Cerrahpaşa Med J 2022; 46(2): 108-114 ORIGINAL ARTICLE

Evaluation of Vitamin B12 Deficiency in Hospitalized Infants: A 5-Year Experience

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Cite this article as: Türkmenoğlu Y, Aksu Uzunhan T, Türkkan E, et al. Evaluation of vitamin B12 deficiency in hospitalized infants: A 5-year experience. *Cerrahpaşa Med J.* 2022;46(2):108-114.

Abstract

Objective: Vitamin B12 deficiency in children can manifest itself with neurodevelopmental retardation, convulsion, hypotonia, tremor, faltering growth, and anemia. This retrospective study aims to compare the clinical and laboratory findings of infants with severe and non-severe vitamin B12 deficiency.

Methods: Children, hospitalized in the infant clinic and administered vitamin B12 therapy between April 2016 and April 2021 were included. A complete blood count, levels of ferritin, vitamin B12, folate, lactate dehydrogenase, and serum homocysteine were measured in all patients. In addition, the laboratory findings of patients with vitamin B12 levels ≤100 pg/mL (severe deficiency) and those with higher levels were compared.

Results: The mean age of the 106 children included in the study was 6.8 ± 4.5 (range: 1-20) months, and 66 (62.3%) of them were male. Fifty-one (48.1%) patients showed neurological symptoms, 29 (27.4%) patients had faltering growth, and 45 (42.5%) patients had anemia. The mean levels of serum B12 in patients were 109.28 ± 40.37 pgm/mL, homocysteine was 18.81 ± 13.54 µmol/L, and levels of hemoglobin were 9.94 ± 2.11 g/dL. Vitamin B12 levels were low in 23 (76.6%) of 30 mothers. The mean hemoglobin and hematocrit levels were statistically significantly lower ($P = .007$; $P = .020$, respectively), and the mean folate, LDH, and homocysteine levels were statistically significantly higher in severe vitamin B12 deficiency group ($P = .047$; $P = .009$; $P = .011$, respectively).

Conclusion: Vitamin B12 deficiency can manifest itself with different symptoms in young children without having anemia. Screening newborns for this deficiency may help prevent these early signs in infants.

Keywords: Child, infant, vitamin B12 deficiency, growth and development

Introduction

Vitamin B12 (cobalamin) is a water-soluble vitamin that is mostly found in foods obtained from animal sources, and cannot be synthesized in the human body. Working closely with folic acid, vitamin B12 serves a crucial function in DNA synthesis, red blood cell production, and neurologic function. The most common causes of vitamin B12 deficiency include insufficient dietary intake, congenital and acquired absorption defects, and impairments in the functional utilization of vitamin B12.[1-3] Vitamin B12 deficiency has been reported with a frequency of 12.5% in children, where is the frequency rises to 70-80% in school children in different geographical regions.[1]

In cobalamin metabolism, cyanocobalamin and hydroxocobalamin are converted to methyl and adenosylcobalamin, which are 2 forms of vitamin B12. Methylcobalamin plays an important role as a cofactor in the synthesis of methionine from homocysteine, and this reaction is essential for the formation of tetrahydrofolate and consequently in the nucleic acid biosynthesis. One of the biologically active forms of vitamin B12, adenosylcobalamin, is required for the conversion of methylmalonyl-CoA to succinyl-CoA. A manufactured form of vitamin B12, cyanocobalamin, has 2 active forms called adenosylcobalamin and methylcobalamin, which play a key role in certain metabolic pathways, and their deficiency often leads to the development of hematological, neurological, and gastrointestinal symptoms. These 2 forms are important co-factors in 2 enzymatic reactions, which play a role in the information of myelin. Some gastrointestinal, hematological, mucocutaneous, and neurological problems may be seen in case of these forms' deficiency.[1-4] The underlying mechanism of neural damage in vitamin B12 deficiency has been suggested to be delayed myelination or demyelination of the nerves caused by the changes in the ratio of S-adenosyl methionine to S-adenosyl homocysteine.[5] The most serious impact of vitamin B12 deficiency in infants occurs during the formation of myelin, causing delayed myelination, or demyelination of the nerves. It has been reported that vitamin B12 deficiency affects the neural functions of the infants through the defective myelin formation—since the myelination process mostly develops in the first 2 years of life, the effect of the neurological involvement in this age group could be

Received: December 31, 2021 **Accepted:** March 14, 2022 **Available Online Date:** May 30, 2022
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DOI: 10.5152/cjm.2022.21115

more pronounced and permanent.[5-8] Insufficient vitamin B12 in the maternal diet may result in its deficiency in the infants.[1,3-6,9] The most common cause of vitamin B12 deficiency in breastfed infants is the breastfeeding mother's voluntary or involuntary vegetarian diet, but it could also occur due to gastrointestinal absorption disorders.[1-4] Infants are more susceptible to vitamin B12 deficiency. Findings may be more pronounced in severe vitamin B12 deficiency. In infants, severe vitamin B12 deficiency often manifests itself with a cluster of clinical symptoms such as anorexia, refusal to feed, pallor, faltering growth, hypotonia, apathy, optic atrophy, neurodevelopmental delay and regression, tremors/involuntary movements, convulsions, hyperpigmentation, and presence of cytopenia of several cell types as the laboratory finding.[1] While such symptoms can be easily relieved with early diagnosis and treatment, they can cause irreversible neurological damage if they become chronic.[5-8]

Serum cobalamin of 148 pmol/L (200 pg/mL) is considered to be a deficiency, but laboratory results do not give accurate results at a rate of 10-20%.[3,4] Severe vitamin B12 deficiency is reported as <73.8 pmol/L or 100 pg/mL.[10,11] Haptocorrin (HC), intrinsic factor (IF), and transcobalamin are proteins that bind vitamin B12 and the levels of vitamin B12 may change due to its binding to these proteins.[4] Therefore, plasma methylmalonic acid and homocysteine elevation are recommended to be used in the diagnosis of vitamin B12 deficiency.[1-4]

In this retrospective study, we aimed to evaluate infants with vitamin B12 deficiency who presented to our infant clinic with various clinical manifestations. In addition, we aimed to compare laboratory and clinical findings of patients with severe and non-severe vitamin B12 deficiency.

Methods

This retrospective observational study was carried out between April 2016 and April 2021 at the infant clinic of University of Health Science Okmeydani Training and Research Hospital. The study population initially consisted of 106 patients aged 124 months, who were admitted to our infant clinic and had vitamin B12 therapy. Patients who were treated with vitamin B12 were searched retrospectively from the treatment records. Children with congenital malformations, dysmorphic findings, congenital heart disease, and known neuromotor diseases were excluded from the study. In addition, tandem mass spectrometry and urine organic acid analyses were performed to exclude congenital metabolic diseases. Approval for this study was obtained from the ethics commitee of University of Health Science Okmeydani Research and Training Hospital (June 11, 2019/1330).

Demographic and laboratory features of the patients were obtained from the records of the patients. Faltering growth was evaluated according to birth weights and current anthropological measurements.[12] Hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), red cell distribution width (RDW), white blood cell (WBC), and the platelet counts were evaluated from complete blood counts, and serum vitamin B12, folate, ferritin, glucose, urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactic dehydrogenase (LDH), and homocysteine levels were analyzed in all patients. Peripheral blood smears (macroovalocytes and hypersegmented neutrophils), radiological results (cranial magnetic resonance imaging), and treatments were obtained from the records. The Hb level <–2 SD for age was accepted as anemia.[13,14] In our laboratory, the breakpoint for homocysteine was 8.3 µmol/L. Vitamin B12 deficiency was confirmed if the serum vitamin B12 level was lower than 200 pg/mL and the homocysteine level was greater than 8.3 µmol/L in the presence of a normal folate level. Severe vitamin B12 deficiency below 100 pg/mL was accepted. If any, maternal vitamin B12 results of exclusively breastfed patients were evaluated from the records. In addition, clinical and laboratory findings of patients with severe vitamin B12 deficiency (<100 pg/mL) and non-severe vitamin B12 deficiency (≥100pg/mL) were compared.

Statistical Analysis

The research data were analyzed using IBM Statistical Package for the Social Sciences 22 software package for statistical analysis (IBM SPSS Corp., Armonk, NY, USA). If the distribution of continuous variables shows normal distribution, they were presented as mean ± SD ($P > .05$ in Kolmogorov-Smirnov test or Shapiro-Wilk), and if the continuous variables show not a normal distribution, they were described as the median (min-max). Descriptive statistical methods were used while evaluating the study data (mean, standard deviation, and frequency). Comparisons between groups were analyzed using Student's *t*-test for normally distributed data and Mann–Whitney *U*-test was used for the data not normally distributed. The categorical variables between the groups were analyzed by using the chi-square test or Continuity (Yates) fix test. A *P*-value less than .05 was considered statistically significant ($P < .05$).

Results

Of the 130 patients initially included in the study, 24 had to be excluded: homocysteine test results were not available for 11 of these patients; whereas 13 were diagnosed with known chronic diseases (one of them Cobalamin E disease). The ages of 106 children ranged from 1 to 20 months, and 66 (62.3%) of them were male. The weight of the patients varied between 3600 and 12 320 g (median: 6900 g). The demographic characteristics of the patients are shown in Table 1.

Apart from respiratory tract symptoms, the most common reason for admission was seizures. The distribution of symptoms of signs of the patient for admission to the hospital is shown in Table 2.

The laboratory tests include complete blood count, ferritin, vitamin B12, folate, glucose, urea, creatinine, ALT, AST, LDH, and serum total homocysteine levels at admission and control vitamin B12 levels after therapy were evaluated. In addition, the results of C3 or propionyl carnitine (N = 0-6.8µmol/L) and methylmalonic

Table 1. Demographic Characteristics of the Patients

	Minimum	Maximum	Mean ± SD	Median
Age (month)	1	20	6.79 ± 4.52	6
Weight (g)	3600	12 000	7007.22 ± 1856.25	6900
Birth weight (g)	2500	4250	3091.56 ± 47.84	3020
		n	**%**	
Gender				
Female		40	37.7	
Male		66	62.3	
Age distribution, month				
<6		47	44.3	
6-12		46	43	
>12		13	12.3	

Table 2. Distribution of Symptoms and Signs of Patients for Admitting to Hospital

Symptoms	**n**	**%**
Respiratory tract symptoms	50	47.2
Afebrile Seizure	38	35.8
Pallor	19	17.9
Problems of feeding	11	10.4
Diarrhea	6	5.7
Vomiting	4	3.8
Weakness	4	3.8
Jaundice	2	1.9
Tremor	2	1.9
Signs	**n**	**%**
Faltering growth	29	27.4
Hipotonia/neurodevelopmental retardation	25	23.6
Lack of social interaction	19	17.9
Periungual skin hyperpigmentation	8	7.5
Tremor	2	1.9
Optic atrophy	1	0.9

*Some patients had multiple symptoms and signs.

acid levels in the urine (N < 50 mg/g creatinine) were evaluated. Laboratory findings of the patients are shown in Table 3.

Anemia was found in 45 (42.5%) of the patients, and hypersegmented neutrophils were detected in 18 patients. The hematological parameters were within the normal range in 47.2% of the patients. The hematological findings of the patients are shown in Table 4.

There were 49 (46.2%) patients with severe vitamin B12 deficiency, and 11 (10.4%) of them had almost undetectable levels (<50 pg/mL). Clinical and demographic features of the patients with severe and non-severe vitamin B12 deficiency were compared. The rate of anemia was statistically significantly higher for severe vitamin B12 deficiency group ($P = .025$) (Table 5).

Laboratory findings (Hb, Htc, MCV, RDW, WBC, ANC, platelet count, ferritin, folate, homocysteine, and LDH) of patients with severe (vitamin B12 <100 pg/mL) and non-severe vitamin B12 deficiency were compared (Table 6). There were no significant differences in the mean of MCV, RDW, RBC, ANC, WBC, or platelet count, and ferritin levels. The mean hemoglobin and hematocrit levels were statistically significantly lower ($P = .007$; $P = .020$, respectively), and the mean folate, LDH, and homocysteine levels were statistically significantly higher for severe vitamin B12 deficiency group ($P = .047$; $P = .009$; $P = .011$, respectively).

In addition, levels of the vitamin B12 levels of the mothers of the 30 children who were exclusively fed breastmilk were revealed. The 30 mothers with vitamin B12 level were found 175.80 ± 92.20 (106-403 pg/mL) and 23 (76.7%) of them were <200 pg/mL vitamin B12 level.

Cranial MRI was performed on 17 patients with neurological findings. Four patients had enlarged lateral and third ventricles. Thinning of the corpus callosum was seen in 2 patients and edema in 1 patient.

All patients received intramuscular vitamin B12 (cyanocobalamin) therapy for 5 months. During the first week, each patient was administered a dose of 250-500 mcg every other day. Then the dose was reduced to 250-500 mcg twice a week; then once weekly for 2 weeks, and after that, they received a single monthly dose for 4 months. In addition, red blood cells were transfused in 11 patients. In addition, erythrocyte suspension was administered to patients with severe anemia and heart failure symptoms. Tremor, hypotonia, and lack of social interaction recovered during the first 2 weeks of vitamin B12 treatment. The involuntary movements of the face and the arms in 1 patient, during the treatment, were evaluated as an adverse reaction to the treatment. Treatment of this patient was continued with clonazepam and hydroxocobalamin. The eye examination of the infant with optic atrophy was evaluated as normal 1 week after the vitamin B12 treatment was initiated.

Discussion

In our study, the mean age was found 6 months and, 44.3% of them were aged 1-6 months. During the antenatal period, vitamin B12 is actively transferred from the placenta to the fetus, and after birth, exclusively breastfed infants are not expected to show any deficiency for 4 or 6 months if they have received sufficient amounts of vitamin B12 before birth.[3,15] However, metabolic and gastrointestinal disorders, which are rare in this age group, may also be responsible for vitamin B12 deficiency.[1-4] In our study, these patients were initially excluded from the study. Voluntary or involuntary vegetarian nutrition causes vitamin B12 deficiency in mothers and deficiency may occur in infants at earlier stages. In infants fed exclusively with breastmilk, the mother's B12 status is more important.[9,16] In our study, only breastfed patients had a frequency of 28.3%, and their mothers' vitamin B12 levels were low at 76.7%. This result suggests that diagnosing vitamin B12 deficiencies of mothers during pregnancy and starting treatment during pregnancy may help to prevent such clinical signs and symptoms that may occur in their children.

Vitamin B12 deficiency can also develop without anemia.[1-3,17] Anemia was found in 42.5% of our patients. In a study conducted in infants and older children with vitamin B12 deficiency, the frequency of anemia was found to be two-thirds. It's suggested hematological abnormalities were more frequent in older children in the same study.[17] Goraya et al[6] reported the incidence of anemia as 83% and macrocytosis as 71% in 27 children aged 6-27 months with vitamin B12 deficiency. Besides anemia, the hematological findings of vitamin B12 deficiency include elevated MCV, leucopenia, thrombocytopenia, bicytopenia, and pancytopenia.[1-4] Previous studies in the relevant literature reported that the presence of anemia, elevated MCV, and hypersegmentation of the neutrophils was not conclusive enough for the diagnosis of vitamin B12 deficiency. In a study conducted with 20 infants, anemia was observed in 80%, leukopenia in 15%, thrombocytopenia in 10%, and MCV elevation in 30%, and they found concomitant iron deficiency in 20% of the patients.[18] The 46.2% of our patients had severe vitamin B12 deficiency, but the anemia rate was low. The low incidence of anemia in our patients suggests that other findings of vitamin B12 deficiency occur before anemia develops.

Vitamin B12 deficiency in adults and older children can manifest itself with neurologic symptoms such as ataxia, difficulty in concentrating, memory loss, dizziness, syncope, tremor, loss of vision, dementia, and convulsions.[1-4] Hypotonia, tremor, and neurodevelopmental retardation are thought to be among the most

Table 3. Laboratory Findings of Patients

Parameters	Minimum	Maximum	Mean ± SD	Median
Hb (g/dL)	4	14.9	9.94 ± 2.11	10.4
Htc (%)	12.1	44.4	30.07 ± 5.77	31.45
MCV (fL)	50.5	104.3	78.3 ± 11.71	77.7
RDW (%)	11	44.5	16 ± 4.57	14.7
RBC count(/mm^3)	1 330 000	54 280 000	4 757 169.81 ± 6 003 993.55	4 130 000
ANC (mm^3)	300	15 670	4279.04 ± 3569.92	3070
WBC count(mm^3)	2440	31 410	10 845.42 ± 5486.8	9975
Plt count (mm^3)	32	746	354.83 ± 159.82	362.5
Ferritin (ng/mL)	2.2	767	70.4 ± 105.5	36.385
Vitamin B12 (pg/mL)	50	194	109.28 ± 40.37	105
Folat (ng/mL)	5.72	24	16.73 ± 4.82	16.635
Homocysteine (µmol/L)	8.5	110.8	18.81 ± 13.54	15
Glucose (mg/dL)	75	136	95.14 ± 11.96	92
Urea (mg/dL)	4	35	14.60 ± 5.67	14
Creatinine (mg/dL)	0.10	0.50	0.22 ± 0.7	0.22
ALT (U/L)	4	41	16.46 ± 7.64	15
AST (U/L)	6	54	37.58 ± 9.94	39.0
LDH (IU/L)	222	2477	414.35 ± 291.95	334.5
C3 or propionyl carnitine (µmol/L)	0.59	4.07	1.62 ± 0.78	1.49
Urine methylmalonic acid (mg/g creatinine)	15	99.5	43.7 ± 26.0	50
Control vitamin B12 (pg/mL)	130	2000	919.37 ± 487.78	825

Hb, hemoglobin; Htc, hematocrit; MCV, mean corpuscular volüme; RDW, red cell distribution width; RBC, red blood cell; ANC, absolute neutrophil count; WBC, white blood cell; Plt, platelet; ALT, alanin aminotransferase; AST, aspartate aminotransferase; LDH, lactic dehydrogenase; MMA, methylmalonic acid.

common findings of vitamin B12 deficiency in infants.[5-8,11,17-20] In a study, it was reported that neurological findings such as hypotonia and neurodevelopmental retardation were more common than hematological findings in children under the age of

Table 4. Hematological Findings of Patients

Hematological Findings	n	%
Normal	50	47.2
Anemia	45	42.5
MCV increase	38	35.8
Leucopenia or neutropenia	14	13.2
Thrombocytopenia	16	15.1
Bicytopenia	15	14.2
Pancytopenia	2	1.9

MCV, mean corpuscular volume.

Table 5. Demographic and Clinical Features of the Patients with Severe and Non-severe Vitamin B12 Deficiency

	Vitamin B12		
	<100 pg/mL Mean ± SD (median)	≥100 pg/mL Mean ± SD (median)	*P*
[a]Age (month)	7.10 ± 4.22 (6)	6.53 ± 4.79 (5)	.302
[b]Gender			
Female	17 (34.7%)	23 (40.4%)	.691
Male	32 (65.3%)	34 (59.6%)	
[c]Neurological sign	26 (53.1%)	32 (56.1%)	.344
[b]Anemia	27 (55.1%)	18 (31.6%)	.025*
[b]Faltering growth	11 (22.4%)	18 (31.6%)	.405

[a]Mann–Whitney U-test. [b]Continuity (yates) correction. [c]Chi-square. *$P < .05$.

Table 6. Comparison of Laboratory Findings of the Patients with Severe and Non-severe Vitamin B12 Deficiency

	Vitamin B12		
	Severe (<100 pg/mL) Mean ± SD (median)	Non-severe (≥100 pg/mL) Mean ± SD (median)	*P*
[a]Hb (g/dL)	9.38 ± 2.31 (9.9)	10.43 ± 1.81 (10.7)	.007*
[a]Htc (%)	28.57 ± 6.59 (31.2)	31.36 ± 4.65 (32.1)	.020*
[b]MCV (fL)	77.78 ± 12.33 (77.1)	78.75 ± 11.23 (78.1)	.673
[a]RDW (%)	17.27 ± 6.12 (15.2)	14.91 ± 2.11 (14.3)	.076
[a]RBC (mm^3)	3 772 040.82 ± 1 026 823.54 (4 130 000)	5 604 035.09 ± 806 889.96 (4 090 000)	.147
[a]ANC (mm^3)	4441.39 ± 4027 (3340)	4139.47 ± 3154.79 (2830)	.897
[a]WBC count (mm^3)	11 043.47 ± 6181.78 (10030)	10 675.18 ± 4860.84 (9660)	.922
[b]Plt count(mm^3)	337.78 ± 177.88 (345)	369.49 ± 142.47 (377)	.311
[a]Ferritin (ng/mL)	50.18 ± 58.82 (29.3)	87.77 ± 131.3 (43,9)	.089
[b]Folat (ng/mL)	17.73 ± 4.9 (17,6)	15.87 ± 4.61 (16)	.047*
[a]Homocysteine (µmol/L)	22.07 ± 18 (18.2)	16.02 ± 7 (13,8)	.011*
[a]LDH (IU/L)	491.08 ± 401.27 (360)	348.39 ± 110.53 (325)	.009*

[a]Mann–Whitney U-test. [b]Student's *t*-test. *$P < .05$.
Hb, hemoglobin; Htc, hematocrit; MCV, mean corpuscular volume; RDW, red cell distribution width; RBC, red blood cell; ANC, absolute neutrophil count; WBC: white blood cell; Plt, platelet; LDH, lactic dehydrogenase.

6.[17] Jain et al[7] observed neurodevelopmental delay or regression due to vitamin B12 deficiency in 14 infants with a mean age of 11 months, and they found serious and permanent disorders in 57% of the patients. In a study, that was conducted on 38 children with neurological findings and vitamin B12 deficiency, 9 children aged <24 months had symptoms associated with hypotonia.[20] In our study, hypotonia or neurodevelopment retardation was seen in only 15.1% of the patients, hypotonia in all the patients improved after vitamin B12 treatment. In addition, lack of social interaction, nystagmus, involuntary movements, tremors, and convulsions are reported due to vitamin B12 deficiency in this age group.[6,19,20-23] Afebrile convulsions have been reported with a frequency of 29-45% in vitamin B12 deficiency.[21,23] Convulsions were at a frequency of 35.8 % among our patients. It has been suggested that high homocysteine levels cause cerebral toxicity and ultimately convulsions. The upper limit homocysteine level has been accepted between 6.5 and 15 µmol/L in different studies.[1,8] In our study, the laboratory limit of 8.3 µmol/L was accepted as the upper limit. Among the patients in our study, lack of social interaction was the most common neurological finding (31.5%), while 15.1% had hypotonia and 1.9% had a tremor. Although described among the findings of vitamin B12 deficiency, optic atrophy is quite rare in adults and can be easily treated if diagnosed early.[1] In our study, optic atrophy was detected in a 2-month-old baby and it resolved upon treatment. Early initiation of treatment helps preventing permanent damage such as optic atrophy.

There are studies investigating vitamin B12 deficiency in hospitalized children in our country.[18,24] A study conducted in our country reported that vitamin B12 deficiency was detected in 30% in the hospitalized children (aged 1-24 months) with diarrhea and respiratory tract symptoms and that the occurrence of an infection triggered the onset of symptoms.[18] About 45.2% of our patients had accompanying diseases such as respiratory tract infections and 3.5% gastroenteritis, but it is also possible that the vitamin B12 deficiency and anemia could have rendered patients susceptible to infections or the presence of such findings during infection-related hospitalizations might have led to the diagnosis of vitamin B12 deficiency.

Vitamin B12 is essential for normal growth and development during the fetal and the neonatal periods as well as in infancy. It plays a key role in energy production and the synthesis of proteins, phospholipids, and fatty acids.[1-4] Faltering growth under the age of 2 in vitamin B12 deficiency has been reported 15-78.% in different studies.[6,11,18] In our study, it was found at a frequency of 27.4%. Knuckle hyperpigmentation is also considered among the specific findings.[6,17] Among our patients, it was seen with a frequency of 7%. These findings are helpful for early diagnosis.

Vitamin B12 deficiency is defined as serum vitamin B12 levels less than 200 pg/mL, and levels below 100 pg/mL are defined as severe deficiency. In the literature, there are limited studies on severe vitamin B12 deficiency.[10,11] However, there is no study in the literature comparing severe and milder vitamin B12 deficiencies. In a study of infants, anemia was found in all patients with severe vitamin B12 deficiency.[11] In our study, 46.2% of the patients had severe vitamin B12 deficiency, 55.1% of whom had anemia. The frequency of anemia was found to be higher in the group with severe vitamin B12 deficiency. In accordance with the frequency of anemia, hemoglobin and hematocrit values were also low in the severe vitamin B12 deficiency group. Folate and homocysteine are involved in the biochemical cycle of vitamin B12.[4] It is reported that LDH levels are high in vitamin B12 deficiency.[1-4,11,24] High LDH is thought to be the result of ineffective erythropoiesis in the bone marrow in vitamin B12 deficiency.[1-4,24] Our results were also found to be compatible with these findings.

In some studies, some findings were found on cranial MRI images in patients with vitamin B12 deficiency and neurological findings. Indicators of neurological damage caused by vitamin B12 deficiency have been demonstrated by MRI findings in some studies, which include cerebral atrophy, thinning in corpus callosum, delayed myelination, ventriculomegaly, and enlargement of the Sylvian fissure.[11,18,25,26] Because of the absence of MRI findings in every patient, the possibility of coincidence comes to our mind. However, some improvements could be achieved with early diagnosis and treatment. Two of our patients who underwent MRI were found to have thinning in the corpus callosum and 4 patients had enlargement of the ventricles, but no follow-up imaging could be performed.

Intramuscular administration of cyanocobalamin and hydroxocobalamin is recommended for the treatment of vitamin B12 deficiency.[1-4] In addition, oral use of vitamin B12 is also possible in children.[27] It has been reported that fasciculation-like involuntary movements are rarely observed in some cases during treatment, which might be attributed to the deterioration of the balance between excitatory-inhibitory pathways. In this case, it is recommended to use hydroxocobalamin and to add clonazepam in severe cases.[21] In our study, facial fasciculations were observed in one patient, yet they improved with clonazepam and hydroxocobalamin therapy and then disappeared completely.

Previous research demonstrated that 58.1-72% of the pregnant women with low socioeconomic status had vitamin B12 deficiency, which led to vitamin B12–deficient newborns as revealed by the newborn screening tests.[16,28,29] Similarly, 49.5% of our patients were infants aged below 6 months, 8 of whom were exclusively breastfed, and one-third of the mothers of these exclusively breastfed infants had low serum vitamin B12 levels. In recent years, the issue of screening pregnant women for prenatal vitamin B12 deficiency has been discussed.[30] It is thought that early diagnosis and treatment of vitamin B12 deficiency in mothers can prevent neurological findings, especially in children. Our study also supports the usefulness of this screening in newborns.

Study Limitations

1. The study sample consisted of a relatively limited number of patients.
2. Vitamin B12 levels in all the mothers were not available.

In conclusion, vitamin B12 deficiency in infants can manifest with neurological symptoms or faltering growth without the presence of anemia. The nutritional status of the mothers appears to exert a substantial impact on such infants. Screening pregnant women or newborns for vitamin B12 deficiency and initiating treatment upon diagnosis in the early period may contribute to the neurological development of infants during the first 2 years.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of University of Health Science Okmeydani Research and Training Hospital (Date: June 11, 2019, No: 1330).

Informed Consent: Written informed consent was obtained from all parents of patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Author Contributions: Concept – Y.T., Ö.F.B., A.K.; Design – Y.T.; Supervision – Y.T., T.A.U., Ö.F.B., A.K.; Materials – Y.T., E.T., N.U., A.L.; Data Collection and/or Processing – Y.T., T.A.U., E.T., N.U., A.L.; Analysis and/or Interpretation – Y.T., D.B.; Literature Review – Y.T., T.A.U., E.T., N.U., A.L., Ö.F.B., A.K.; Writing – Y.T.; Critical Review – D.B.

Declaration of Interests: The authors declare that they have no competing interests.

Funding: The authors declared that this study has received no financial support.

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