**ORIGINAL ARTICLE**

# Comparison of Vitamin B12 and Folic Acid Serum Levels in patients with obsessive-compulsive disorder versus healthy group

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## ABSTRACT

**Background:** There are prior evidences in regard to the relationship between folate deficiency and depressive disorders,whichemphasizedthe importance of vitamin B12 and folate in carbon transfer metabolism required for the production of serotonin. It is indicated that vitamin B12 and folic acid levels can be related to certain neuropsychiatric disorders like Obsessive-compulsive disorder (OCD).
**Aim:** To compare vitamin B12 and folic acid serum levels in patients with obsessive-compulsive disorder versus healthy group.
**Methods:** This was a cross sectional study, which was performed on patients with OCD during October 2018 to August 2019, referred to Imam Reza and Ibne-Sina hospital's clinics. Patients who were diagnosed with OCD according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria were approached and informed about the aims and methods of the study. We evaluated the serum level of Vitamin B12 and folate and compared it between OCD patients and healthy control groups.
**Results:**Thirty two patients in each group were evaluated. The mean age of them was 37.14± 11.00 years old (20-68). Twenty one patients were male (32.8%) and others were female. Vitamin B12 deficiency was significantly higher in OCD patients in comparison with control group (24 patients (75%) versus 14 patients (43.75%); P=0.011). However, folate deficiency was not significantly different between two groups (9.37% in OCD group versus 12.5% in control group; P=0.68). there was significant negative correlation between severity of OCD and level of vitamin B12 level (r=-0.301, P=0.016).
**Conclusion:** Our study showed that there is significant vitamin B12 deficiency in patients with OCD that is negatively correlated with severity of disease. Therefore, using vitamin B12 supplements in patients resistant to routine treatment can be helpful.
**Keywords:** Obsessive-compulsive disorder, vitamin B12, folate

## INTRODUCTION

The prevalence of Obsessive-compulsive disorder (OCD) is about 1%–3% globally, and it follows a chronic course with increased rates of comorbidity. Thus, it is a global burden on the patients and their families which can decrease the quality of life for both of these groups[1,2]. OCD is a psychiatric disease characterized by obsessions (all kinds of images and impulses that are involuntary and persistent) and compulsions (repetitive involuntary behaviors that are performed to clear the mind of the obsessive thoughts and to eliminate the stress caused by them)[3]. OCD is a complex psychiatric disorder that may occur due to genetics[4], alterations in fronto-striatal connections[5], psychosocial experiences, perinatal injuries, toxic pathogens, stress and traumatic events and environmental factors like infections, particularly streptococcal infections[6].

Earlier studies focused on the relationship between folate deficiency and depressive disorders[7]. These observations may be explained by the importance of vitamin B12 and folate in carbon transfer metabolism (methylation), which is required for the production of serotonin, other monoamine neurotransmitters, and catecholamines(8). It is demonstrated that vitamin B12 and folic acid levels can be associated with certain neuropsychiatric disorders. Moreover, B12 and folate deficiency were shown to have an impact on brain functions and cause non-specific psychiatric symptoms[9]. In a few studies on adult patients with OCD, there is some evidence of deficient levels of folic acid and vitamin B12 in adult patients with OCD[10,11]. There are some cases of OCD that are due to a vitamin B12 deficiency have been reported[12,13].

According to low level of evidence, in this study, we compared vitamin B12 and folic acid serum levels in patients with obsessive-compulsive disorder versus healthy group.

## METHODS

**Study Population:** This was a cross sectional study, which was performed on patients with OCD during October 2018 to August 2019, referred to Imam Reza and Ibne-Sinahospital's clinics. IbneSina hospital is a referral center of psychiatric disorders in north eastern of Iran with 700 beds capacity. Imam Reza hospital is the biggest general hospital of Mashhd in north eastern Iran and had a psychiatric ward with .. beds.
**Study design:** Patients who were diagnosed with OCD according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria

were approached and informed about the aims and methods of the study.

All patients provided their informed consent and then enrolled in the study. We enrolled 95 participants and finally because of no cooperation of 31 patients, 64 of them were finally evaluated. We entered 32 patients with OCD diagnosis and 32 healthy persons in a control group that were matched with age and gender.

**Eligibility:** We included patients with a definite diagnosis of OCD. Patients with mental retardation, growth disorders, psychotic disorders, substance and alcohol abuse, history of endocrine disorders and pregnant or breastfeeding patients or more than 60 years old were excluded. We also excluded patientsconsumpedsupplements in recent one year or vegetarians and patients who had food limitations following OCD. In addition, both groups did not have a history of major mood disorder, dementia, mental retardation, or psychosis in their first-degree relatives.

**Tools:** The patients were diagnosed with the Structured Clinical Interview for DSM-V Axis I Disorders[14]. Diagnosis of depression or anxiety was based on clinical interview. The Yale–Brown Obsessive–Compulsive Scale27 were used for evaluating severity and comorbidities. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is a clinician-administered instrument, consists of 10 items which are 5-point Likert-type scales characterizing the time spent on compulsions (item 1), interference from obsessions (item 2), distress associated with obsessions (item 3), resistance to obsessions (item 4), subject's control over obsessions (item 5) and equivalent items for compulsions (items 6–10). The total number is between 0-40 and the score 16 is considered as threshold of disorder for administration of drug[15]. Optimal levels of internal consistency scores (symptom checklist 0.97, severity scale 0.95) reliability (symptom checklist 0.93, severity scale 0.89), and test-retest reliability (0.99) were calculated before in Iranian population study[16].

**Sampling:** Venous blood samples were collected after overnight fasting. Folate, and vitamin B12 levels were measured in all subjects. Blood was drawn into tubes containingethylenediaminetetraacetic acid, immediately placed on ice, and centrifuged at 4°C. Plasma was separated and immediately stored at -80°C before it was analyzed. Cutoffs were used to determine vitamin deficiency.

**Statistic:** All data were entered in SPSS version 11.5 Descriptive data analysis was performed and it was analyzed. To compare the quantitative variables in two groups, independent T-Test or Mann-Whitney test was used. The chi square test was used for comparison of categorical variables. Pearson correlation or Cohen's D were also used for effect size. P value lesser than 0.05 was considered as significant.

**Ethics:** This study evaluated by an editorial review board of medical faculty and approved by the ethical committee of Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1397.402).

## RESULTS

In this study, we evaluated 64 patients (32 patients in control and 32 patients in case group). The mean age of participants was 37.14± 11.00 years old (20- 68). Twenty one patients were male (32.8%) and others were female. Demographics of two groups are listed in Table1.

The mean of Y-BOCS score was 12.63± 13.59 in OCD participants. Table2 shows the level of vitamin B12 and folic acid in the OCD group versus the control group.

According to the results of vitamin B12 and folic acid level, vitamin B12 deficiency was significantly higher in OCD patients in comparison with control group (24 patients (75%) versus 14 patients (43.75%); P=0.011). However, folate deficiency was not significantly different between two groups (3 patients (9.37%) versus 4 patients (12.5%); P=0.68) (Figure1).

Our correlation analysis showed that there was significant negative correlation between severity of OCD and level of vitamin B12 level (r=-0.301, P=0.016) (Table3).

Table1- Demographic characteristics of patients in both groups

| Variable | Group | | P |
|---|---|---|---|
| | Case (n= 32) | Control (n= 32) | |
| Gender (n, %) | Male (10, 47.6)<br>Female (22, 51.2) | Male (11, 52.4)<br>Female (21, 48.8) | 0.79 |
| Age (years) (mean± S.D) | 37.50± 11.48 | 36.78± 10.66 | 0.64 |

OCD= obsessive convulsive disorder, SD: standard deviation.

Table2- The mean and effect size level of vitamin B12 and folic acid in two groups

| Variable | Group | | Cohen's d |
|---|---|---|---|
| | OCD patients (n=32) | Control patients (n=32) | |
| Folic acid (mean± S.D) | 12.87± 6.98 | 9.66± 6.04 | 0.070 |
| Vitamin B12 (mean± S.D) | 738± 205.50 | 879.00± 294.21 | 0.048 |

OCD= obsessive convulsive disorder, SD: standard deviation.

*The interpretation of the effect size was as follows: 0.0–0.19, trivial; 0.20–0.49, small;0.50-0.79,moderate; and >0.80, large (17).*

Figure1- The difference between folate deficient cases and vitamin B12 cases in OCD and control groups

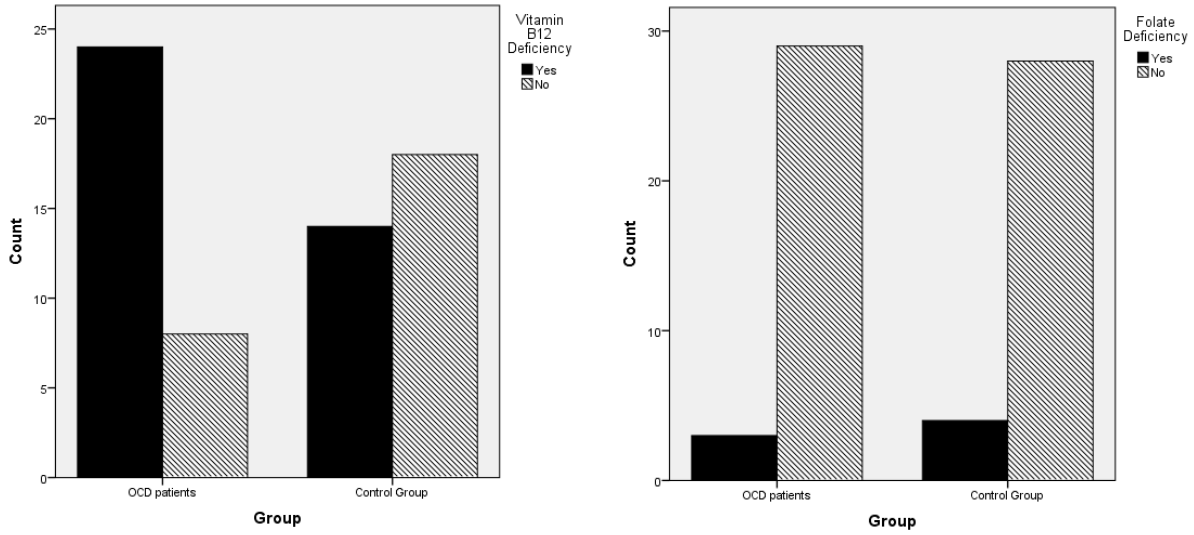


Table-3: Inter-correlations of VIT 12, folic acid and YBOCS with age

| Variables | | Age | VITB12 | Folic acid | YBOCS |
|---|---|---|---|---|---|
| Age | Pearson Correlation | 1 | 0.105 | 0.035 | 0.044 |
| | Sig. (2-tailed) | | 0.410 | 0.781 | 0.731 |
| VITB12 | Pearson Correlation | 0.105 | 1 | .181 | -0.301* |
| | Sig. (2-tailed) | 0.410 | | .152 | 0.016 |
| Folic acid | Pearson Correlation | 0.035 | 0.181 | 1 | 0.244 |
| | Sig. (2-tailed) | 0.781 | 0.152 | | 0.052 |
| YBOCS | Pearson Correlation | 0.044 | -0.301* | 0.244 | 1 |
| | Sig. (2-tailed) | 0.731 | 0.016 | 0.052 | |

*YBOCS= The Yale-Brown Obsessive-Compulsive Scale; *. Correlation is significant at the 0.05 level (2-tailed).*

## DISCUSSION

To our knowledge, investigations regard to evaluate the level of vitamin B12 and folate level in OCD patients. Our main findings were significant difference between vitamin B12 level in OCD patients versus control group and not folate level. We also showed that there was significant correlation between serum level of vitamin B12 and OCD severity.

It was reported a case of a middle-aged male patient presenting with OCD, low levels of serum vitamin B12, and a positive family history of vitamin B12 deficiency who responded well to methylcobalamin replacement. Accordingly, it was suggested a possible etiological role of vitamin B12 in OCD[13]. Similar to our study, Turksoy et al. demonstrated in their study that vitamin B12 levels were decreased significantly in some OCD patients. However, there was no significant difference between folate level in OCD and control group participants[11]. In a previous investigation, it is indicated that vitamin B12 deficiency was more frequent in OCD patients than controls. This suggests that obsessive–compulsive symptoms can be a marker for vitamin B12 deficiency and predicts more well-known symptoms of it[18]. Atmaca et al reported that serum folate values were significantly lower in OCD patients than controls, while homocysteine concentrations were higher in patients compared to controls[10]. It was in contrast with our results that shows higher level of folate level probably because of different race in study population or geographical difference. It was demonstrated in another study that vitamin B12 and vitamin D levels were significantly lower in patients compared to healthy controls, whereas homocysteine was higher in the patient group. There was no significant difference between groups in terms of folic acid levels[19].

It is suggested that it might point to the possibility that vitamin B12 deficiency characterizes a subgroup of OCD patients[18]. It is also indicated that folate levels in those patients were significantly and negatively correlated with the scores on the Yale–Brown Obsessive–Compulsive Scale while levels of homocysteine were positively correlated with the duration of illness and Yale–Brown Obsessive–Compulsive Scale scores[10]. Considering patients who had received previous anti-obsessive therapy with no benefit from it, the high rates of B12 deficiency may be indicative of a selected group featuring a larger than usual representation of a patient subgroup resistant to treatment in addition to high rates of vitamin B12 deficiency.

Our study had some limitations. The most important was low sample size. Determination of other disorders were evaluated by clinical interview not a standardized questionnaire.

## CONCLUSION

Our study showed that there is a significant vitamin B12 deficiency in patients with OCD that is negatively correlated with severity of disease. Therefore, using vitamin B12 supplement in patients who are resistant to usual therapeutic agents or evaluation of vitamin B12 level are helpful approaches in management of OCD patients.

**Conflict of interest:** There was no conflict of interest.

**Acknowledgement:** This study funded by Mashhad University of Medical Sciences.

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