

Original article

# Impact of Serum Folate and Vitamin B12 on Mental Health in Patient Admitted at Razi Psychiatric Hospital

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## ABSTRACT

Vitamin B12 (cobalamin) is one of the essential vitamins that affect various systems in the body, including the central nervous system and plays an important role in the metabolism of the nervous system, although its exact role under pathological conditions is not fully understood. The present study aimed to assessing vitamin B12 & serum folate in patient admitted at Razi psychiatric hospital. A cross section study subjects were inpatients with psychiatric disorder, patients from 21 to 60 years old. In this group of 40 psychiatric patients, there is no evidence of clinically relevant changes in serum vitamin B12 and folate level. Vitamin B12 deficiency can occur despite "normal" serum cobalamin levels; therefore, measuring homocysteine and methyl malonic acid can decrease false-negative findings.

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## INTRODUCTION

Vitamin B12 (cobalamin) are water-soluble micronutrients that have to be consumed in adequate quantities from diet, The incidence appears to be increase with age , cobalamin plays a key role in DNA synthesis and neurologic function, deficit can lead to a wide spectrum of hematologic and neuropsychiatric disorders that can often be reversed by quick diagnosis and immediate treatment [1]. Vitamin B12 is extremely important vitamins that affect different systems in the body, as the central nervous system and plays a significant role in the metabolism of the nervous system, whereas under pathological conditions is incompletely understood [2]. There is another study explain two possible mechanisms linking vitamin B12 deficiency and abnormal behavior and development possibly through demyelination and inflammation; possibly simulating an autoimmune process that blocks intrinsic factor for cobalamin absorption, similar to pernicious anemia an autoimmune disease that blocks intrinsic factor [3]. The goal of this study was to high light the importance of early diagnosis of vitamin B12 deficiency given pattern of the patients enrolled [2]. Cobalamin is crucial for maintaining neuronal health and deficiency leading to myeloneuropathy is rare in developed countries [1], cobalamin deficiency has been implicated in a spectrum of neuropsychiatric disorders, the true prevalence of vitamin B12 deficiency in the general population is unknown [1].

Subclinical vitamin B12 deficiency, defined as less than 200 p mol/L of serum vitamin B12, frequently remains asymptomatic over years predicated on the anti-oxidative property of vitamin B12, cobalamin deficiency might lead to oxidation of lipids, proteins and nucleic acids and might contribute to the development of age-related diseases, in which oxidative stress is believed to be a major factor; including Parkinson disease and others [4]. Nutrition support is very important in all age groups, especially in the elderly and children, nutritional B12 deficiency is rare in children with nonspecific symptoms, including, vomiting, anorexia and neurological changes with or without hematologic disturbances. Symptoms cover expansive spectrum, including weakness, tiredness, lightheadedness, rapid heartbeat and breathing, pale skin, soreness, easy bruising and bleeding, sore tongue, gastric upset, weight loss, diarrhea or

constipation, lack of motivation and energy, muscle weakness and tingling in the extremities. Other neurological findings include altered sensation, paresthesia in the extremities, gait ataxia, poor vision, dizziness [5], urinary or fecal incontinence, and loss of cutaneous sensation, impaired sense of vibration, psychiatric manifestation, memory impairment, personality changes, convulsions, hypotonia, developmental delay, poor activity. While it is common during infancy and adolescence in developing and underdeveloped countries, a high level of awareness is required in order to prevent permanent neurological damage from B12 deficiency, especially in children with mild symptoms [5]. Vitamin B12 is cofactor dependency for enzymatic reactions involved in one-carbon (1-C) metabolism [2]. Neuropsychiatric manifestations of vitamin B12 deficiency as the early 20th century, studies have reported psychiatric symptoms in patients with pernicious anemia that is associated with B12 deficiency, the wide range of vitamin B12 related neuropsychiatric disorder include major depression, bipolar disorder, schizophrenia. An early recognition of the vitamin B12 deficiency followed by adequate supplementation of B12 often is clinically rewarding as patients are likely to recover [2].

Folate deficiency in the per conception period donate to neural tube defects; deficits in vitamin B12 (cobalamin) have negative outcome on the developing brain during infancy, and deficits of both vitamins are associated with a greater risk of depression during adulthood [3]. Folate plays vital role in the metabolic regulation of amino acids and nucleic acids, and in one-carbon metabolism. Folate must be acquired from the diet, and supplementation is absolutely recommended in populations at risk for deficiency due to specific conditions. Folic acid is the synthetic form of the vitamin, usually incorporated into foods and supplements. In the body, it must be reduced into the bioactive folate derivative (6S) 5-MTHF by cell metabolism. Folate deficiency is related to many health issues such as neurological disorders and can increase cardiovascular disease risk. Women of childbearing age and pregnant women, are the main populations at risk for folate deficiency. Folate supplementation is broadly used for fertility, for the obstacle of embryonal neural tube defects (NTDs) in pregnancy [6].

Vitamin B12 and folate play a key role involved in different brain processes, altered levels have been reported in neuropsychiatric disorders, particularly in major depression, while the information is limited. Therefore, this study aimed to assessing serum vitamin B12 & folate in patient admitted at Razi Psychiatric Hospital.

## METHODS

In this cross-sectional study, we extracted data collected between 01/05/2024 and 05/05/2024 from Razi Psychiatric Hospital at the Department of Psychiatry and Psychotherapy. Subjects were inpatients with psychiatric disorder who were psychiatrically stable on antipsychotic treatment. Patients age from 21 to 60 years old. Records were individually screened by five authors using the following inclusion criteria manually extracted data; Inpatients, Collect blood sample for assessment of vitamin levels (folate & vitamin B12). Then blood parameters of serum vitamin B12, folate were measured according to common clinical-chemical methods. Vitamin B12 levels were assayed by Siemens IMMULITE 1000 Immunoassay System and results obtained in pmol/L [7]. This cross-section study was approved by the Ethics committee of the Faculty of Medicine, at University of Zawia and Administration of Razi Psychiatric Hospital, waived informed consent. Then data was analyzed by using SPSS version 26 and results obtained.

## RESULTS

Table 1 shows the distribution of 40 patients based on age group. There is a fairly even spread of patients a cross the different adult age groups from 21 to 60 years old. The 51-60 years group has slightly more patients than the other groups. There are no patients under 21 or over 60 in this sample.

*Table 1. Patients' distribution based on age*

Age group	Count	%
21-30	10	25.0
31-40	9	20.0
41-50	10	25.0
51-60	12	30.0
<b>Total</b>	40	100.0

From table 2, it can be seen that test some variables for patients with psychological and mental illnesses The mean values for MCV, MCH, MCHC, folate and VB12 all fall within their respective normal reference ranges Standard deviations indicate there is some variability around these means, particularly for VB12 and folate levels the t-tests evaluate whether the sample means differ significantly from population means (the standard values). In all cases, the

high p-values (0.841 to 0.999) indicate no statistically significant difference between the sample averages and normal averages. In summary, these findings do not identify any hematological abnormalities in this group of psychiatric patients relative to healthy populations. Levels align with normal reference standards.

**Table 2. Test some variables for patients with psychological and mental illnesses**

Variable	N	Standard value	Mean	Standard deviation	T value	P-value
MCV	40	80-96	86.46	8.66	2.11	0.964
MCH	40	27-33	30.58	2.53	8.95	0.999
MCHC	40	32-36	33.07	4.90	1.38	0.912
Folate	40	2.7-17.0	3.49	3.46	1.44	0.922
VB12	40	200-900	320.74	129.52	1.01	0.841

Table 3 compares mean values for several red blood cell and micronutrient indices between psychiatric male patients (n=32) and female patients (n=8), for MCV, MCHC and folate levels the mean values are very similar between genders. T-tests confirm there is no statistically significant difference in averages between the groups as evidenced by low t-statistics and high p-values, for MCH and VB12, males have slightly higher averages compared to females. However, the t-tests yield p-values > 0.05, indicating these differences are still not considered statistically significant. In summary, when comparing psychiatric patients directly along gender lines, there are no significant differences found in red blood cell parameters or nutritional markers. Larger subsample sizes, especially for females, could provide validation of trends. Exploring differences based on specific mental health conditions rather than broad gender categories may reveal more insights as well.

**Table 3. Comparison between males and females' patients with psychological and mental illnesses according to some variables.**

Variable	Gender	N	Mean	Standard deviation	T value	P-value
MCV	Male	32	86.89	9.37	0.623	0.537
	Female	8	84.74	4.91		
MCH	Male	32	30.90	2.26	1.617	0.114
	Female	8	29.31	3.28		
MCHC	Male	32	33.04	5.46	-0.083	0.934
	Female	8	33.20	1.38		
Folate	Male	32	3.15	3.33	-1.231	0.226
	Female	8	4.83	3.87		
VB12	Male	32	337.37	127.78	1.660	0.105
	Female	8	254.24	121.78		

## DISCUSSION

Vitamin B12 is linked to large scale of symptoms, though the classical presentation of vitamin B12 deficit is hematological, it is predominant to note that neuropsychiatric manifestations could be the early symptom of a developing vitamin B12 and folate deficiency syndrome or sometimes the only manifestation of vitamin B12 deficit. Over the last century, several manifestations related to neuropsychiatry have been reported concerning vitamin B12, folate deficiency. It is interesting to note that patients admitted to mental institutions [8]. The deficiency of vitamin B12 can masquerade as a psychiatric presentation. It is essential to identify the underlying cause as psychiatric manifestation could be the initial and only manifestation of vitamin B12 deficiency. The elderly, vegetarian diet, chronic mental illness, and alcohol abuse are common predisposing factors for B12 deficiency. In a realized psychiatric disorder, it is preferable to maintain the serum vitamin B12 levels at elevated normal range [2].

Our results come from a study analyzing vitamin b12 and folate markers in a sample of 40 psychiatric patients (32 males, 8 females). Multiple metrics were compared between genders and against normal reference ranges. Key findings show that overall, the averages for folate, and vitamin B12 levels in these patients largely fell within expected ranges for healthy populations of the corresponding gender. Statistical tests did not detect significant deviations between the psychiatric population means and standard values. When compared directly along gender lines, there were also no statistically significant gaps identified for any markers between male and female psychiatric patients. So, their some studies support these results due to effect of antidepressant drugs can increase vitamin B12 and other studies explain

false negative results. In this study in adults and children the use of valproic acid was found to correlate with a higher vitamin B12 level. Nearly all studies found an increase in vitamin B12 in adults and children using carbamazepine. Among the users of valproic acid, it was only children who showed a clear association with a rise in vitamin B12 [8]. Vitamin B12 deficiency definitions vary and usually rely on population statistics to establish normal serum-level thresholds (normal range: 200 pg/ml–900 pg./ml). This can be problematic because individual metabolic requirements may vary, and active deficiency can be present despite a “normal level.” False-negative results can also be explained because vitamin B12 levels are altered by the concentration of its binding proteins, and radio immunoassays may detect in active forms of cobalamin that may mask tissue deficiencies of active cobalamin [9]. Higher homocysteine (Hcy) levels have been recognized in bipolar disorder (BD) patients, and BD patients appear circadian rhythm disorders even during diminution of intensity [1].

Vitamin B12 deficiency impairs the enzymatic functions of L-methyl- malonyl–coenzyme a mutase and methionine synthase leading to elevated plasma levels of accumulation of methyl malonic acid (MMA) and homocysteine, respectively. Hence, the elevated MMA and Hcy concentration in the peripheral blood could be used as an early and sensitive marker of vitamin B12 deficiency [2].

It is known that vitamin B12 deficiency associated with depression. Vitamin B12 deficiency plays a role in the formation of depression with its effects on the adrenergic system, glutamatergic system, serotonin system, and dopamine system [10]. It was reported that the incidence of depression is higher in vegetarians due to insufficient intake of vitamin B12. In the case of vitamin B12 deficiency, it is not sufficient to measure serum vitamin B12 levels alone. Methyl malonic acid (MMA) and homocysteine levels (Hcy) should also be checked [11].

Deficiencies in cobalamin or folate have also been related to symptoms of depression in adults. For example, investigators have found inverse relationships between symptoms of depression and plasma folate or plasma cobalamin. One possible mechanism linking these vitamin deficiencies to depressive symptoms may be through elevated homocysteine and intracellular one-carbon metabolism. Plasma vitamin B12 and folate are required for the synthesis of methionine from homocysteine (Hcy) [12].

## CONCLUSION

Both cobalamin and folate play a big part in the developing nervous system, Folate is necessary during early fetal development to arrest NTD, and cobalamin deficiency may interfere with early development through disruptions in myelination and dendritic formation or inflammation. Vitamin B12 deficiency is a common and often missed problem in geriatric patients. Neuropsychiatric manifestations can be the presenting and only sign of deficiency even in the absence of hematologic abnormalities. Vitamin B12 deficiency can occur even through “normal” serum cobalamin levels; therefore, measuring Hcy and MMA can decrease false-negative findings. Early spotting and treatment are crucial to prevent structural and irreversible damage leading to treatment-resistant symptoms. So, it is significant to maintain plasma cobalamin and folate levels in the mid-ordinary range among elderly and children and recommend to: Screen annually for vitamin B12 deficiency in at-risk patients by measuring MMA and Hcy levels in patients especially with serum cobalamin levels <350 pg/ml, monitor vitamin B12 serum levels & folate at least yearly in patients who have stopped supplementation after symptoms have improved or cobalamin levels have been replenished.

*Conflict of interest.* Nil.

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## أثر مستوى حمض الفوليك وفيتامين ب12 على الصحة النفسية لدى المرضى المقيمين في مستشفى الرازي للأمراض النفسية

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### المستخلص

فيتامين ب12 (الكوبالامين) هو أحد الفيتامينات الأساسية التي تؤثر على أنظمة مختلفة في الجسم، بما في ذلك الجهاز العصبي المركزي و تهدف الدراسة الحالية إلى تقييم فيتامين ب12 وحمض الفوليك في المصل لدى المرضى الذين تم دخولهم لمستشفى الرازي للأمراض النفسية. كانت الدراسة على مرضى داخليين يعانون من اضطرابات نفسية تتراوح أعمارهم بين 21 إلى 60 عامًا. في هذه المجموعة من 40 مريضًا نفسيًا، لا توجد أدلة على تغييرات سريرية ذات صلة بمستوى فيتامين ب12 وحمض الفوليك في المصل. يمكن أن يحدث نقص في فيتامين ب12 بالرغم من أن مستويات الكوبالامين في المصل طبيعية؛ لذلك، يمكن أن يؤدي قياس الهوموسيستئين وحمض الميثيل مالونيك إلى تقليل النتائج السلبية الكاذبة.

**الكلمات الدالة:** مستوى فيتامين ب12, مستوى حمض الفوليك.