MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2024.18.10.381.385

Prevalence and Clinical Manifestations of Vitamin B12 Deficiency Anemia in Adults: A Cross-sectional Study

[1]Maulik Pradipbhai Panchal, [2]Chintan Pravinchandra Patil, [3]Karmarajsinh Dilipsinh Vaghela, [4]Smithkumar Narendrakumar Modi

[1-4]General Medicine, GMERS Medical College and Hospital, Himmatnagar, Gujarat, India

ABSTRACT

Vitamin B12 deficiency is a prevalent condition associated with various systemic manifestations, particularly among older people. The deficiency can arise due to inadequate dietary intake or impaired absorption, with sources of Vitamin B12 primarily being animal products. The study aims to explore the incidence, clinical manifestations and biochemical correlations of Vitamin B12 deficiency anaemia. The present research was conducted to determine the prevalence of Vitamin B12 deficiency anaemia in adults and to investigate its clinical manifestations and relation with other blood investigations. A hospital-based, cross-sectional study was conducted at a tertiary care centre. One hundred adult patients presenting with symptoms indicative of Vitamin B12 deficiency, such as tingling, giddiness and unsteady gait, were included. Laboratory investigations included Complete Blood Count (CBC), serum Vitamin B12 levels and other biochemical markers. Data analysis was performed using SPSS software, with chi-square tests for statistical significance ($p<0.05$). Out of 100 participants, 64% were diagnosed with Vitamin B12 deficiency anaemia. The highest incidence (32%) was in the 51-60 age group. Male patients comprised 52% of the study group. Giddiness (47%) was the most common symptom, followed by tingling (13%). Significant correlations were observed with mean corpuscular volume (MCV), platelet count and serum urea levels, while no significant association was found between Vitamin B12 deficiency and Vitamin D3 levels. Vitamin B12 deficiency anaemia is prevalent, especially in older people. Timely diagnosis and treatment can prevent irreversible damage and significant haematological parameters like MCV and platelet count are crucial in diagnosis.

OPEN ACCESS

Key Words

Vitamin B12 deficiency, anaemia, elderly, MCV, platelet count, neurological symptoms, biochemical correlations

Corresponding Author

Smithkumar Narendrakumar Modi, General Medicine, GMERS Medical College and Hospital, Himmatnagar, Gujarat, India
smithmodi95@gmail.com

Author Designation

[1-4]Assistant Professor

Received: 01 Sep 2024
Accepted: 11 Sep 2024
Published: 20 Sep 2024

Citation: Maulik Pradipbhai Panchal, Chintan Pravinchandra Patil, Karmarajsinh Dilipsinh Vaghela, Smithkumar Narendrakumar Modi, 2024. Prevalence and Clinical Manifestations of Vitamin B12 Deficiency Anemia in Adults: A Cross-sectional Study. Res. J. Med. Sci., 18: 381-385, doi: 10.59218/makrjms.2024.18.10.381.385

INTRODUCTION

Vitamin B12, also known as cobalamin, is a vital nutrient necessary for DNA synthesis, red blood cell formation and the proper functioning of the nervous system. Deficiency of this nutrient can lead to megaloblastic anaemia, a condition characterized by the production of abnormally large and immature red blood cells. Megaloblastic anaemia often presents with symptoms such as pallor, fatigue, shortness of breath and neurological disturbances like numbness, tingling and cognitive impairment[1]. Vitamin B12 deficiency can arise from various causes, including poor dietary intake, particularly in individuals following vegetarian or vegan diets, impaired absorption due to gastrointestinal disorders such as pernicious anaemia and conditions that affect the terminal ileum, the site of Vitamin B12 absorption. This deficiency can manifest across various age groups, though it is notably prevalent among older adults[2].

Age-related gastric atrophy and reduced intrinsic factor production, necessary for Vitamin B12 absorption, contribute to the higher incidence of deficiency in elderly populations. Among vegetarians, particularly those who have adhered to a plant-based diet for extended periods, the risk is significantly elevated[3]. For instance, older Chinese vegetarian women have shown a high prevalence of subclinical Vitamin B12 deficiency, which is associated with lowered haemoglobin levels and, in some cases, anaemia, though macrocytosis may not always be present[4].

In clinical settings, Vitamin B12 deficiency is often associated with increased mean corpuscular volume (MCV), a marker of macrocytic anaemia. However, cases of deficiency with normal or borderline MCV levels have also been reported, complicating the diagnosis based solely on red blood cell indices. Hematological abnormalities such as pancytopenia, characterized by all blood cell type reductions, are often observed in severe cases. This can lead to a wide array of systemic effects, from haematological to neurological and gastrointestinal manifestations, such as peripheral neuropathy and altered bowel habits, as seen in a significant proportion of patients[5].

The role of other nutrients like folate in developing megaloblastic anaemia has also been explored[6]. Vitamin B12 and folate deficiency can result in overlapping clinical symptoms, making it necessary to differentiate between them for appropriate treatment. The complexity of Vitamin B12 deficiency lies not only in its multifactorial aetiology and the variability of its clinical presentation, which may range from subtle neurological symptoms to severe anaemia and pancytopenia. Early detection and management are critical, as prolonged deficiency can lead to irreversible neurological damage[7,8]. In many cases, dietary supplementation or Vitamin B12 injections can effectively reverse haematological abnormalities and prevent further complications. However, the challenges of early diagnosis, especially in individuals without classic signs of macrocytosis, underscore the importance of routine screening for at-risk populations, such as the elderly and vegetarians[9,10].

The need for this study arises from the growing concern over Vitamin B12 deficiency's widespread impact on adult populations. The primary aim is to investigate the status of Vitamin B12 deficiency anaemia in adults. Additionally, the study seeks to determine the prevalence of various clinical manifestations associated with Vitamin B12 deficiency.

METHODS AND MATERIALS

Study Setting, Design and Duration: The study was a hospital-based, descriptive, cross-sectional investigation conducted over two years in the General Medicine Department of a tertiary care hospital.

Study Population: The study targeted one hundred adult patients who were evaluated purposively for symptoms suggestive of Vitamin B12 deficiency for the first time. Participants were included if they exhibited one or more of the following symptoms or risk factors: tingling and numbness in extremities, dizziness, unsteady gait, chronic headache, altered bowel habits, strict vegetarian diet, alcohol consumption, use of anti-tubercular medications, or a history of surgery involving the terminal ileum. Exclusion criteria included patients under 18 years of age, pregnant women, those with a history of bleeding from any site, the presence of evident structural or metabolic diseases, or normocytic normochromic or microcytic findings on a peripheral blood smear.

Data Collection: Data was collected using a structured interview form designed for this study, which the principal investigator personally completed during patient interviews to ensure consistency and data completeness. Laboratory investigations conducted for each participant included Complete Blood Count (CBC), serum Vitamin B12 level, serum Vitamin D3 level, Random Blood Sugar (RBS), blood urea, serum creatinine and serum Thyroid-Stimulating Hormone (TSH) level.

Measurement of Vitamin B12: Vitamin B12 levels were measured using an automated chemiluminescence system, a sensitive method for detecting Vitamin B12 concentrations in serum. In this assay, Vitamin B12 from the patient's serum competed with acridinium ester-labeled Vitamin B12 for a limited amount of intrinsic factor, covalently bound to paramagnetic particles in the solid phase. Sodium hydroxide was

employed as the releasing agent to liberate Vitamin B12 from endogenous binding proteins, ensuring that rebinding was prevented after the introduction of the solid phase. Following the competitive binding reaction, the bound and free forms of Vitamin B12 were separated and the chemiluminescent signal was measured to quantify Vitamin B12 concentration in the sample. In this study, Vitamin B12 levels were classified as sufficient when they were above 156 pg/mL and insufficient when below 156 pg/mL.

Measurement of Vitamin D3: Vitamin D levels were measured using an automated chemiluminescence system, a precise method for quantifying serum 25-hydroxyvitamin D concentrations. In this assay, 25-hydroxyvitamin D from the patient's serum competed with a labelled 25-hydroxyvitamin D analogue for a limited amount of specific binding protein attached to paramagnetic particles in the solid phase. A releasing agent was used to dissociate Vitamin D from its binding proteins in the serum, preventing rebinding after the introduction of the solid phase. After the competitive binding reaction, the unbound and bound fractions were separated and the chemiluminescent signal was detected to determine the 25-hydroxyvitamin D concentration in the sample. Vitamin D3 levels were classified as sufficient when they exceeded 75 ng/mL and insufficient when below 75 ng/mL.

Data Analysis: The data entry and analysis were performed using Epi info CDC 7. Descriptive and inferential statistics were employed to present the findings, with frequencies and percentages calculated for categorical variables. The chi-square test was used to compare qualitative categorical variables, while an independent sample t-test was employed for continuous variables. Statistical significance was established at a p-value of less than 0.05.

RESULTS

As shown in Table 1, most participants were in the 51-60 age group (33%), followed by the 41-50 age group (31%). A smaller percentage of participants were aged 18-30 (3%) and over 60 years (17%). Regarding gender distribution, there was a nearly equal representation of males (52%) and females (48%). The most common symptoms reported were giddiness (47%), followed by tingling (13%), chronic headache (10%), altered bowel habits (7%) and both difficulties in walking and palpitations (6% each).

In our research, a significant 64% of the sample population is deficient in Vitamin B12 (vitamin B12 level less than 156 pg/ml) (Fig. 1).

Significant findings in Mean Corpuscular Volume (MCV) and platelet counts among participants suggest that these parameters can serve as reliable indicators of Vitamin B12 deficiency. The statistical significance of MCV and platelets in this study reinforces their potential utility in routine screening for this condition, helping in early diagnosis and timely management of the deficiency (Table 2).

Table 3 shows no significant association between Vitamin B12 and Vitamin D3 levels, as sufficient and insufficient Vitamin B12 were similarly distributed across Vitamin D3 levels.

Fig. 1: Vitamin B12 Status Distribution

Table 1: Socio-demographic variables of study participants

Variables	Number (%)
Age groups	
18-30 years	3 (3%)
31-40 years	16 (16%)
41-50 years	31 (31%)
51-60 years	33 (33%)
>60 years	17 (17%)
Gender	
Male	52 (52%)
Female	48 (48%)
Symptoms	
Tingling	13 (13%)
Giddiness	47 (47%)
Difficulties in Walking	6 (6%)
Palpitation	6 (6%)
Altered Bowel Habit	7 (7%)
Chronic Headache	10 (10%)

Table 2: Relation of various blood parameters with vitamin B12 level

Parameter	Sufficient vitamin B12	Insufficient vitamin B12	p-value
Haemoglobin	11.8±2.27	12.6±3.27	0.1785
MCV*	91.57±3.17	78.91±5.21	<0.0001
WBC**	7100±2300	6600±1600	0.2072
Platelet	226000±8900	206000±6200	<0.0001
Creatinine	0.62±0.21	0.68±0.39	0.4055
Serum Urea	19.70±4.53	21.95±3.87	0.0109
RBS[#]	94.64±7.21	95.27±6.98	0.6734
TSH[$]	3.20±1.01	3.37±0.76	0.3471

*MCV: Mean Corpuscular Volume, **WBC: White Blood Cells, [#]RBS: Random Blood Sugar, [$]TSH: Thyroid-Stimulating Hormone

Table 3: Association of vitamin B12 and Vitamin D3 Level (n = 100)

Vitamin D3 Level	Sufficient vitamin B12	Insufficient vitamin B12	p-value
>75 ng/mL	4 (11.72%)	9 (13.63%)	0.9599
<75 ng/mL	30 (88.82%)	57 (86.36%)	

DISCUSSION

Vitamin B12 deficiency is a widespread health issue with significant implications, particularly in the form of megaloblastic anaemia and neurological disturbances. This condition is common among middle-aged and elderly populations, particularly those with restrictive diets, such as vegetarians. The current study aims to evaluate the prevalence, clinical manifestations and diagnostic markers of Vitamin B12 deficiency anaemia and compares the results with key findings from other significant studies to better understand the broader implications of the deficiency. In the present study, the age group most affected was 41-60 years, similar to Nizamani et al., who reported a mean age of 34.48±6.71 years, indicating that Vitamin B12 deficiency frequently affects middle-aged individuals[11]. Kwok et al. specifically studied older women (>55 years), reporting that this demographic was highly susceptible to Vitamin B12 deficiency, particularly among vegetarians, where advanced age and dietary restrictions further exacerbate the risk[12].

Regarding prevalence, the current study found that 64% of participants were Vitamin B12 deficient, a finding closely aligned with Nizamani et al., who reported a 57.5% prevalence[12] and Kwok *et al*., who observed a significantly higher prevalence of 75% among older vegetarians. Kwok *et al*.[12] also found that 42% of their participants had a definitive Vitamin B12 deficiency, with levels below 150 pmol/L and an additional 33% had a possible deficiency, defined by a combination of low Vitamin B12 levels and elevated methylmalonic acid (MMA) levels. These findings collectively highlight the widespread nature of Vitamin B12 deficiency across various age groups and dietary habits. The gender distribution in the current study (52% male, 48% female) reflects an almost equal impact of Vitamin B12 deficiency across genders, consistent with findings by Nizamani et al., though they observed a slightly higher proportion of females (67.2%)[11]. In contrast, Kwok et al. focused exclusively on older women, reporting a significant prevalence of Vitamin B12 deficiency in this subgroup, particularly in vegetarian populations. This suggests that while both genders are susceptible to Vitamin B12 deficiency, older women, particularly those with restricted diets, may face heightened risk[12].

Regarding Mean Corpuscular Volume (MCV), the present study found that MCV values were 91.57±3.17 in non-deficient participants and 78.91±5.21 in those with deficiency, supporting the use of MCV as an important diagnostic marker. Nizamani et al. similarly found elevated MCV values of 100.64±19.27 among deficient individuals, further underscoring the utility of MCV in diagnosing megaloblastic anaemia[11]. Kwok *et al*.[12] found that while Vitamin B12 deficiency was associated with a reduction in haemoglobin, it was not consistently linked to macrocytosis (increased MCV). They observed that macrocytosis was present in only 23% of patients with severe deficiency, suggesting that MCV alone may not reliably detect all cases of Vitamin B12 deficiency, particularly in less advanced stages. This highlights the need for more comprehensive diagnostics, such as serum methylmalonic acid levels, in certain populations. Neurological symptoms were prominent in the current study, with 47% of participants reporting giddiness and 13% reporting tingling. These findings are consistent with those of Kwok *et al*.[12], who observed that neurological issues such as cognitive decline were common in older, Vitamin B12-deficient women, even without significant haematological markers[12]. Similarly, Mahajan *et al*.[13] reported that 34% of their participants exhibited neurological involvement, particularly posterior column impairment. The consistent reporting of neurological symptoms across these studies underscores the significant neurological impact of Vitamin B12 deficiency, reinforcing the need for early detection and intervention to prevent long-term damage. Regarding haemoglobin levels, the current study found no significant differences between deficient (12.6±3.27) and non-deficient (11.8±2.27) participants, suggesting that haemoglobin alone may not be a reliable indicator of Vitamin B12 deficiency in early stages. This aligns with the findings of both Nizamani *et al*.[11], who reported a mean haemoglobin level of 11.3 g/dL and Kwok *et al*.[12], who noted that a decrease in haemoglobin was more apparent in severe deficiency cases. Kwok *et al*.[12] highlighted that Vitamin B12 deficiency reduced haemoglobin concentrations by up to 0.9 g/dL, but anaemia was rarely macrocytic unless methylmalonic acid levels exceeded 1.0 µmol/L. These findings indicate that while haemoglobin remains a useful diagnostic marker, it may not fully capture the extent of Vitamin B12 deficiency, particularly in its early stages.

Limitations: This study, while valuable, has several limitations. As a hospital-based study, it may introduce selection bias by including only individuals who sought medical care for Vitamin B12 deficiency symptoms, potentially overlooking asymptomatic or mildly deficient individuals and underestimating the true prevalence. Additionally, factors like genetic predispositions, dietary habits and socio-economic status, which may influence deficiency and symptom variability, were not considered. Finally, the cross-sectional design limits the ability to establish causal links between Vitamin B12 deficiency and its systemic effects.

CONCLUSION

In conclusion, this study highlights the high prevalence of Vitamin B12 deficiency, particularly in adults aged 51-60, with a slightly higher occurrence in

males. Neurological symptoms like giddiness and tingling were the most common manifestations. The association of mean corpuscular volume, platelet count and serum urea levels with Vitamin B12 deficiency anaemia underscores their diagnostic value. However, no significant link was found between Vitamin D3 levels and Vitamin B12 deficiency. These findings stress the need for timely screening and intervention to prevent the health risks of untreated Vitamin B12 deficiency. Larger, more diverse studies are required to generalize these results, explore genetic and environmental factors and examine potential interactions between Vitamin B12 and other micronutrients while assessing different treatment approaches.

REFERENCES

1. Smith, A.D. and H. Refsum, 2016. Homocysteine, B Vitamins and Cognitive Impairment. Annu. Rev. Nutr., 36: 211-239.
2. Stabler, S.P., 2013. Clinical practice. Vitamin B12 deficiency. N Engl. J. Med., 368: 149-160.
3. Green, R., L.H. Allen, A.L. Bjørke-Monsen, A. Brito and J.L. Guéant *et al*., 2017. Vitamin B12 deficiency. Nat. Rev. Dis. Prim., 3: 1-20.
4. Sobczyńska-Malefora, A., E. Delvin, A. McCaddon, K.R. Ahmadi, D.J. Harrington, 2021. Vitamin B12 status in health and disease: A critical review. Diagnosis of deficiency and insufficiency-clinical and laboratory pitfalls. Critical reviews in clinical laboratory sciences. 58: 399-429.
5. Green, R., 2017. Vitamin B12 deficiency from the perspective of a practicing haematologist. Blood, J. Am. Soc. Hematol., 129: 2603-2611.
6. Wolffenbuttel, B.H., H.J Wouters, M.R. Heiner-Fokkema, M.M. van der Klauw, 2019. The many faces of cobalamin (vitamin B12) deficiency. Mayo Clinic proceedings: innovations, quality and outcomes. 3: 200-214.
7. Aaron, S., S. Kumar, J. Vijayan, J. Jacob, M. Alexander, C. Gnanamuthu, 2005. Clinical and laboratory features and response to treatment in patients presenting with vitamin B12 deficiency-related neurological syndromes. Neurol. India 53: 55-58.
8. Suijker, K.I., C.H. Plattel, C.H. Seage, N. Ward, D.H. James and J.Y. Vis, 2024. Development of a Vitamin B12 Deficiency Patient-Reported Outcome Measure for Clinical Practice and Research. Food Nut. Bull., 45: S73-S79.
9. Remacha, A.F., J.C. Souto, J.L. Piñana, M.P. Sardà, J.M. Queraltó and J. Martí-Fabregas *et al*., 2011. Vitamin B12 deficiency, hyperhomocysteinemia and thrombosis: a case and control study. Int. J. Hematol., 93: 458-464.
10. Andrès, E., A.A. Zulfiqar, K. Serraj, T. Vogel and G. Kaltenbach, 2018. Systematic Review and Pragmatic Clinical Approach to Oral and Nasal Vitamin B12 (Cobalamin) Treatment in Patients with Vitamin B12 Deficiency Related to Gastrointestinal Disorders. J. Clin. Med., 7: 304.
11. Nizamani, G.S., I.A. Memon, A. Memon, H.K. Khoharo, 2014. Vitamin B12 deficiency with megaloblastic anaemia: An experience at Tertiary Care Hospital of Sindh. JLUMHS. 13: 13.
12. Kwok, T., G. Cheng, J. Woo, W.K. Lai, C.P. Pang, 2002. Independent effect of vitamin B12 deficiency on haematological status in older Chinese, vegetarian women. Am. J. Hematol., 70: 186-190.
13. Mahajan, S.K., S.C. Aundhakar, 2015. A study of the prevalence of serum vitamin B12 and folic Acid deficiency in Western Maharashtra. J. Family Med. Prim. Care, 4: 64-68.