

Assessment of Folate and Vitamin B12 Levels According to Gender in Psychiatric Patients in Şırnak Region

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Abstract

The most severe and prevalent type of neuropsychiatric condition affecting millions of people globally is major depressive disorder. The aim of our study is to evaluate the folate and vitamin B12 levels of outpatient psychiatric patients in Şırnak province, according to gender. The patients who applied to the Psychiatric Services of the state hospitals in the Şırnak region between January 1, 2021, and January 5, 2022, were found by conducting a retrospective search of the hospital databases for folate and vitamin B12 levels. Device reference ranges between 200-771 pg/mL were accepted for the evaluation of vitamin B12 levels and 4.6-18.7 ng/mL for the evaluation of folate levels. 9.6% of the males and 13.7% of the women who applied to the psychiatry service in Şırnak during the study period had B12 levels below 200 pg/mL, whereas 86.5% of the men and 84.3% of the women had B12 levels between 200 and 771 pg/mL. It was found that 3.8% of men and 2% of women were above 771 pg/mL. It was found that there was no significant difference in the statistical analysis results according to gender ($P>0.05$). In folate levels, 56.3% of male patients and 42.9% of females had folate levels below 4.6 ng/mL, while 43.7% of men and 50% of women had folate levels between 4.6-18.7 ng/mL. It was observed that there was no statistically significant difference in the folate levels of the patients according to gender ($P>0.05$). In our study, we did not find any evidence that the rate of vitamin B12 deficiency differs according to gender in psychiatric patients. Although Folate level was not statistically significant according to gender, it was found to be significant as a percentage. Eating habits can be linked to depression by changing serum folate and vitamin B12 levels depending on gender.

Keywords: Biochemistry, psychiatry, B12, folate

INTRODUCTION

A chronic and recurrent mental illness called major depressive disorder (MDD) is characterized by low mood, social withdrawal, and anhedonia (Dudek et al., 2021). Today, depression, which takes its place among important diseases all over the world, especially in developed countries, increases its severity day by day like an epidemic. Depression, which is the second most disabling disease for the 15-44 year-olds worldwide, ranks fourth after AIDS, diarrhea and respiratory tract disorders among all age groups (Acarcan and Nazlıkul, 2017). Deprivation of micronutrients concerns the living conditions of approximately two billion people worldwide and can lead to deficiencies triggered by different biochemical mechanisms. Drug components such as "phenothiazines", a tricyclic antidepressant derivative that affects coenzyme Q10 and vitamin B2, "benzodiazepine", a psychotherapeutic drug derivative that affects melatonin and calcium metabolism, and selective serotonin reabsorption inhibitors (SSRIs) that affect folic acid metabolism, are effective in endogenous production. Has been reported to cause deficiencies (Karadima et al., 2016). The negative effects of drugs used on the basis of the pathophysiology of psychiatric diseases on neurological, hematological, gastrointestinal and endocrinological systems are widely mentioned (Demirkol et al., 2019; Moretti et al., 2021). Folate and vitamin B12 mechanisms with proven effects on mood disorders in psychiatric cases play a role in many important processes related to neurodegenerative diseases. Small molecule folic acid is also referred to as vitamin B9. Folic acid is a very significant molecule, especially in its ionic form, which is involved in numerous critical metabolic processes in

humans (Gazzali et al., 2016). It is crucial for DNA replication and methylation, homocysteine metabolism, and the synthesis of purines and pyrimidines (Vorobei and Vorobei, 2011; Borradale et al., 2014). Since humans cannot produce vitamin B12 and must instead receive it from animal protein, vitamin B12 is a crucial micronutrient. Vitamin B12 that has been consumed must go through a protracted assimilation and absorption process. Cellular activity requires vitamin B12 to function. 15% of patients over the age of 65 are said to be affected by deficiency, which has been linked to neurological and hematological diseases (Romain et al., 2016). Additionally, there is strong evidence that persons with depression have lower levels of folate and vitamin B12 (Kar et al., 2018). In this respect, the relationship between mental disorders and folate and vitamin B12 levels is very important. This study aims to shed light on future comprehensive research by retrospectively evaluating the folate and vitamin B12 status of psychiatric patients in the Şırnak region according to gender.

MATERIALS and METHODS

This study was carried out on patients who applied to the Psychiatry Service of Şırnak State Hospital between January 1, 2021, and January 5, 2022, after receiving approval from the Şırnak University Ethics Committee (dated 26.05.2022, numbered 2022/82). It was done retrospectively by scanning the soles. Device reference ranges of 200-771 pg/mL were accepted for the evaluation of vitamin B12 levels and 4.6-18.7 ng/mL for the evaluation of folate levels. Folate concentration below 4.6 ng/mL and vitamin B12 concentration below 200 pg/mL were considered inadequate levels. All diagnostic groups were included in the study for objective

evaluation. In total, folate and vitamin B12 values of 133 patients were reached. While evaluating the findings, SPSS 21 program was used for statistical analysis and Fisher's Exact test was applied. $P < 0.05$ was considered significant.

RESULTS

In this study, serum vitamin B12 levels of 103 patients were evaluated. B12 levels were evaluated according to gender. It was determined that 9.6% of men and 13.7% of women had B12 levels below 200 pg/mL. Additionally, it was determined that the B12 levels of 86.5% of men and 84.3% of women were between 200-771 pg/mL, and 3.8% of men and 2% of women were above 771 pg/mL. There was no significant difference in the statistical analysis results according to gender ($P > 0.05$). (Table 1). However, even though the data were not statistically significant, it

was noteworthy that serum vitamin B12 levels were higher in men compared to women (Figure 1). At the same time, serum folate levels of 30 patients were evaluated. and according to the results obtained, serum folate levels of 56.3% of male patients and 42.9% of females were below 4.6 ng/mL, while serum folate levels of 43.7% of males and 50% of females were below 4.6 ng/mL. It was below 4.6 ng/mL. women had serum folate levels. It was observed that the levels were between 4.6-18.7 ng/mL. Additionally, it was determined that the serum folate level of 0.0% of men and 7.1% of women was above 18.7 ng/mL. It was observed that the difference between the serum folate levels of the patients according to gender was not statistically significant (Table 2) ($P > 0.05$). However, it is mathematically possible to say that men have lower serum folate levels than women.

Table 1. Evaluation of B12 Levels by Gender

B12 level, pg/mL	Male	Female	X ² value* P value
<200 deficiencies	5/52 (%9.6)	7/51 (%13.7)	
200-771 Normal	45/52 (%86,5)	43/51 (%84,3)	X ² =0.798 p=0.739
>771 high	2/52 (%3.8)	1/51 (%2.0)	

* Fisher's Exact Test was used ($p < 0.05$)

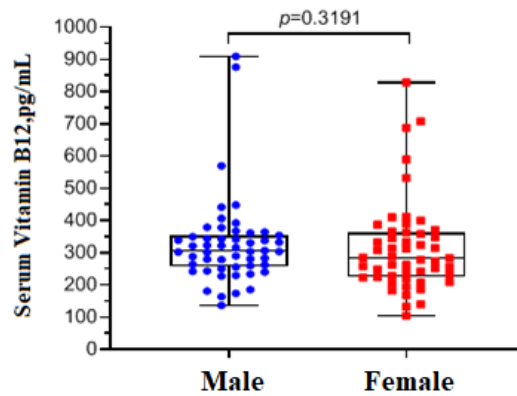


Figure 1. Graph showing the relationship of vitamin B12 between men and women

Table 2. Evaluation of Folate Levels by Gender

Folate, ng/mL	Male	Female	X ² value* P value
<4.6 deficiencies	9/16 (%56.3)	6/14 (%42.9)	X ² =1.432 p=0.582
4.6<x<18.7 Normal	7/16 (%43.8)	7/14 (%50.0)	
>18.7 high	0/16 (%0.0)	1/14 (%7.1)	

* Fisher's Exact Test was used (p<0.05)

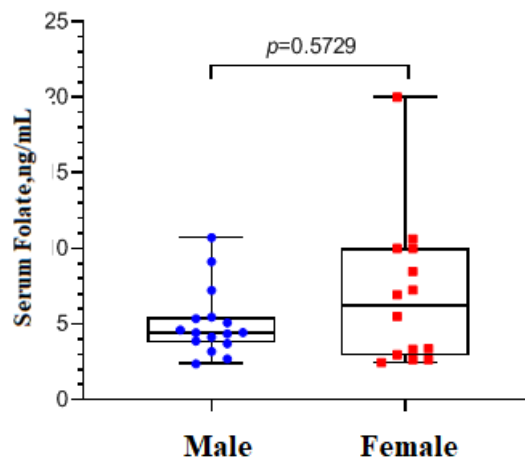


Figure 2. Graph showing the relationship between folate male and female

DISCUSSION

The most severe and prevalent type of neuropsychiatric condition, major depressive disorder, affects millions of people worldwide. The brain monoamine hypothesis and traditional antidepressants, which block the reuptake of monoamine neurotransmitters to increase synaptic monoamine concentrations to interact with postsynaptic receptors, are the mainstays of current treatment. In the drug treatment of major depressive disorder, the treatment processes become quite complicated due to reasons such as the lack of awareness of the sick individuals, the deficiencies in their drug intake and the inability to get a positive response to the treatment. Recent research suggests that the dietary status of people with major depressive disorder affects how the disease progresses and that vitamins and minerals in particular have an impact on the central nervous system. Major depressive illnesses are caused by the central nervous system's mechanism of action. Among the metabolites that have a significant impact on the central nervous system are folate and vitamin B12. These metabolites' significance and role in psychiatric illnesses have established themselves in an unchallengeable position. For this reason, the focus of psychiatric studies focuses on folate and vitamin B12 levels. In this study, it was determined that 9.6% of men and 13.7% of women had serum vitamin B12 levels below 200 pg/mL, while 86.5% of men and 84.3% of women had B12 levels in the range of 200-771 pg/mL. has been found to be. It was found that 3.8% of men and 2% of women were above 771 pg/mL. The importance of serum vitamin B12 levels in hematopoiesis, the preservation of gastrointestinal mucosal activity, the maintenance of central nervous system activities, and the

maintenance of other metabolic pathways influenced by vitamin B12 has been established (Baytan et al., 2007). Research similar to ours on mental patients in Eskişehir revealed that 15.5% of patients had overall low vitamin B12 levels (Kar et al., 2018). Another similar study by Atada et al. found that there was a 16.1% vitamin B12 deficiency in the association between depression and anxiety (Atadağ et al., 2017). In another study investigating depression patients of Turkish and German origin, it was stated that Turkish patients had lower levels of vitamin B12, which was statistically significant compared to German patients. Even if the underlying reasons for this situation have not been fully clarified yet, additional food supplements should be recommended for Turkish patients to maintain their vitamin B12 levels (Yener and Van Loon., 2009). In a study conducted to evaluate the risk of depression, no correlation was found between vitamin supplementation and depression in women who were given vitamin B6 and B12 supplements regularly for a certain period of time (Okereke et al., 2015). In another study, Hintikka et al. evaluated vitamin B12 and folate levels in individuals diagnosed with major depressive disorder. Hintikka et al. found better clinical pictures in people with high vitamin B12 levels. However, they reported that they could not observe any significant change after 6 months of follow-up (Hintikka et al., 2003). Although the relationship between depression and anxiety disorders and vitamin B12 levels is known, it is possible to come across studies claiming that this relationship could not be established. In this study, we found that vitamin B12 deficiency in psychiatric patients was generally within acceptable limits. Folate levels of 56.3% of male patients and 42.9% of female patients

were below 4.6 ng/mL, and 43.7% of men and 50% of women had folate levels between 4.6-18.7 ng/mL. detected. In addition, 0.0% of men and 7.1% of women were found to be above 18.7 ng/mL. In a study that included psychiatric patients, it was reported that folate levels were 10-33%, while it was between 5-8% in individuals without psychiatric disorders (Lerner et al., 2006). Another study conducted on 213 American outpatients diagnosed with depression revealed the association of low folate levels with depressed patients. It is also said that although they receive standard antidepressant treatment according to treatment protocols, their response to treatment is very low (Abou-Saleh and Coppen., 2006). In a study conducted on individuals from Hong Kong, it was mentioned that serum folate levels were within normal ranges in patients diagnosed with major depressive disorder. and researchers added that they owe these levels to the Chinese diet, which is rich in green vegetables, which is a natural antioxidant and vitamin store, so they maintain their folate levels in this way (Lee et al., 1998). In our study, although the level of folate in psychiatric patients was not statistically significant when we evaluate the percentage rate, it is seen that the level of folate in psychiatric patients is important. The mechanism by which folate and vitamin B12, which are known to be effective in the pathophysiology of the aforementioned disease, work has not yet been clarified. For this reason, obtaining different results gives rise to the idea that comprehensive studies are needed. The extent to which changing nutrition and vitamin intake will be effective in psychiatric patients is within the limitations of this subject. Our biggest limitation was that our study was retrospective and the number of patients accessible was small. However, the

study is extremely important as it is the first study conducted in Şırnak province and reveals the relationship between folate and B12 in the psychiatric patient profile of the region. It is important to carry out prospective and controlled studies that will include the surrounding provinces in order to provide a clearer interpretation within the possibilities in the future. Additionally, interactions between various meals may enhance the antidepressant benefits of folate and vitamin B12. For instance, in addition to folate and vitamin B12, fruits and vegetables also include non-nutrients that are good for the body when consumed in a healthy diet. Dietary fiber is a remarkable example of a non-nutrient since it influences the gut microbiota to enhance immunological and inflammatory responses. Additionally, dietary fibre and phytochemicals together help lessen inflammation and oxidative stress. Numerous illnesses, including depression, have been linked to inflammation and impaired immunological function. Additionally, the antidepressant effects of folate and vitamin B12 may be diminished by the interactions between various foods and unhealthy eating patterns. It is significant to emphasize that healthy diets with reduced intakes of unhealthy foods may also lower the incidence of depression (Khosravi et al., 2020). As a result; The first goal should be to take additional precautions and maintain folate and vitamin B12 levels, which are known to be related. This is in addition to pharmacological treatments for mentally ill patients. Eating habits can be linked to depression by changing serum folate and vitamin B12 levels according to gender. More research is needed to confirm this mechanism. A balanced diet can reduce the risk of depression by increasing blood levels of folate and

vitamin B12. However, poor nutrition may increase the risk of depression by reducing the level of vitamins in the serum. We have obtained significant evidence supporting the literature showing that there is a mathematical decrease in folate levels according to gender. Since we found the folate levels in this study to be compatible with some studies in the literature, we can say that especially folate and vitamin B12 levels should be routinely evaluated to prevent the symptoms and treatment resistance of psychiatric patients. Essentially, it will be very important for people with depression to start taking vitamin supplements and reduce their use of antidepressants as the disease progresses. More extensive research is recommended to confirm the results.

REFERENCES

- Abou-Saleh, M.T., Coppen, A. 2006. Folic acid and the treatment of the depression. *Journal of Psychosomatic Research* 61: 285-287.
- Acarcan, T., Nazlıkul, H. 2017. Depresyona tamamlayıcı tıp yaklaşımı. *Journal of Complementary Medicine, Regulation and Neural Therapy* 11: 20-23.
- Atadağ, Y., Aydın, A., Köşker, H.D. 2017. Vitamin B12 ve depresyon-aksiyete bozuklukları ilişkisi: Retrospektif kohort çalışma. *Arch Clin Exp Med.* 2:6-8.
- Baytan, B., Özdemir, Ö., Erdemir, G. 2007. Çocukluk çağında vitamin B12 eksikliği klinik bulgular ve tedavi. *Uludağ Üniversitesi Tıp Fakültesi Dergisi.* 33(2): 61-64.
- Borradale, D., Isenring, E., Hacker, E. 2014. Exposure to solar ultraviolet radiation is associated with a decreased folate status in women of childbearing age. *J Photochem Photobiol B.* 131:90-95.
- Demirkol, M.E., Tamam, L., Çakmak, S. 2019. Şizofreni tanılı hastalarda metabolik sendrom ve D vitamini düzeyleri ilişkisi. *Cukurova Medical Journal* 44:1110-1117
- Dudek, K.A., Dion-Albert, L., Kaufmann, F.N. 2021. Neurobiology of resilience in depression: immune and vascular insights from human and animal studies. *Eur J Neurosci.* 53:183-221.
- Gazzali, A.M., Lobry, M., Colombeau, L. 2016. Stability of folic acid under several parameters. *Eur J Pharm Sci.* 93:419-430.
- Hintikka, J., Tolmunen, T., Tanskanen, A. 2003. High vitamin B12 level and good treatment outcome may be associated in major depressive disorder. *BMC Psychiatry* 3: 17.
- Kar, F., Hacıoğlu, C., Küskü Kiraz, Z. 2018. Eskişehir'deki Psikiyatrik Hastalarda Folat ve B12 Vitamin Seviyelerinin Değerlendirilmesi. *TJLS.* 3: 210-213.
- Karadima, V., Kraniotou, C., Bellos, G. 2016. Drug-micronutrient interactions: food for thought and thought for action. *EPMA J.* 7(1):10.
- Khosravi, M., Sotoudeh, G., Amini, M. 2020. The relationship between dietary patterns and depression mediated by serum levels of Folate and vitamin B12. *BMC Psychiatry.* 20:63.
- Lee, S., Wing, Y.K., Fong, S. 1998. A controlled study of folate levels in Chinese inpatients with major depression in Hong Kong. *J Affect Disorders,* 49:73-77

- Lerner, V., Kanevsky, M., Dwolatzky, T. 2006. Vitamin B12 and folat serum levels in newly admitted psychiatric patients. *Clinical Nutrition* 25:60-67.
- Moretti, R., Giuffré, M., Caruso, P. 2021. Homocysteine in Neurology: A Possible Contributing Factor to Small Vessel Disease. *Int J Mol Sci.* 22: 2051.
- Okereke, O.I., Cook, N.R., Albert, C.M. 2015. Effect of long-term supplementation with folic acid and B vitamins on risk of depression in older women. *Br J Psychiatry* 206: 324-331.
- Romain, M., Sviri, S., Linton, D.M. 2016. The role of Vitamin B12 in the critically ill--a review. *Anaesth Intensive Care.* 44: 447-452.
- Vorobei, A.V., Vorobei, P.A. 2011. Photosensitized degradation of folic acid *J. Appl. Spectrosc.,* 78:614-616
- Yener, G., Van Loon, P. 2009. Vitamin B12 status in patients of Turkish and dutch descent with depression: a comparative cross-sectional study. *Ann General Psychiatry* 8: 18.