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Frequency Of Depression In Patients With Vitamin B12 Deficiency

Anam Fatima[1], Faridullah Shah[2], Hareema Saeed Khan[3], Kashif Rauf[4], Safdar Ali[5], Shahid Ali Khan[6]

Abstract

Objective: To determine the frequency of depression in patients with vitamin B12 deficiency.
Methodology: This cross-sectional study was carried out from January 2020 to March 2021 on a total sample size of n=100 patients (age 49.84 ± 0.91 years) using a simple random sampling technique, visiting the medical department of the federal government polyclinic hospital, in Islamabad. Patients presenting with macrocytic anaemia secondary to vitamin B12 deficiency were included while the patients with previously diagnosed depression were excluded from the study. Serum vitamin B12 levels were measured through the ELISA technique. Patient Healthcare Questionnaire-9 (PHQ-9) was designed and presented to patients with vitamin B12 deficiency for depression assessment. Patients with PHQ-9 score ≤5 were rated as having no depression and the patients with score ≥5 were rated as having depression. Data were analyzed using GraphPad Prism and the correlation coefficient was measured through non-linear fit and linear regression curves while ordinary ANOVA (non-parametric) was applied for study variables.
Results: The average level of vitamin B12 in the serum and PHQ-9 score were recorded as 158 ± 4.94 (pg/uL) and 5.85 ± 0.30, respectively. Vitamin B12 levels and PHQ-9 score depicted an inverse correlation, however, no association was found between gender and PHQ-9 score.
Conclusion: Data depicted that the patients presenting low levels of vitamin B12 in their serum have shown corresponding high PHQ-9 scores which is an indicator of depression. However, depression prevails in all age groups without any discrimination of gender.
Keywords: Vitamin B12; Clinical Depression; PHQ-9; Malnutrition; Social Factors

[1] Post Graduate trainee, Federal Government Poly Clinic; [2,3] Consultant Medicine, Federal Government Poly Clinic; [4] Senior Demonstrator, Rawalpindi Medical University; [5] Assistant Professor; [6] Head of Department, Psychiatry.
Correspondence: Dr Anam Fatima, Post Graduate Trainee, Federal Government Poly Clinic. **Email:** anamfatima.rmc14@gmail.com
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1. Introduction

Vitamin B12 is predominantly acquired through the intake of meat products [1]. Deficiency of vitamin B12 is associated with feelings of lethargy, clinical depression, feebleness, steadiness, tickling and [2]. Numerous studies reported the association between deficiency of vitamin B12 and clinical expression [3, 4]. The provision of vitamin B12 supplements to patients depicting clinical depression has shown improvements in their mental health. A vitamin B12 diet helps improve the blood levels which subsequently recovers the patients' clinical depression [5]. Malnutrition is reported to worsen the mental health of adult patients by lowering the vitamin B12 levels in their serum Vitamin B12 supplementation in treating major depressive disorder: a randomized controlled trial [2]. Monitoring the serum levels of vitamin B12 is highly recommended to control the onset of clinical depression [6]. It also helps in the timely management of depression [2]. Moreover, vitamin B12 plays a vital role in the formation of *S*-adenosylmethionine in the body. Deficiency of *S*-adenosylmethionine is associated with lower levels of vitamin B12. *S*-adenosylmethionine helps in the methylation of neurons in the brain which imparts the antidepressant effect [7]. Vitamin B12 deficiency and to a lesser extent folate deficiency were also related to depressive disorders [8]. Synthesis of monoamines (dopamine and serotonin) is dependent on both folate and vitamin B12. Hence the deficiency of vitamin B12 hinders the monoamine synthesis which subsequently causes depression [9]. Previous studies have also reported an association between vitamin B12 deficiency and depressive symptoms in elderly patients [10, 11]. Those a with deficiency of vitamin B12 reported more fatigue and depressive symptoms than those without the deficiency [12]. Consideration of vitamin B12 deficiency is recommended in all patients with organic mental disorders and B12 levels should be evaluated in patients with treatment-resistant depressive [3, 13]. In Pakistan, data presenting the association of clinical depression with vitamin B12 deficiency was lacking.
The present study aimed to determine the frequency of depression in patients presenting with vitamin B12 deficiency. Moreover, it would help clinical management of depression in patients with vitamin B12 deficiency.

2. Materials & Methods

For this cross-sectional study, patients (male and female over 12 years of age) visiting the medical department (both indoor and outdoor) of the federal

government polyclinic hospital (FGPC), Islamabad from January 2020 to March 2021 were included in the study after informed consent. A minimum sample size of 100 was worked out with an alpha error of 0.05, an acceptable difference of 0.15 and a CI of 95% according to the sampling technique mentioned elsewhere [14]. Sampling was done using a simple random sampling method. Patient Healthcare Questionnaire-9 (PHQ-9) was verbally presented by the nurses in the native language of the patients to fill in all the required information for the assessment of depression. Patients presenting with macrocytic anaemia secondary to vitamin B12 deficiency were included while the patients with previously diagnosed depression were excluded from the study. The study was approved by Bio-Ethical Committee (No. FGPC.1/12/2021) of FGPC, Islamabad. Blood Samples were also collected from the patients in gel tubes (DB, USA) for the measurement of vitamin B12 in serum.

Serum was separated from the blood samples and stored at -20°C. Serum levels of vitamin B12 were measured by AccuDiag™ vitamin B12 ELISA kit (Cortez Diagnostics, USA) according to the manufacturer's instructions. Briefly, 50µl of vitamin B12 calibrator, control or serum was loaded into the wells followed by the addition of biotin reagent (50µl). After 45min incubation at room temperature (RT), enzyme (50µl) was added. Unreacted content was decanted and wash buffer (350µl) was added followed by the addition of substrate (100µl). The reaction mixture was incubated for 20 min at room temperature (RT) followed by the addition of stop solution (50µl). The plate was read at 450nm on the microplate reader (ThermoFisher, USA) after 30min of the addition of the stop solution. Patients with vitamin B12 levels below the reference range will be assessed regarding the presence of depression using the PHQ-9 questionnaire. Patients with a score ≤5 were rated as having no depression and the patients with a score ≥5 were rated as having depression. Data were analyzed by GraphPad PRISM 8.0.1 software. Data in Figure 1 is analyzed through Ordinary one-way ANOVA (non-parametric) as a mean ± SD. Data in Figures 2 and 3 are the correlation coefficients measured as non-linear fit and linear regression curves, respectively.

3. Results

Males to female ratio of study participants were 3:1. Average concentration of vitamin B12 in the serum was measured as 158±4.94 (pg/uL) in the patients presenting average age of 49.84 ± 0.91. The mean PHQ-9 score in the study participants was recorded as 5.85±0.30 (Figure 1).

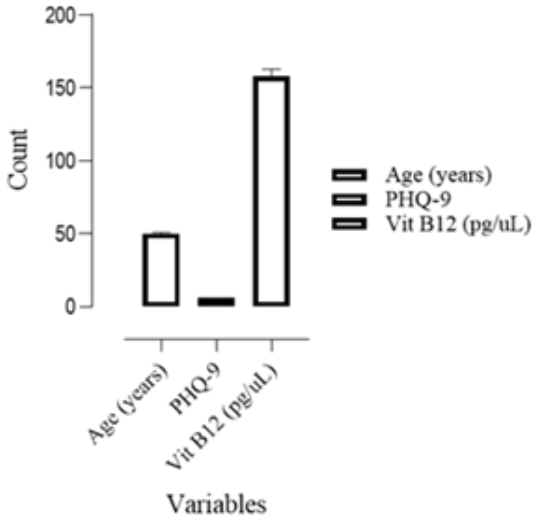

Figure-1 Description of the variables included in the study. The bar graph represents with average age of the participants, mean PHQ score and vitamin B12 concentration. Error bars represent ±SD

Data depicted a negative correlation between PHQ-9 scores and vitamin B12 concentrations. It was not surprising to note that higher PHQ-9 scores were corresponding to vitamin B12 deficiencies in the patients (Figure 2).

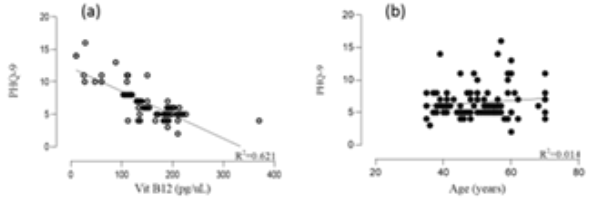

Figure-2 Correlation between PHQ-9 scores and the concentrations of vitamin B12 (a) and age (b). (a) Open circles represent individual values of vitamin B12 concentrations corresponding to the PHQ-9 score. The correlation coefficient (R^2=0.621) is calculated as a non-linear fit curve. (b) Correlation between PHQ-9 scores and age. Filled circles represent individual values of age (years) corresponding to PHQ-9 score. The correlation coefficient (R^2=0.014) is calculated as a linear regression curve. Moreover, data did not show any correlation between the PHQ-9 scores of the patients with their age (Figure 2b). PHQ-9 score remained independent of age and gender.

5. Discussion

Data indicated that the frequency of depression is higher in patients presenting vitamin B12 deficiency. Vitamin B12 deficiency causes neuropsychiatric symptoms [10] through variable effects on myelination of the neurons [10, 15, 16]. Hence, vitamin B12 is required for normal brain and nervous system function and its deficiency can lead to various neuropsychiatric symptoms and most commonly depression [16]. Previous studies indicated that vitamin B12 supplements can improve depression symptoms in patients [2, 3, 17, 18] which helps to improve the quality of life of patients, their families and society. Depression is not only affecting the individual but also causes a social and economic burden on society [19, 20]. Data also showed that the frequency of depression prevails independent of age and gender if the patient is vitamin B12 deficient. Depression is almost equally prevalent in males and females [21] and there is no specific age limitation [22]. However, the intensity and severity of the depression may vary depending on the exposure to critical biological or social factors. A minimal gender difference was found in dimensional depression scores and prevalence rates of depression [21]. Both these measures were found to increase continuously with age in both genders [23]. After analyzing carefully, data may suggest some intrinsic factors contributing to the development of clinical depression. Moreover, the social and economic conditions of the patients might be the vital factors contributing to the clinical manifestation. People living in resource-poor set-ups may have more chances to develop vitamin B12 deficiency due to malnutrition (24-26) as compared to people living in prosperity [27]. Even though depression or other mental health concerns are very common and expensive to manage, previously, many studies have depicted that depression lowers the quality and living standards. [28-30]. It is therefore mandatory to understand the importance of social factors contributing to the lowering of life quality. It would help manage mental health concerns with improved outcomes. [31]

It is in clinical practice that the onset of depression can be delayed with dietary intake of vitamin B12 which subsequently helps to improve the depressive conditions of the patients as well as the efficacy of anti-depression treatment. Folate and vitamin B6 are also reported to improve the clinical symptoms of depression [3, 31]. The study depicted the frequent relationship between vitamin B12 deficiency and the onset of depression. It also warrants further investigation into the dietary habits of our social strata which would help to improve the clinical symptoms of depression by scaling up the serum levels of vitamin B12.

5. Conclusion

The present study concluded that vitamin B12 deficiency causes depression in patients. Moreover, the frequency of depression prevails in all age groups without any discrimination of gender.

CONFLICTS OF INTEREST- None

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Potential competing interests: None to report

Contributions:

A.F, F.S, S.A.K - Conception of study
A.F, F.S - Experimentation/Study conduction
A.F, F.S, H.S.K, S.A -Analysis/Interpretation/Discussion
A.F, F.S, H.S.K, K.R - Manuscript Writing
A.F, F.S, H.S.K, K.R - Critical Review
A.F, F.S,H.S.K, K.R, S.A.K - Facilitation and Material analysis

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