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### Review Article

# Psychiatric Manifestations and Bone Marrow Findings in Vitamin - B-12 Deficiency

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### Abstract

**Background:** Vitamin B-12 deficiency is a common nutritional disorder with diverse clinical manifestations involving the hematological, neurological, and psychiatric systems. Psychiatric symptoms may precede or occur in the absence of overt anemia, leading to underdiagnosis and delayed treatment. Bone marrow examination often reveals characteristic megaloblastic changes that aid in confirming the diagnosis. **Objectives:** To evaluate the spectrum of psychiatric manifestations and bone marrow findings in patients with vitamin B-12 deficiency and to assess their association with hematological parameters. **Methods:** This hospital-based observational study included 30 patients diagnosed with vitamin B-12 deficiency. Detailed clinical evaluation with emphasis on psychiatric symptoms was performed. Hematological investigations, including hemoglobin levels, mean corpuscular volume, and serum vitamin B-12 levels, were analyzed. Bone marrow examination was carried out where indicated. Statistical analysis was performed using appropriate tests, and a p-value <0.05 was considered statistically significant. **Results:** The mean age of patients was  $45 \pm 12$  years, with a male predominance. Depression was the most common psychiatric manifestation (40%), followed by cognitive impairment (30%), anxiety or irritability (20%), and psychotic symptoms (10%). Most patients had moderate macrocytic anemia, with a mean hemoglobin of  $8.5 \pm 1.8$  g/dL and mean MCV of  $110 \pm 9$  fL. Bone marrow examination revealed hypercellularity in 73% of patients and megaloblastic changes in 83%. Psychiatric manifestations were significantly associated with lower hemoglobin levels and reduced serum vitamin B-12 concentrations. **Conclusion:** Vitamin B-12 deficiency commonly presents with psychiatric manifestations alongside characteristic bone marrow changes. Early recognition and prompt treatment are essential to prevent potentially reversible neuropsychiatric complications.

**Keywords:** Vitamin B-12 deficiency; Psychiatric manifestations; Megaloblastic anemia; Bone marrow; Macrocytosis.

### Introduction:

Vitamin B-12 (cobalamin) is an essential water-soluble vitamin required for normal hematopoiesis, DNA synthesis, and proper neurological and psychiatric functioning. It acts as a cofactor in critical enzymatic reactions, including the conversion of homocysteine to methionine and methylmalonyl-CoA to succinyl-CoA, processes vital for myelin synthesis and cellular maturation [1]. Deficiency of vitamin B-12 is a common yet often underdiagnosed condition, particularly in developing countries, the elderly population, vegetarians, and individuals with malabsorption syndromes [2]. The clinical manifestations of vitamin B-12 deficiency are diverse and can involve hematological, neurological, and psychiatric systems, either in isolation or in combination.

Traditionally, vitamin B-12 deficiency has been associated with megaloblastic anemia characterized by macrocytosis, hypersegmented neutrophils, and ineffective erythropoiesis. Bone marrow examination typically reveals hypercellularity with megaloblastic changes affecting erythroid, myeloid, and megakaryocytic lineages [3]. However, it is now well recognized that neuropsychiatric manifestations may precede hematological abnormalities or occur even in the absence of anemia, making diagnosis challenging if reliance is placed solely on peripheral blood findings [4].

Psychiatric manifestations of vitamin B-12 deficiency range from subtle behavioral and cognitive changes to severe neuropsychiatric syndromes. These include depression, irritability, anxiety, apathy, memory impairment, delirium, dementia, psychosis, and, rarely, manic or catatonic states [5]. The term "megaloblastic madness" has historically been used to describe acute psychosis associated with vitamin B-12 deficiency. Cognitive dysfunction due to cobalamin deficiency can mimic Alzheimer's disease or other dementias, highlighting the importance of early recognition, as these changes may be partially or completely reversible with timely treatment [6].

The pathophysiology underlying psychiatric manifestations in vitamin B-12 deficiency is multifactorial. Proposed mechanisms include impaired myelin formation, accumulation of neurotoxic metabolites such as methylmalonic acid and homocysteine, altered monoamine neurotransmitter synthesis, and cerebral white matter changes [7]. These biochemical derangements may result in neuronal dysfunction even before structural damage becomes evident. Additionally, elevated homocysteine levels have been independently associated with cognitive impairment and mood disorders, further linking vitamin B-12 deficiency to psychiatric illness [8].

Bone marrow findings in vitamin B-12 deficiency provide crucial diagnostic evidence, especially in cases with unexplained cytopenias or atypical presentations. Megaloblastic changes, nuclear-cytoplasmic asynchrony, giant metamyelocytes, and abnormal megakaryocytes are characteristic features [9]. In some patients, bone marrow examination may reveal dysplastic changes that mimic myelodysplastic syndromes, leading to potential misdiagnosis if nutritional deficiency is not considered. Therefore, correlating bone marrow morphology with clinical and biochemical parameters is essential for accurate diagnosis and management.

Despite the high prevalence of vitamin B-12 deficiency, particularly in the Indian subcontinent, limited attention has been paid to the combined evaluation of psychiatric manifestations and bone marrow findings in affected patients. Many psychiatric symptoms are often attributed to primary psychiatric disorders, while hematological abnormalities may be treated symptomatically without addressing the underlying nutritional deficiency [10]. Early identification of vitamin B-12 deficiency is crucial, as prompt supplementation can lead to significant improvement in psychiatric symptoms and normalization of bone marrow changes.

The aim of this study is to evaluate psychiatric manifestations and

bone marrow findings in patients with vitamin B-12 deficiency, and to analyze the spectrum of psychiatric symptoms, assess associated bone marrow changes, and correlate psychiatric features with hematological abnormalities.

## MATERIALS AND METHODS

- **Study Design:** Hospital-based, observational cross-sectional study.
- **Study Place:** Rishi Pathological Laboratory, Kolkata.
- **Study Duration:** One year.
- **Sample Size:** 30 patients.
- **Study Population:** Patients diagnosed with vitamin B-12 deficiency and evaluated for psychiatric and haematological abnormalities.

### Inclusion Criteria:

- Age  $\geq 18$  years
- Biochemically confirmed vitamin B-12 deficiency
- Presence of psychiatric symptoms and/or hematological abnormalities
- Patients undergoing bone marrow examination

- Informed consent obtained

### Exclusion Criteria:

- Known primary psychiatric illness
- Folate or iron deficiency anemia
- Chronic systemic illness or malignancy
- Prior vitamin B-12 supplementation
- Refusal to consent

### Statistical Analysis

For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and subsequently analyzed using SPSS software (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized as mean  $\pm$  standard deviation, while categorical variables were expressed as frequencies and percentages. Comparisons between independent groups were performed using the two-sample (unpaired) t-test, whereas paired t-tests were applied for comparisons involving paired observations. Associations between categorical variables were analysed using the Chi-square test, and Fisher's exact test was employed where expected cell counts were small. A p-value  $\leq 0.05$  was considered statistically significant.

## RESULT

**Table 1: Age and Sex Distribution (n = 30)**

| Variable         | Number      |
|------------------|-------------|
| Mean age (years) | 45 $\pm$ 12 |
| Male             | 18          |
| Female           | 12          |

**Table 2: Psychiatric Manifestations**

| Psychiatric symptom  | Number (%) |
|----------------------|------------|
| Depression           | 12 (40%)   |
| Cognitive impairment | 9 (30%)    |
| Anxiety/Irritability | 6 (20%)    |
| Psychosis            | 3 (10%)    |

**Table 3: Hematological Parameters**

| Parameter                  | Mean $\pm$ SD |
|----------------------------|---------------|
| Hemoglobin (g/dL)          | 8.5 $\pm$ 1.8 |
| MCV (fL)                   | 110 $\pm$ 9   |
| Serum Vitamin B-12 (pg/mL) | 140 $\pm$ 35  |

**Table 4: Bone Marrow Findings**

| Bone marrow finding   | Number (%) |
|-----------------------|------------|
| Hypercellular marrow  | 22 (73%)   |
| Megaloblastic changes | 25 (83%)   |
| Giant metamyelocytes  | 18 (60%)   |

**Table 5: Psychiatric Symptoms vs Hemoglobin Level**

| Hemoglobin     | Psychiatric symptoms present | Psychiatric symptoms absent |
|----------------|------------------------------|-----------------------------|
| < 8 g/dL       | 10                           | 3                           |
| $\geq 8$ g/dL  | 6                            | 11                          |
| <b>p-value</b> | <b>0.04</b>                  |                             |

**Table 6: Vitamin B-12 Levels and Psychiatric Symptoms**

| Group                        | Mean Vitamin B-12 (pg/mL) | p-value |
|------------------------------|---------------------------|---------|
| With psychiatric symptoms    | 125 $\pm$ 30              | 0.02    |
| Without psychiatric symptoms | 165 $\pm$ 28              |         |

**Figure: 1: Psychiatric Manifestations**

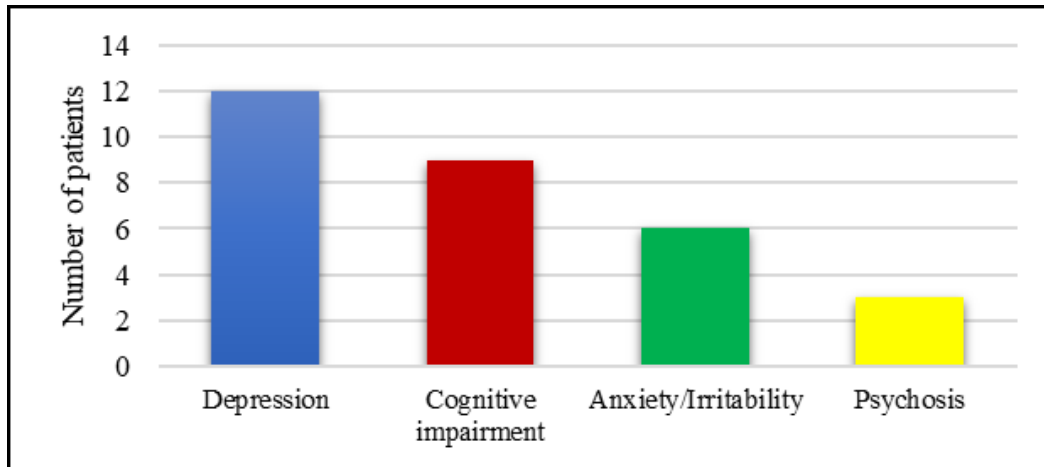


Figure: 2. Bone Marrow Findings

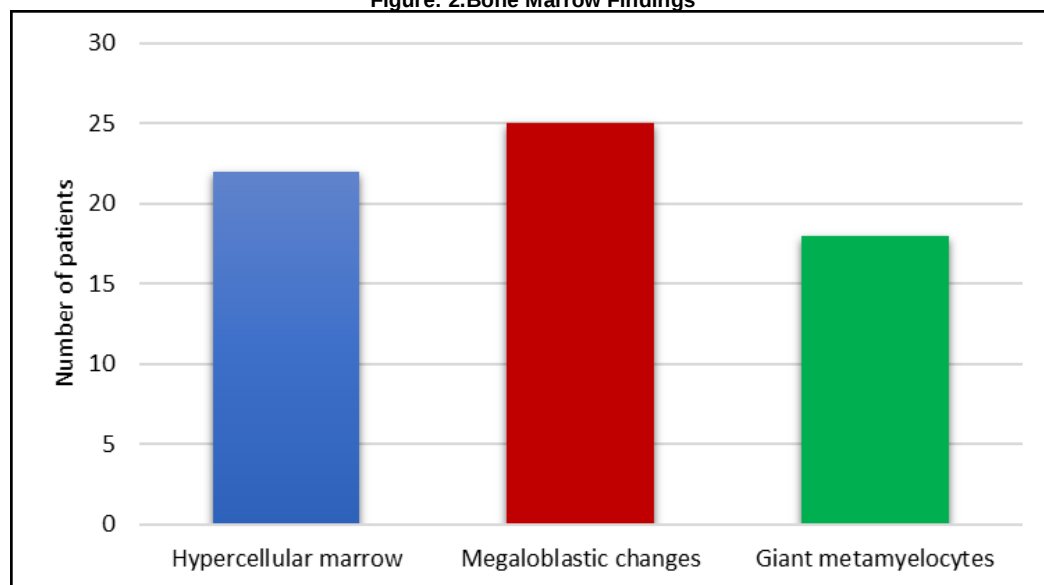


Table 1 shows the demographic profile of the study participants. The mean age of the patients was  $45 \pm 12$  years. Males (18 patients) outnumbered females (12 patients), indicating a male predominance in the study population.

Table 2 depicts the distribution of psychiatric manifestations among patients with vitamin B-12 deficiency. Depression was the most common psychiatric presentation, observed in 40% of patients, followed by cognitive impairment (30%) and anxiety/irritability (20%). Psychotic symptoms were present in 10% of cases.

Table 3 summarizes the hematological parameters of the study subjects. The mean hemoglobin level was  $8.5 \pm 1.8$  g/dL, indicating moderate anemia. The mean mean corpuscular volume (MCV) was  $110 \pm 9$  fL, suggestive of macrocytosis. The mean serum vitamin B-12 level was  $140 \pm 35$  pg/mL, confirming vitamin B-12 deficiency in all patients.

Table 4 shows the bone marrow findings in patients with vitamin B-12 deficiency. Hypercellular marrow was observed in 73% of patients. Megaloblastic changes were the most common finding, present in 83% of cases, while giant metamyelocytes were noted in 60% of patients.

Table 5 demonstrates the association between hemoglobin levels and psychiatric manifestations. Psychiatric symptoms were more frequently observed in patients with hemoglobin levels  $< 8$  g/dL compared to those with hemoglobin  $\geq 8$  g/dL. This association was found to be statistically significant ( $p = 0.04$ ).

Table 6 compares serum vitamin B-12 levels in patients with and without psychiatric manifestations. Patients with psychiatric symptoms had significantly lower mean vitamin B-12 levels ( $125 \pm 30$  pg/mL) compared to those without psychiatric symptoms ( $165 \pm 28$  pg/mL). This difference was statistically significant ( $p = 0.02$ ).

## DISCUSSION

The present study highlights the wide spectrum of neuropsychiatric and hematological manifestations associated with vitamin B-12 deficiency and demonstrates a significant association between severity of anemia, low serum vitamin B-12 levels, and psychiatric symptoms. The male predominance and mean age observed in our cohort are comparable to findings reported by Reynolds et al. [11] and Lindenbaum et al. [12], who noted that middle-aged males frequently present with clinically overt vitamin B-12 deficiency, possibly due to dietary habits, alcohol intake, and malabsorption states.

Psychiatric manifestations were common in our study, with depression being the most frequent presentation, followed by cognitive impairment and anxiety, findings consistent with earlier studies by Tiemeier et al. [13] and Moore et al. [14], who reported

depressive symptoms and cognitive decline as the predominant psychiatric features in vitamin B-12-deficient patients. The occurrence of psychotic symptoms in 10% of our patients is also in line with observations by Hector and Burton [15], who emphasized that severe deficiency may precipitate frank psychosis even in the absence of profound anemia. These similarities reinforce the role of vitamin B-12 in neurotransmitter synthesis and myelin maintenance.

Hematological findings in our study, including macrocytic anemia and megaloblastic bone marrow changes, closely mirror those described by O'Leary and Samman [16] and Savage et al. [17]. The high prevalence of hypercellular marrow with megaloblastic erythropoiesis further supports the classical pathological picture of vitamin B-12 deficiency. Importantly, the statistically significant association between lower hemoglobin levels and psychiatric

manifestations observed in our study corroborates findings by Klee [18], who reported that neuropsychiatric symptoms tend to be more frequent and severe in patients with advanced hematological involvement.

Furthermore, patients with psychiatric manifestations in our cohort had significantly lower serum vitamin B-12 levels compared to those without such symptoms. Similar associations have been documented by Morris et al. [19] and Lerner et al. [20], suggesting that the degree of vitamin B-12 depletion, rather than anemia alone, plays a critical role in the development of psychiatric symptoms. Collectively, these comparisons emphasize the need for early recognition and prompt treatment of vitamin B-12 deficiency to prevent potentially reversible psychiatric and neurological complications.

## CONCLUSION

Vitamin B-12 deficiency is a common yet often underrecognized condition with diverse hematological and neuropsychiatric manifestations. The present study demonstrates that psychiatric symptoms, particularly depression and cognitive impairment, are frequently associated with low serum vitamin B-12 levels and greater severity of anemia. Macrocytic anemia and characteristic megaloblastic bone marrow changes remain important diagnostic clues, but psychiatric manifestations may occur even before severe hematological abnormalities become evident. The significant association between lower hemoglobin levels, reduced vitamin B-12 concentrations, and psychiatric manifestations underscores the importance of considering vitamin B-12 deficiency in patients presenting with unexplained psychiatric symptoms. Early diagnosis and timely supplementation can lead to significant clinical improvement and prevent irreversible neurological damage. Routine screening for vitamin B-12 deficiency should therefore be considered in patients with anemia and neuropsychiatric symptoms, especially in middle-aged and elderly individuals, to improve overall patient outcomes.

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