</sup> Larger, prospective studies are needed to support our findings and determine the efficacy of VitD supplementation in patients with OCD.

In our study, no significant difference was found between the OCD and HC groups in terms of serum ferritin levels. In a study involving all psychiatric patients treated at the hospital, a non-significant lower ferritin level was found in the group with OCD compared to other psychiatric diseases such as depression, bipolar, and schizophrenia.<sup>[43]</sup> In another study conducted in children with Tourette's syndrome, which is known to be associated with OCD, ferritin levels were found to be low. In this study, it was reported that patients' tics decreased with iron supplementation.<sup>[44]</sup> This study suggests that there may be a relationship between ferritin and OCD. Large prospective studies are needed to determine whether there is a relationship between OCD and ferritin. Considering the limited number of studies in the literature, our study can contribute to the literature at this point.

## Limitations

Our study had some limitations. Our sample was small. It is a separate limitation that remission and subclinical OCD cases were not included in the study and the severity of OCD was not taken into account. In addition, the fact that the subtypes and severity of the disease were not evaluated was a limitation.

## CONCLUSION

The low levels of serum VitB12, FA and VitD in OCD patients compared to the HC group in our study may lead to new studies to find pathways related to etiopathogenesis. Although there is sufficient evidence that deficiencies of these vitamins play a role in the etiopathogenesis of other psychiatric disorders, there is still no consensus on their relationship with OCD. It is possible that the deficiencies of these vitamins play a role in the etiopathogenesis of OCD through very different mechanisms. It may also guide studies encouraging the use of these vitamins in patients with treatment-resistant OCD. For this, prospective studies, including the post-treatment phase, are needed.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Karamanoglu Mehmetbey University Clinical Researches Ethics Committee (Date: 01.06.2023, Decision No: 5-17).

**Informed Consent:** All participants in the study provided informed consent and written permission to publish their data.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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