

Characteristics of Patients with Megaloblastic Anemia: A Retrospective Analysis – A Pediatric Center Experience

Adnan Erseçkin^{1*}, Bilal Arslan¹, Serap Karaman², Kamuran Karaman³

¹Department of pediatric, Yüzüncü Yıl University, Van, Turkey

²Department of Neonatology, Yüzüncü Yıl University, Van, Turkey

³Department of pediatric hematology oncology Yüzüncü Yıl University, Van, Turkey

ABSTRACT

This study aimed to evaluate the clinical and hematological characteristics of 39 pediatric cases diagnosed with megaloblastic anemia who were investigated and treated at the Pediatric Hematology Clinic of Van Yüzüncü Yıl University Faculty of Medicine between 2020 and 2025.

A retrospective review of patient files was performed. Bone marrow aspiration findings, peripheral blood smear results, serum vitamin B12, and folic acid levels were analyzed and evaluated for the diagnosis of megaloblastic anemia.

Of the patients, 19 (48.7%) were female and 20 (51.3%) male, with a mean age of 37.8 months (range: 11–168). The most common presenting symptoms were loss of appetite, pallor, and fatigue. Folic acid deficiency was detected in 4 patients, and vitamin B12 deficiency in 35 patients. The mean hemoglobin concentration was 6.1 g/dL, mean MCV 97.2 fL, mean white blood cell count 8104/mm³, and mean RDW 23.8. Proteinuria was observed in 3 patients (7.7%). All patients were treated with parenteral vitamin B12 and oral folic acid, resulting in significant improvement in laboratory parameters. Post-treatment, iron deficiency anemia developed in 2 patients (5.1%). In 14 patients (35.9%), the initial MCV value was below 90 fL.

By presenting these cases, we aimed to emphasize that megaloblastic anemia may present without macrocytosis and highlight the importance of adequate nutrition in infants and pregnant women in our region.

Keywords: Megaloblastic anemia, hematological findings, clinical features, children

Introduction

Megaloblastic anemias are a group of anemias characterized by morphological abnormalities, particularly in erythroid lineage cells in bone marrow and peripheral blood. Morphologically, they fall under the macrocytic anemia classification. As they commonly result from deficiencies in vitamin B12 and folic acid—nutrients essential for nucleic acid synthesis—nuclear maturation is impaired while cytoplasmic maturation proceeds normally. This discrepancy between nuclear and cytoplasmic development is morphologically described as megaloblastic change. The prevalence of vitamin B12 deficiency has been reported to be as high as 22–66% in impoverished regions worldwide due to malnutrition. A study conducted in Şanlıurfa, Turkey, reported vitamin B12 deficiency rates of 40% in infants aged 6–11 months and 60% in

pregnant women.

Megaloblastic anemia particularly affects rapidly dividing tissues such as bone marrow, gastrointestinal mucosa, and the neuromotor system. Common clinical features include growth and developmental delay, irritability, loss of appetite, mucosal changes of the tongue and oral cavity, and gastroenteritis. In severe deficiency, sensory disturbances, paralysis, and psychosis may occur. The most significant hematological finding is anemia, with hemoglobin levels dropping as low as 2–3 g/dL. Peripheral blood smear typically reveals macrocytic erythrocytes and hypersegmented neutrophils. Leukopenia, thrombocytopenia, and pancytopenia may also be present.

*Corresponding Author: Adnan Erseçkin, Department of Pediatrics, Van Yüzüncü Yıl University, Faculty of Medicine, Van 65080, Türkiye
Email: dr.adnanerseckin@hotmail.com, Telephone: +90 (432) 216 00 00, Fax: +90 (432) 216 75 25

ORCID ID: Adnan Erseçkin: 0000-0002-3105-2749, Bilal Arslan: 0009-0001-3907-0888, Serap Karaman: 0000-0002-9143-6883,
Kamuran Karaman: 0000-0003-2991-3551

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Materials and Methods

A total of 39 patients with megaloblastic anemia who were followed and treated at the Pediatric Hematology Clinic of Van Yüzüncü Yıl University Faculty of Medicine between 2020 and 2025 were evaluated. Among patients presenting with anemia, bicytopenia, or pancytopenia, diagnosis was established based on clinical history, laboratory findings (Hb, MCV, platelets, leukocytes, LDH, reticulocyte count), bone marrow aspiration, and serum vitamin B12 and folic acid levels. All patients demonstrated megaloblastic changes in bone marrow aspiration. The study was approved by the Van Yüzüncü Yıl University Non-Interventional Ethics Committee (Decision No: 2025/04-22).

Statistical Analysis: Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean \pm standard deviation (SD) and minimum–maximum values, while categorical variables were presented as frequencies and percentages. The normality of data distribution was assessed using visual methods and analytical tests as appropriate. Comparisons of continuous variables between categorical groups were performed using one-way analysis of variance (ANOVA) for normally distributed data and the Kruskal–Wallis test for non-normally distributed data. Relationships between continuous variables were evaluated using Pearson correlation coefficients. Associations between categorical variables were analyzed using the chi-square test or Fisher’s exact test when appropriate. A p -value < 0.05 was considered statistically significant.

Results

Among the 39 patients, 19 (48.7%) were female and 20 (51.3%) were male, with a mean age of 37.8 months (range: 10–168). The most common presenting symptoms were loss of appetite, pallor, and fatigue. Folic acid deficiency was detected in 4 patients, while 35 patients had vitamin B12 deficiency. The mean serum vitamin B12 level in deficient patients was 103.4 ± 49.3 pg/mL (83–178), while the mean serum folic acid level in folic acid-deficient patients was 2.1 ng/mL (1.8–2.4). Mean hemoglobin was 6.1 g/dL (3.7–10.8), mean MCV 97.2 fL (54–122), mean white blood cell count $8104/\text{mm}^3$ (1800–69000), mean RDW 23.8 (13–46), mean LDH 3114 U/L (218–15326), and

mean reticulocyte count $<0.5\%$. Proteinuria was detected in 3 patients (7.7%). All patients received appropriate doses of parenteral vitamin B12 replacement, leading to normalization of serum vitamin B12 levels. Post-treatment, 2 patients (5.1%) developed iron deficiency anemia. In 14 patients (35.9%), the initial MCV value at presentation was below 90 fL. Ten patients (25.6%) were ≤ 12 months old at diagnosis. Leukopenia was observed in 2 patients (5.1%), thrombocytopenia in 11 patients (28.2%), and pancytopenia in 1 patient (2.5%) (Table 1).

Discussion

Vitamin B12 was first isolated in 1947 and plays a critical coenzyme role in DNA synthesis. There are four types of cobalamin: methylcobalamin, hydroxocobalamin, cyanocobalamin, and deoxyadenosylcobalamin. Cyanocobalamin and hydroxocobalamin are stable forms used in pharmaceutical preparations, while methylcobalamin and deoxyadenosylcobalamin act as active coenzymes in cells, functioning as cofactors in two key metabolic reactions: conversion of methylmalonyl-CoA to succinyl-CoA and homocysteine to methionine. Unlike other B vitamins, vitamin B12 is not synthesized by plants and must be obtained primarily from animal-based foods. The daily requirement is approximately 3 μg . Among B vitamins, B12 is the only one stored in significant amounts in the body, with a healthy adult containing about 3–5 mg, meaning deficiency symptoms may take several years to manifest. Term newborns have around 25 μg of stored B12, usually preventing deficiency-related anemia during the first year of life.

Megaloblastic anemia can develop in infants of mothers with B12 or folic acid deficiency, in breastfed infants of deficient mothers, or in individuals following poorly planned vegan or phenylketonuria diets. In our study, 10 patients (25.6%) were ≤ 12 months old, suggesting inadequate maternal nutrition during pregnancy. Megaloblastic anemia may also present with thrombocytopenia and neutropenia, and RDW and MCV are typically elevated. However, concurrent conditions such as iron deficiency anemia, infections, hereditary elliptocytosis, thalassemia trait, or chronic inflammatory disease may mask the expected macrocytosis. Previous studies have reported normal or even low MCV values in some megaloblastic anemia cases. Durmuş et al. reported that 25% of adult patients with

Table 1: Laboratory Values of Patients With Megaloblastic Anemia

	Average	± SD (Distribution)
Age (months)	37,8	36,7 (10-168)
Hemoglobin (gr/dl)	6,1	3,12 (3,7-10,8)
MCV (fl)	97,2	17,4 (54-122)
WBC (mm ³)	8104	10297 (1800-69000)
RDW	23,8	8,6 (13-46)
LDH (U/L)	3114	2643 (218-15326)
Serum B 12 (Pg/ml)	103,4	49,3 (83-178)
Serum Folic Acid (ng/ml)	7,8	5,1 (1,6-22)

Tables note: Data are presented as mean ± standard deviation (SD) and minimum–maximum values. Abbreviations: MCV, mean corpuscular volume; WBC, white blood cell count; RDW, red cell distribution width; LDH, lactate dehydrogenase; SD, standard deviation

megaloblastic anemia did not have elevated MCV, and Ali et al. found this rate to be one-third. In our study, 14 patients (35.9%) had MCV values below 90 fL at initial presentation, without any other identifiable cause for low MCV.

Recently, RDW has been increasingly used in differentiating megaloblastic anemia from other macrocytic anemias. Gupta et al. reported significantly higher RDW in megaloblastic anemia compared to aplastic anemia, suggesting its diagnostic utility. Similarly, in our study, 29 patients (74.3%) had RDW >17, while only 2 patients (5.1%) had RDW <15. This highlights the importance of considering RDW in evaluating vitamin B12 deficiency.

In conclusion, megaloblastic anemia should be considered even in patients presenting without macrocytosis. Moreover, the findings emphasize the importance of balanced nutrition for infants and especially pregnant women in our region.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Ethics Declarations

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Van Yüzüncü Yıl University Non-Interventional Ethics Committee with decision number 2025/04-29.

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