



ANATOMICAL AND PHYSIOLOGICAL CHANGES IN CHILDREN WITH VITAMIN B12 DEFICIENCY ANEMIA AND ITS TREATMENT

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ABSTRACT

Background: Vitamin B12 deficiency anemia is a prevalent nutritional disorder among children, especially in resource-poor countries, with considerable hematological, neurological and developmental complications.

Objectives: To evaluate the anatomical and physiological changes in children with vitamin B12 deficiency anemia and to assess the response to treatment.

Methods: This descriptive analytical study was conducted at Gomal Medical College, Dera Ismail Khan, from January 2024 to January 2025. Non-probability consecutive sampling was used to enroll 72 children (1-12 years) with vitamin B12 deficiency anemia. Clinical, neurological, hematological, and biochemical data were collected. The children were treated with vitamin B12 and response to therapy was observed. Data were analyzed using SPSS version 26. Paired t-test and chi-square test were used, with $p \leq 0.05$ being significant

Results: The mean age of participants was 6.8 ± 2.9 years, with male predominance (55.6%). Pallor (90.3%) and fatigue (80.6%) were the most common symptoms. Neurological involvement was observed in 30–40% of cases. Hematological analysis showed macrocytic anemia (MCV 104.6 ± 8.5 fL, Hb 7.9 ± 1.3 g/dL). Serum vitamin B12 levels were significantly low, with elevated homocysteine levels. Post-treatment, significant improvement was observed in hemoglobin (11.2 ± 1.4 g/dL), MCV, and vitamin B12 levels ($p < 0.001$). Complete recovery was achieved in 69.4% of patients.

Conclusions: Vitamin B12 deficiency anemia in children leads to significant anatomical and physiological alterations. Early diagnosis and timely treatment are essential to prevent long-term neurological complications and improve clinical outcomes.

Keywords: Vitamin B12 deficiency, macrocytic anemia, children, neurological changes, treatment response

INTRODUCTION

Vitamin B12 deficiency anemia is a significant nutritional and blood disorder in children, especially in third-world countries with poor nutrition and dietary deficiencies. Cobalamin (vitamin B12) is an essential vitamin for DNA synthesis, hematopoiesis, and the central nervous system. When deficient, this causes defective cell division, ineffective erythropoiesis and a form of macrocytic anemia. Beyond hematological changes, vitamin B12 deficiency is also associated with severe neurological manifestations, especially during the growing years, and can result in developmental delay and permanent neurological deficits (1-3). Children with vitamin B12 deficiency may present with a range of symptoms, including fatigue, pallor, severe neurodevelopmental delay with hypotonia, cognitive deterioration and developmental delay. Structural abnormalities, including cerebral atrophy and delayed myelination, have also been noted in severe or chronic vitamin B12 deficiency. These signs point to the systemic nature of the disease and its capacity to impact both growth and brain development (4-7). Vitamin B12 deficiency remains poorly recognised and screened for in low-resource countries such as Pakistan. Its prevalence is increased by low dietary intake, exclusive breastfeeding without supplementation and maternal vitamin B12 deficiency. A recent study has highlighted the need for early screening and treatment to prevent permanent neurological impairment (8-10). Despite its clinical importance, there is limited local data evaluating both the anatomical and physiological consequences of vitamin B12 deficiency in children, along with treatment outcomes. Therefore, this study was designed to assess the clinical, hematological, biochemical, and neurological changes associated with vitamin B12 deficiency anemia in children and to evaluate the effectiveness of vitamin B12 therapy in improving these parameters.

METHODOLOGY

This descriptive analytical study was conducted at Gomal Medical College from January 2024 to January 2025. This study was to assess the anatomical and physiological changes in children with vitamin B12 deficiency anemia, and treatment outcomes. Seventy-two children were enrolled in the study by a non-probability consecutive sampling method. The sample size of 72 was calculated using the WHO sample size formula for prevalence studies: $n = Z^2 \times p(1-p) / d^2$, where $Z = 1.96$ at 95% confidence level, $p = 5\%$ (estimated prevalence of vitamin B12 deficiency in children based on previous regional studies), and $d = 5\%$ margin of error. The calculated sample size was 73, which was adjusted to 72 based on feasibility and patient availability during the study period. The study included children between 1-12 years with vitamin B12 deficiency anemia defined as hemoglobin <11 g/dl and vitamin B12 level <200 pg/ml. Exclusion criteria included children with iron deficiency anemia, chronic systemic disease, congenital anomaly or on vitamin B12 supplements. A proforma was used to gather data after parental/guardian consent. Age, sex, weight, height, BMI and social class were noted. Clinical assessment included symptoms of pallor, lethargy, irritability, delayed physical and intellectual growth, and neurological symptoms such as hypotonia, paresthesia, and ataxia. Structural changes were evaluated by physical examination and radiology (where available) including signs of cerebral atrophy and delayed myelination. Investigations comprised of complete blood count (CBC) with hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and reticulocyte count. Laboratory tests included serum vitamin B12, folate, homocysteine, lactate dehydrogenase (LDH) and bilirubin. A peripheral blood film was examined for macrocytosis and hypersegmented neutrophils. Patients were treated with vitamin B12 injections or oral vitamin B12 supplementation as per the pediatric protocol. Patients were followed up for clinical and laboratory improvement over a defined period. The efficacy of the treatment was evaluated through comparison of various hematological and biochemical parameters before and after treatment, and improvement in clinical and neurological symptoms. Data were entered and analyzed using IBM SPSS Statistics. Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables as number and percentage. Normality of data was

assessed using the Shapiro–Wilk test. We used paired t-test to compare pre- and post-treatment measures and chi-square to compare qualitative characteristics. P-value ≤ 0.05 was taken as significant.

RESULTS

A total of 72 children with vitamin B12 deficiency anemia were included. The average age is 6.8 ± 2.9 years and there is a male preponderance. Majority of children were of low socioeconomic background and had poor nutritional indices.

Table 1: Demographic and Baseline Characteristics of Participants (n = 72)

Variable	Category	Frequency (%) / Mean $\pm$ SD
Age (years)	—	6.8 ± 2.9
Gender	Male	40 (55.6%)
	Female	32 (44.4%)
Weight (kg)	—	18.6 ± 5.2
Height (cm)	—	108.4 ± 12.7
BMI (kg/m ²)	—	15.2 ± 2.1
Socioeconomic Status	Low	45 (62.5%)
	Middle	20 (27.8%)
	High	7 (9.7%)

Clinical manifestations were dominated by pallor and fatigue. Neurological and anatomical changes were also observed, indicating systemic and neurodevelopmental involvement.

Table 2: Clinical, Neurological, and Anatomical Features

Variable	Frequency (%)
Pallor	65 (90.3%)
Fatigue	58 (80.6%)
Shortness of breath	30 (41.7%)
Irritability	42 (58.3%)
Developmental delay	25 (34.7%)
Glossitis	20 (27.8%)
Jaundice	18 (25.0%)
Paresthesia	28 (38.9%)
Hypotonia	22 (30.6%)
Ataxia	15 (20.8%)
Cognitive impairment	26 (36.1%)
Delayed milestones	24 (33.3%)
Cerebral atrophy (MRI)	10 (13.9%)
Delayed myelination	14 (19.4%)
Hepatomegaly	18 (25.0%)
Splenomegaly	12 (16.7%)

Baseline investigations demonstrated macrocytic anemia with significant biochemical abnormalities consistent with vitamin B12 deficiency.

Table 3: Hematological and Biochemical Parameters (Baseline)

Parameter	Mean $\pm$ SD
Hemoglobin (g/dL)	7.9 ± 1.3
MCV (fL)	104.6 ± 8.5
MCH (pg)	34.2 ± 3.1

MCHC (g/dL)	32.1 ± 2.0
RBC count (×10 ¹² /L)	3.1 ± 0.6
Reticulocyte count (%)	0.8 ± 0.3
Serum Vitamin B12 (pg/mL)	142.5 ± 35.8
Serum folate (ng/mL)	6.8 ± 1.9
Homocysteine (μmol/L)	18.6 ± 5.2
Serum LDH (U/L)	520 ± 110
Serum bilirubin (mg/dL)	1.6 ± 0.5

Peripheral smear showed **macrocytosis and hypersegmented neutrophils in 85% cases.**

A statistically significant improvement was observed in hematological and biochemical parameters following vitamin B12 supplementation.

Table 4: Treatment Response (Pre vs Post Therapy)

Parameter	Pre-treatment (Mean ± SD)	Post-treatment (Mean ± SD)	p-value
Hemoglobin (g/dL)	7.9 ± 1.3	11.2 ± 1.4	<0.001*
MCV (fL)	104.6 ± 8.5	90.3 ± 5.7	<0.001*
Reticulocyte count (%)	0.8 ± 0.3	2.5 ± 0.6	<0.001*
Vitamin B12 (pg/mL)	142.5 ± 35.8	410.2 ± 75.3	<0.001*

*Statistically significant (paired t-test)

Most children showed clinical recovery, with improvement in systemic and neurological symptoms.

Table 5: Clinical and Neurological Outcomes after Treatment

Outcome	Frequency (%)
Improvement in pallor	60 (83.3%)
Improved energy levels	55 (76.4%)
Neurological improvement	40 (55.6%)
Weight gain	48 (66.7%)
Complete recovery	50 (69.4%)
Partial recovery	18 (25.0%)
No improvement	4 (5.6%)

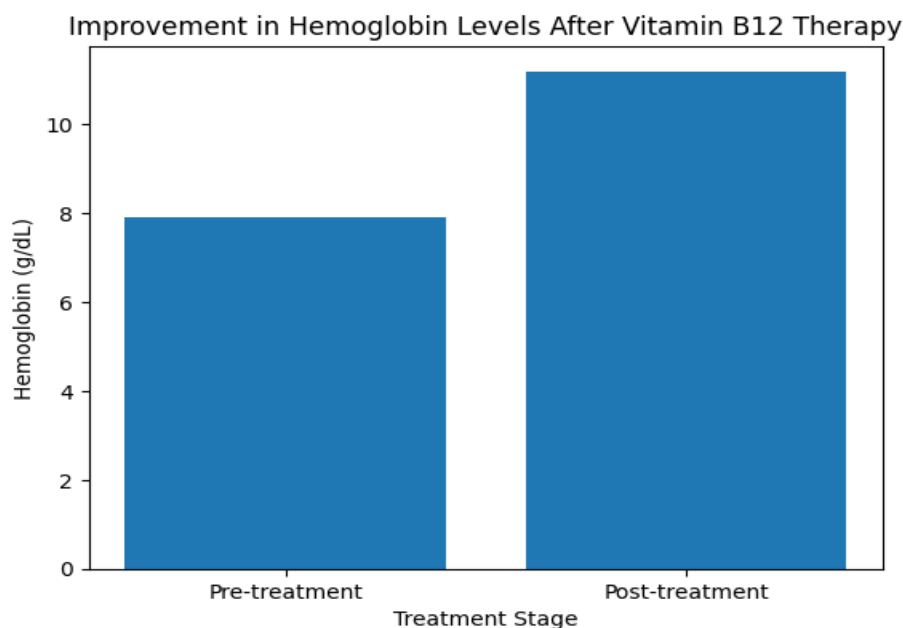


Figure 1: Bar chart showing significant improvement in mean hemoglobin levels (g/dL) among children with vitamin B12 deficiency anemia before and after treatment.

DISCUSSION

This study evaluated the anatomical and physiological changes in children with vitamin B12 deficiency anemia and assessed the response to treatment. The findings demonstrated that vitamin B12 deficiency in children is associated with significant hematological abnormalities, neurological manifestations, and structural changes, with substantial improvement following appropriate therapy. Our study population had a mean age of 6.8 ± 2.9 years with a male predominance. This age profile is similar to those reported in recent studies in children from South Asia, where malnutrition remains a major cause of anemia. The large number of children from low economic strata (62.5%) in our study also suggests that suboptimal nutrition and lack of access to nutritious food are other important contributing factors, as has been shown in recent Pakistani and regional studies (11-13). Pallor (90.3%) and fatigue (80.6%) were the most frequent clinical symptoms, which conform to the typical symptoms of anemia. But we also found a significant number of infants and children with irritability, mental retardation, and glossitis, which suggests systemic spread. There is growing recognition that vitamin B12 deficiency presents with subtle neurobehavioral symptoms in children, which may be missed in the early stages, resulting in a delay in diagnosis (14-16).

Our study also identified a significant proportion of patients with neurological symptoms, including paresthesia (38.9%), hypotonia (30.6%) and cognitive impairment (36.1%). This is in line with recent evidence that vitamin B12 is essential for the production of myelin and its role in the nervous system. Research have shown that sustained deficiency may lead to delayed myelination and cerebral atrophy, which was also found in a proportion of our patients (13.9%). This highlights the importance of early diagnosis to prevent irreversible neurological damage (17, 18).

Our study showed typical features of macrocytic anemia with high mean corpuscular volume (MCV 104.6 ± 8.5 fL) and low hemoglobin titer (7.9 ± 1.3 g/dL). The results obtained in our study accumulate to various other recent reports from the international literature that include macrocytosis and hyper-segmented neutrophils as the characteristic haemoglobinil picture of vitamin B12 deficiency (19).

Furthermore, it was found low levels of serum vitamin B12, hyperhomocysteinemia, and elevated LDH, indicating defective DNA synthesis and increased cell death, consistent with recent biochemical studies. The response to this intervention was highly significant, with a significant elevation of hemoglobin, normalization of MCV and reticulocytosis ($p < 0.001$). This is in agreement with recent clinical studies showing a rapid improvement in hematological abnormalities

after vitamin B12 supplementation. Crucially, 55.6% of patients, but not all, showed improvement in neurological symptoms. This is in line with recent reports that while hematological abnormalities improve rapidly, to some extent neurological improvement might take longer and is not always complete, especially in cases presenting late (20).

Our study showed a high overall recovery rate (69.4% complete recovery and 5.6% no recovery). This rate is similar to recent studies in children and highlights the importance of early diagnosis and treatment. The ongoing presence of some patients with partial recovery highlights the need for early screening and intervention programs, particularly in at-risk groups.

CONCLUSION

Vitamin B12 deficiency anemia in children is associated with significant hematological, neurological, and anatomical alterations, reflecting its systemic impact on growth and development. The condition commonly presents with macrocytic anemia, neurodevelopmental impairment, and biochemical abnormalities.

Timely diagnosis and appropriate vitamin B12 supplementation result in substantial hematological and clinical improvement; however, neurological recovery may be incomplete if treatment is delayed. These findings highlight the critical importance of early detection, nutritional awareness, and preventive strategies in pediatric populations.

Future studies should focus on long-term neurological outcomes and the implementation of community-based screening programs to reduce the burden of vitamin B12 deficiency in children.

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