

Clinical presentation of vitamin B12 deficiency in pediatric patients at a tertiary care centre

ABSTRACT

Background: Vitamin B12 deficiency is a common and preventable problem in children. If not treated, it can cause serious nerve and blood-related problems. In areas where many people follow a vegetarian diet and malnutrition is common, this deficiency is often not properly reported. This study aims to look at the symptoms and possible causes of vitamin B12 deficiency in affected children.

Methods: This cross-sectional study was conducted at Rani Durgavati Medical College from 1 June 2025 to 31 December 2025. It included 110 children aged 0–18 years who had vitamin B12 deficiency. Information was collected about their diet, appetite, neurological symptoms, and other health conditions. Laboratory tests were done to check hemoglobin levels, peripheral blood smear, vitamin B12 levels, and platelet count. Informed consent was taken from the guardians of all participants.

Conclusions: This study shows that vitamin B12 is very important for the health of children and adolescents. It found that deficiency is more common in infants, children who start complementary feeding late, and those following a vegetarian diet. The vitamin B12 levels of mothers also affect the health of breastfed infants. The study also found that lower vitamin B12 levels are linked with poorer nutritional status, highlighting the need for early detection, regular monitoring, and timely treatment.

Keywords: Vegetarian diet, Malnutrition, Developmental delays, Maternal vitamin B12 levels

INTRODUCTION

Vitamin B12 deficiency in children is an important but preventable public health problem. If it is not diagnosed early, it can lead to long-term neurological problems. In developing countries, it is often underreported, with prevalence rates ranging from 21–45%. Several factors contribute to this deficiency, including low vitamin B12 levels in mothers, delayed complementary feeding, low intake of animal-based foods, poverty, and malnutrition.

Vitamin B12 is a water-soluble vitamin that contains a cobalt atom. Its active forms, such as methylcobalamin and adenosylcobalamin, are important for many metabolic processes in the body.

These include converting homocysteine to methionine and methylmalonyl-CoA to succinyl-CoA, which help in the production of DNA, RNA, and proteins. Since vitamin B12 is produced only by microorganisms, the main dietary sources are animal products such as meat, eggs, fish, and milk. Older children and adults usually have vitamin B12 stores that last for about 3–5 years, but infants born to mothers with low vitamin B12 levels may develop deficiency symptoms within 6–18 months.

In the acidic environment of the stomach, vitamin B12 (Cbl) is released from food proteins and binds to haptocorrin (R binder) present in saliva and gastric juice. In the duodenum, pancreatic enzymes release vitamin B12 from this complex so that it can bind with intrinsic factor. This complex then attaches to receptors in the ileum, where vitamin B12 is absorbed.

Usually, about 1.5–2.5 micrograms of vitamin B12 are absorbed from each meal, along with a small amount through passive absorption. Inside the intestinal cells, vitamin B12 binds to transcobalamin II for transport in the body. About one-third of the body's vitamin B12 is stored in the liver, which delays the appearance of deficiency symptoms.

Vitamin B12 status is usually checked by measuring its level in serum or plasma. Most laboratories consider levels below 200–250 pg/ml as vitamin B12 deficiency. Serum methylmalonic acid (MMA) is a sensitive marker for detecting deficiency; levels above 0.271 micromol/l may indicate vitamin B12 deficiency, although MMA levels can also increase in people with kidney problems. Total plasma homocysteine levels also rise when vitamin B12 levels decrease, and values above 15 micromol/l may suggest deficiency. However, homocysteine is a less specific marker because it can also increase due to low folate levels or reduced kidney function.

According to the World Health Organization (WHO), vitamin B12 deficiency is defined as serum vitamin B12 levels below 203 pg/ml, and folate deficiency is defined as erythrocyte folate levels below 151 ng/ml.

The average vitamin B12 level in the breast milk of women who consume more than the recommended daily intake is about 0.44 mcg/l. The absorption of vitamin B12 from food depends on the amount consumed, as absorption decreases when the capacity of intrinsic factor is exceeded (around 1–2 mcg). Dairy products provide about three times higher bioavailability of vitamin B12 compared to meat, fish, and poultry. Vitamin B12 from dietary supplements has about 50% higher bioavailability than that from food sources.

About 70% of vitamin B12 transported across the placenta is bound to transcobalamin, compared to about 30% in maternal blood. Higher levels of transcobalamin in the placenta are associated with higher vitamin B12 levels in cord blood.

Maternal vitamin B12 deficiency, which may occur due to a vegan diet or poor absorption, can lead to low vitamin B12 supply to the fetus during pregnancy. As a result, newborns may have low vitamin B12 stores. In addition, mothers with vitamin B12 deficiency also have low levels of the vitamin in their breast milk, so breastfed infants may not receive enough vitamin B12 to build adequate stores.

Globally, vitamin B12 deficiency affects about 10% of the population, and children in developing countries are particularly at risk. In developed countries such as the United States and Europe, the prevalence in children is relatively low, ranging from 0.3% to 1.5%. In contrast, in developing countries, the prevalence can be as high as 30% due to dietary habits and socioeconomic factors.

In India, vitamin B12 deficiency affects about 14% of preschool children, 17% of school-age children, and 31% of adolescents. The prevalence is higher in boys (35%) compared to girls (27%). Among children aged 1–4 years, the prevalence ranges from 2% in West Bengal to 29% in Gujarat. In children aged 5–9 years, it ranges from 0% in Nagaland and 1% in Kerala to 31% in Uttar Pradesh and 32% in Punjab. Among adolescents aged 10–19 years, it ranges from 2% in Kerala and Nagaland to 45.5% in Karnataka.

Vitamin B12 deficiency in children mainly occurs due to three reasons: low intake, poor absorption, and genetic problems affecting transport and metabolism. Low intake is common in breastfed infants whose mothers have undiagnosed vitamin B12 deficiency, often because of strict vegetarian diets or conditions like pernicious anemia. Poor absorption can occur due to lack of intrinsic factor, competition for absorption in the ileum, or reduced stomach acid, which may happen with long-term use of acid-reducing medicines. Genetic disorders may also affect the body's ability to produce the active forms of vitamin B12 needed for important metabolic processes. Understanding these causes is important for proper diagnosis and treatment.

Children with vitamin B12 deficiency often show nonspecific symptoms such as weakness, tiredness, poor feeding, failure to gain weight, and irritability. Other common signs include pallor, glossitis, vomiting, diarrhea, and jaundice. The deficiency can also cause neurological problems such as developmental delay, muscle weakness, learning difficulties, and loss of previously acquired skills.

The blood-related effects of vitamin B12 and folate deficiency are similar. They usually cause macrocytic anemia, where red blood cells are larger than normal, along with macro-ovalocytes and hypersegmented neutrophils. In severe cases, neutropenia and thrombocytopenia may occur, which can resemble conditions like aplastic anemia or leukemia. In vitamin B12 deficiency, serum vitamin B12 levels are low, while methylmalonic acid and homocysteine levels are increased. Serum iron and folate levels are usually normal or high, and lactate dehydrogenase levels may increase due to ineffective red blood cell production. Urinary methylmalonic acid (normal: 0–3.5 mg/24 hours) is a sensitive indicator of vitamin B12 deficiency, especially when serum levels are borderline. High homocysteine levels may also occur in folate deficiency, homocystinuria, and kidney failure.

Treatment of vitamin B12 deficiency in children depends on age and severity. The dose may range from 100 µg to 1000 µg and can be given orally or by injection. Oral vitamin B12 is usually taken on an empty stomach. Infants are generally given 500 µg and older children 1000 µg daily at first, with the dose gradually reduced over three months. Parenteral treatment may start with 25 µg daily, then increase to 100 µg, and later to 1000 µg weekly if required, especially in children who are severely malnourished or anemic. In cases of infantile tremor syndrome, vitamin B12 supplementation is essential, and severe tremors may require additional medicines such as propranolol or phenytoin.

Vitamin B12 deficiency in children is an important preventable public health problem and can cause long-term neurological damage if not diagnosed early. Since our region has a predominantly vegetarian diet and a high rate of severe acute malnutrition and delayed complementary feeding, studying vitamin B12 deficiency is particularly important. Therefore, this study was undertaken.

Aims and objectives

104 The aims and objectives of this study were to examine the different clinical manifestations of vitamin B12
105 deficiency and to identify the factors that contribute to vitamin B12 deficiency.

106 **METHODS**

107 This cross-sectional survey was conducted over 6 months, from 01 July 2025, to 31 December 2025 at Department
108 of Pediatrics, Rani Durgavati Medical College , Banda , Uttar Pradesh, India.

109 Sample size calculation for a continuous outcome measure was done.

110 Sample size was 110.

111 A total of 110 children aged 0-18 years who were admitted to the hospital with vitamin B12 deficiency were
112 included in the study. The sample comprised children with vitamin B12 deficiency either as a stand-alone condition
113 or in conjunction with other diseases. Participants were selected consecutively based on their admission records
114 during the study period.

115 Upon enrollment, each child's data were recorded using a pre-designed proforma. Written consent was obtained
116 from the parents or guardians before the collection of data. The following variables were systematically evaluated.

117 ***Dietary pattern***

118 Information on the child's dietary habits was collected through a detailed dietary recall and assessment. This
119 included dietary intake frequency and types of foods consumed, focusing on sources of vitamin B12.

120 ***Appetite***

121 The child's appetite was assessed based on parental reports and clinical observations, noting any deviations from
122 normal eating patterns.

123 ***Neurological symptoms***

124 A detailed clinical evaluation was performed to identify any neurological symptoms associated with vitamin B12
125 deficiency, such as developmental delays, tremors, or other cognitive and motor dysfunctions.

126 ***Co-morbid conditions***

127 Any additional health conditions that might affect vitamin B12 levels or be associated with its deficiency were
128 recorded.

129 ***Laboratory investigations***

130 ***Hemoglobin levels***

131 It was measured to assess the severity of anemia.

132 ***Peripheral smear***

133 A peripheral blood smear was performed to identify any hematological abnormalities associated with vitamin B12
134 deficiency.

135 ***Vitamin B12 levels***

136 Serum vitamin B12 concentrations were measured to confirm the deficiency.

137 ***Platelet count***

138 Platelet counts were recorded to evaluate any related hematological manifestations.

139 ***Statistical analysis***

140 Data were analyzed to determine the vitamin B12 deficiency among the study population and to explore its
141 association with various clinical and laboratory parameters. Statistical methods were employed to assess
142 correlations between vitamin B12 levels and variables such as dietary patterns, neurological symptoms, and

comorbid conditions. Descriptive statistics were used to summarize the findings, and inferential statistics were applied to determine the significance of observed associations.

A p value of <0.05 will be considered as significant.

Inclusion criteria

Children admitted with signs and symptoms of vitamin B12 deficiency were included.

Exclusion criteria

Non-nutritional causes of vitamin B12 deficiency were excluded.

Children with seizure and on anti-epileptic drug were excluded.

RESULTS

A total of 110 children aged 0-18 years who were admitted to the hospital with vitamin B12 deficiency were included in the study. The sample comprised children with vitamin B12 deficiency either as a stand-alone condition or in conjunction with other diseases. Participants were selected consecutively based on their admission records during the study period.

The study observed that, out of 110 cases, 25 (22.7%) were under 1-year-old, 55 (50%) were between 10 and 18 years old, and 20 (18.1%) were between 1 and 6 years old. The minimum age of a case was 3 months, while the maximum age was 17 years, with a mean age of 6.16 years which is depicted in Table 1.

Table 1: Age-wise distribution of cases.		
Age in years	Number of cases	Percentage
<1	25	22.7
1-6	20	18.1
7-9	10	9.0
10-18	55	50
Total	110	100.0

Out of 110 study samples; 58 (52.7%) cases were males and 52 (47.2%) of cases were females.

Table 2: Presenting complaints-wise distribution of cases.

Presenting complaints	Number of cases	Percentage
General weakness	30	27.3
Poor appetite	15	13.6
Comorbidities	55	50.0
Failure to thrive	10	9.1

Table 3: Distribution of cases based on diet history of cases

Dietary history	Number of cases	Percentage
Veg	70	63.6
Mixed	22	20
Exclusive breastfeeding	18	16.3
Total	110	100.0

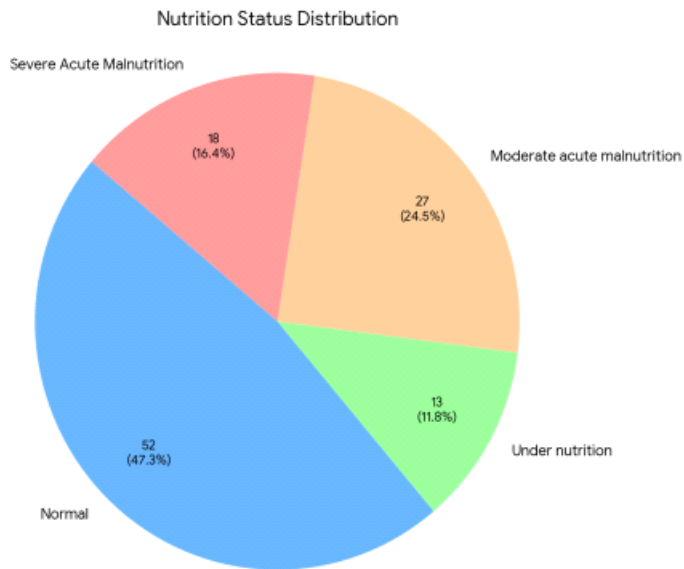


Figure 1: Nutritional status among children

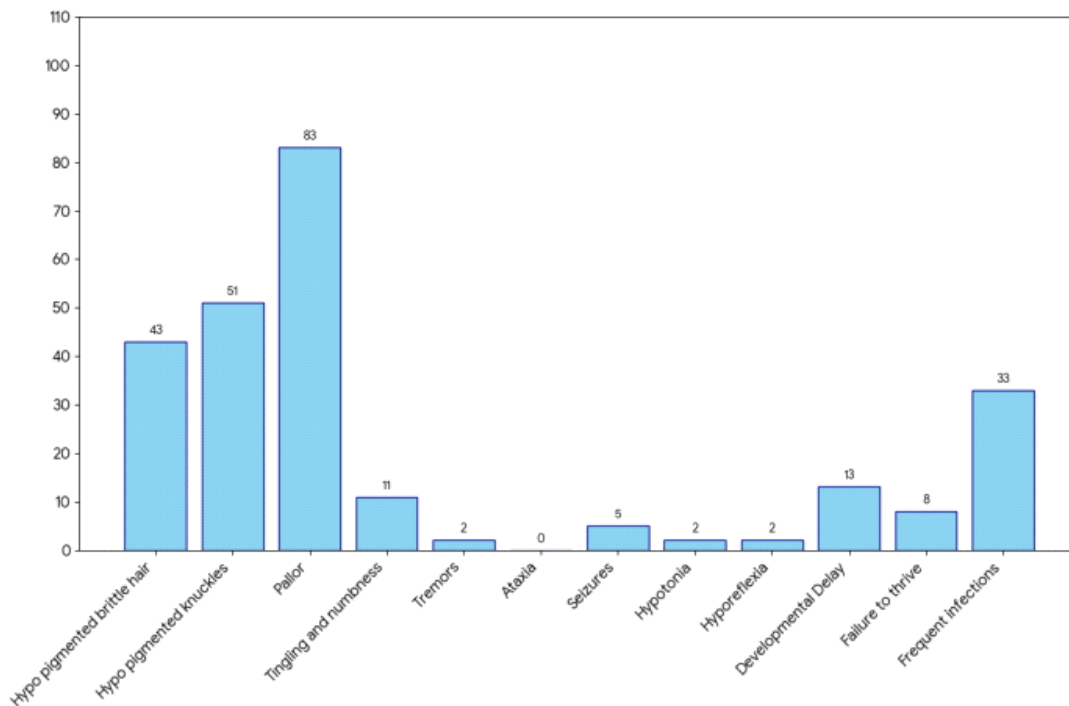


Figure 2: Clinical presentation-wise distribution of cases

The study observed that the majority of cases, 64 (85.3%), had vitamin B12 levels in the range of 100–200 pmol/l. The mean vitamin B12 level in the children was 165.34 pmol/l which is shown in Table 5.

Table 5: Distribution of cases based on serum vitamin B12 levels in children.

Variables	Number of cases	Percentage
Vitamin B12 levels		
<100	7	6.7
100-200	93	84.5
200-250	10	9.0
Total	110	100.0

The study found that out of 101 cases, (92.0%) were new diagnoses of co-morbidities, while 9 (8.0%) were preexisting co-morbid conditions.

Neurological manifestations were observed in 3% (n=3) of cases in the <2 years age group. Tremors, seizures, and hypotonia were each noted in 2 cases. Developmental delay was reported in 5 cases, while hyporeflexia and neuroregression were seen in 1 case each.

The study found that out of 110 cases, 9 (8.1%) had global developmental delays.

Table 6: Association of diet and vitamin B12 levels.

Dietary history	Number of cases	Vitamin B12 levels		
		<100	100-200	200-250
Veg	63	7	53	3
Mixed	14	1	9	4
Total	77	8	62	7

As depicted in Table 6, individuals on a vegetarian diet exhibited a higher prevalence of vitamin B12 deficiency compared to those on a mixed diet, indicating a statistically significant association between a vegetarian diet and vitamin B12 deficiency ($p<0.05$).

Table 7: Association of mother's and EBF infants sr. vitamin B12 levels.

Mother's vitamin B12	Number of cases	Vitamin B12 levels		
		<100	100-200	200-250
≤200	5	1	4	0
200-250	7	0	2	5
Total	12	1	6	5

As depicted in Table 7, the study reveals a statistically significant association between mothers' vitamin B12 levels and the vitamin B12 levels in their exclusively breastfed (EBF) infants ($p<0.05$).

Table 8: Correlation between vitamin B12 with nutritional status.

Nutritional status	Number of cases	Vitamin B12 (mean±SD)
Normal	52	
Undernutrition	13	
Moderate acute malnutrition	27	
Severe acute malnutrition	18	
Total	110	

Correlation between vitamin B12 with nutritional status demonstrates a significant inverse correlation between vitamin B12 levels and the severity of nutritional status which is depicted in Table 8.

In infants aged 3–12 months, the mean age was 9.1 months, with 70.4% male. Key issues included 77.2% pallor, 42.8% failure to thrive, and 42.8% frequent infections. Anemia was widespread, with 49.6% having microcytic hypochromic anemia. Infantile Tremor syndrome was observed in 3 cases (7.1%) magnetic resonance imaging (MRI) revealed hypomyelination in one case. The high prevalence of anemia and infections highlights significant nutritional and health challenges.

In preschoolers aged 1–4 years, the mean age was 2.3 years, with 70.7% male. Key issues included 70% pallor and 45% frequent infections. Nutritional deficiencies were prevalent, with 67.5% having microcytic hypochromic anemia. Infantile Tremor syndrome was observed in 1 case (6.7%), and MRI showed diffuse cortical thinning in 1 case (6.7%).

In school-aged children (5–10 years), with a mean age of 7.3 years, 82% were underweight and 77% had pallor. Nutritional deficiencies were evident, with 60% having microcytic hypochromic anemia. Notable comorbidities included dengue fever, viral fever, and Down's syndrome, each affecting 17%.

In adolescents aged 11–17 years, with a mean age of 13.8 years, 77.8% were female. The dietary data for adolescents reveals that a significant majority, 81.5%, follow a vegetarian diet, while 18.5% have a mixed diet. 85.2% had pallor and 55.6% had a generalized weakness. Tingling and numbness were seen in 40.4% of cases. Nutritional deficiencies were notable, with 37.3% having microcytic hypochromic anemia and 25.9% underweight. Comorbidities included dengue fever and viral fever (7.4% each), and 22.2% had pancytopenia.

LIMITATIONS

Lack of comprehensive biomarker analysis

The study could not measure important biomarkers like methylmalonic acid, homocysteine, and folate. These are essential for properly evaluating vitamin B12 deficiency and its metabolic effects, especially in cases where serum vitamin B12 levels are normal but patients still show clinical features of deficiency.

Small sample size

The small sample size may limit how widely the results can be applied. A larger cohort would make the findings more reliable and improve understanding of vitamin B12 deficiency and its relationship with nutritional and dietary factors.

CONCLUSION

This study shows that vitamin B12 is essential for the nutritional status and neurological health of children and adolescents. It also identifies certain high-risk groups. Vitamin B12 deficiency was more common in infants, children with delayed complementary feeding, and adolescents. These groups have a higher risk of developing neurological complications, making early diagnosis and treatment important.

The study also found that children on a vegetarian diet had lower vitamin B12 levels and a higher prevalence of deficiency compared to those on a mixed diet. This indicates that regular monitoring and possible supplementation may be necessary for vegetarians.

245 Additionally, maternal vitamin B12 levels directly influence the health of exclusively breastfed infants, highlighting
246 the importance of adequate maternal nutrition.
247 Children with severe malnutrition were also found to have lower vitamin B12 levels, showing a clear association
248 between poor nutritional status and vitamin B12 deficiency. This emphasizes the need for proper nutritional
249 assessment and management in such cases.

250
251 Overall, the study highlights the importance of adequate intake and regular monitoring of vitamin B12, especially in
252 high-risk groups such as infants and children following vegetarian diets.

253 254 **ACKNOWLEDGEMENTS**

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