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The frequency of vitamin B12, iron, and folic acid deficiency in the neonatal period and infancy, and the relationship with maternal levels

Yenidoğan ve süt çocukluğu döneminde B 12 vitamini, demir, folik asit eksikliğinin sıklığı ve maternal düzeylerle ilişkisi

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The known about this topic

Vitamin B12 is important for cell growth and DNA synthesis. It cannot be synthesized by the human body, so it must be obtained from the diet. In deficiency of vitamin B12, hematologic, intestinal, and neurologic findings are observed. The most important reason for deficiency in infancy is deficiency in the mother.

Contribution of the study

Our study is the first to demonstrate the frequency of vitamin B12 deficiency in pregnant women and newborns in the region of Trakya. In this study, it was found that there was a moderate positive correlation between the vitamin B12 levels in mothers and newborns, and the cord B12 levels in babies whose mothers had adequate vitamin B12 levels were higher compared with the group whose mothers had deficient vitamin B12 levels.

Abstract

Aim: The most important function of vitamin B12 is to accomplish DNA synthesis, which is necessary for cell division and proliferation. Deficiency of vitamin B12 causes megaloblastic anemia, retardation of growth, and delay in neuromotor maturation. Newborns whose mothers have vitamin B12 deficiency are born with low vitamin B12 storages, and are at risk in terms of vitamin B12 deficiency symptoms during infancy. The aim of our study was to investigate the frequency of anemia and deficiency of vitamin B12, folic acid, and iron in pregnant women living in our region, in their newborn babies, and during the infancy period of these babies. Another aim of our study was to investigate the correlation between the levels of these vitamins in newborns and in their mothers.

Material and Methods: In our study, 250 pregnant women at 38–42 gestational weeks, who were admitted for delivery to Gynecology and Obstetrics Clinic and their babies with a birth weight over 2500 g were included in the study.

Öz

Amaç: B 12 vitamininin en önemli işlevi hücre bölünmesi ve çoğalması için gerekli olan DNA sentezini desteklemesidir. Eksikliği süt çocuklarında megaloblastik anemi, büyüme ve nöromotor gelişimde geriliğe yol açabilir. Annelerinde eksiklik olan ve düşük B 12 vitamini depolarıyla doğan yenidoğanlar süt çocukluğu döneminde eksiklik bulguları gelişmesi açısından risk altındadır. Bu çalışmada bölgemizdeki gebelerde, onların yenidoğan bebeklerinde ve süt çocukluğu dönemlerinde anemi, B 12 vitamini, folik asit ve ferritin eksikliği sıklığı ve yenidoğandaki düzeylerin maternal düzeyler ile ilişkisinin araştırılması amaçlandı.

Gereç ve Yöntemler: Çalışmaya Kadın Hastalıkları ve Doğum Servisi'ne doğum amacıyla başvuran 38–42 gebelik haftasında olan 250 gebe ve onların 2 500 g üstünde doğan sağlıklı bebekleri alındı.

Bulgular: Çalışmamızdaki gebelerin %24,8'i anemikti, %28'inde ise
Cont. ➡

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Results: We determined that 24.8% of the pregnant women had anemia, 28% had low ferritin levels, 90.4% had vitamin B 12 deficiency, and 22.4% had folic acid deficiency. Some 3.2% of the newborns had anemia, 2.8% had low ferritin levels, and 72.4% had vitamin B12 deficiency. Among the infants who presented for a follow-up visit at 6 months of age, 22.3% had anemia, 14.9% had low ferritin levels, 40.4% had vitamin B12 deficiency, and 1.06% had folic acid deficiency. In addition, we found that the levels of vitamin B12 and folic acid in newborns were related to the levels of vitamin B12 and folic acid in their mothers.

Conclusion: Development of low vitamin B12 stores in newborns and the development of vitamin B12 deficiency during infancy, which may result in irreversible complications including neurologic complications, can be prevented by preventing vitamin B12 deficiency during pregnancy.

Keywords: Anemia, infant, newborn, pregnancy, vitamin B12 deficiency

ferritin düşüklüğü, %90,4'ünde B 12 vitamini eksikliği, %22,4'ünde de folik asit eksikliği saptandı. Yenidoğanların %3,2'sinde anemi, %2,8'inde ferritin düşüklüğü, %72,4'ünde B 12 vitamini eksikliği saptandı. Kontrole getirilen süt çocuklarının %22,3'ünde anemi, %14,9'unda ferritin düşüklüğü, %40,4'ünde B 12 vitamini eksikliği, %1,06'sında folik asit eksikliği gözlendi. Ayrıca yenidoğanlardaki B 12 vitamini ve folik asit düzeylerinin annelerindeki düzeylerle ilişkili olduğu saptandı.

Çıkarımlar: Sonuç olarak, gebelerdeki B 12 vitamini eksikliği önlenerek yenidoğanların düşük depo ile doğmaları ve süt çocukluğu döneminde eksikliğe bağlı geri dönüşümsüz olabilen özellikle nörolojik bulguların gelişmesi önlenebilir.

Anahtar sözcükler: Anemi, B 12 vitamini eksikliği, gebelik, süt çocuğu, yenidoğan

Introduction

The most important function of vitamin B12 is to support DNA synthesis required for cell division and cell growth in association with folic acid. The system that is maximally sensitive to a deficiency of vitamin B12 is the hematopoietic system in which the cellular growth rate is high (especially erythropoietic series). The second most important function of vitamin B12 is to enable the maintenance of some normal structures and functions in the central and peripheral nervous system (1).

Children with vitamin B12 deficiency frequently present with nonspecific findings such as weakness, fatigue, growth retardation, and restlessness. Vitamin B12 deficiency is usually associated with signs of the hematologic and intestinal systems in which rapid cell growth occurs. In addition, neurologic findings may also be present. Although neurologic findings progress slowly, the signs and symptoms may not regress with vitamin B12 treatment in patients who have had deficiency for a long period (2, 3).

The most important reason for megaloblastic anemia in infancy is vitamin B12 deficiency in mothers. In babies born from mothers with vitamin B12 deficiency, severe vitamin B12 deficiency may be observed if they are being exclusively breastfed, because intake of vitamin B12 by the placenta in the prenatal period and by breastmilk in the postnatal period is insufficient (4, 5).

In our study, it was aimed to demonstrate the frequency of anemia, vitamin B12 deficiency, iron deficiency, and folic acid deficiency in pregnant women, newborns, and infants, and to investigate the relationship between the maternal levels and the levels in the neonatal and infancy periods.

Material and Methods

The study was planned prospectively between June 2008 and May 2009, and 250 pregnant women at the 38th–42nd gestational week and their healthy babies who were born with a birth weight above 2500 grams, were included in the study. The study exclusion criteria included maternal chronic disease, multiple pregnancy, premature labor, placenta previa, placental detachment, preeclampsia, and bleeding during pregnancy (gastrointestinal, urinary system).

Approval was obtained from Trakya University, Faculty of Medicine, Scientific Researches Ethics Committee for the study (TÜTFEK 2008/66). The study was conducted in accordance with the Declaration of Helsinki and informed consent was obtained from the pregnant women. Questionnaire forms that included the pregnant women's ages, weights, heights, gravida numbers, parity numbers, gestational weeks, education levels, use of vitamins and iron during pregnancy, and socioeconomic status were completed. Socioeconomic level (SEL) was evaluated using a scale adapted from Toukan et al. (6). The women were called again for a follow-up visit when their babies were aged 6–9 months. The return rate was found as 37.6%. The body weight, height and head circumference values were measured and physical examinations were performed in 94 babies. Nutritional status and iron prophylaxis were interrogated.

Blood samples were obtained 1–2 hours before birth from the pregnant women, cord blood samples were obtained from the newborns during delivery, blood samples were obtained at the age of 6–9 months, and complete blood count (Coulter LH 780 Hematology Analyzer, Beckman Coulter/USA), ferritin, folic acid, and vitamin B12 levels (UniCel DxI 800 Access, Beckman Coulter/USA) were studied. A hemoglobin (Hb) value below 13 g/dL in newborns, below 11 g/dL in pregnant women, and below 10.5 g/dL in infants was considered as anemia. A mean corpuscular volume (MCV) value below 95 fL in newborns, below 80 fL in pregnant women, and below 70 fL in infants, was considered microcytosis. A MCV value above 100 fL in pregnant women, above 120 fL in newborns, and above 86 fL in infants was considered as macrocytosis. The lower limit for ferritin was considered 25 ng/mL in newborns and 12 ng/mL in pregnant women and in infants (7). A vitamin B12 level below 200 pg/mL was considered as deficiency. A folic acid value below 3 ng/mL was considered as deficiency in all three groups (2).

The relationship of vitamin B12, folic acid, ferritin, and Hb values in the pregnant women with SEL, education levels, use of vitamins and iron, and with the level in newborns and infants was investigated. In addition, the relationship of the use of solid foods and iron in infants with the levels of vitamin B12, folic acid, ferritin, and Hb levels was investigated. The levels in the newborns were evaluated according to the status of vitamin B12, folic acid, and iron deficiency in the pregnant women.

Statistical Analysis

Statistical analysis was performed using the statistics program STATISTICA AXA 7.1 (serial number AXA507C775506FAN3). After the compatibility of the measurable data with normal distribution was tested using the Shapiro–Wilk test, Kruskal–Wallis variance analysis was used for comparisons between more than two groups because they did not show normal distribution. The Mann–Whitney U test was used for comparisons of two groups. The post hoc Dunn test was used following Kruskal– Wallis variance analysis. In in-group comparisons, the dependent t-test was used for variables that showed normal distribution, Wilcoxon's paired two-sample test was used for variables that did not show normal distribution, and Spearman and Pearson correlation analysis was used for the assessment of the relationship between variables. Arithmetic mean±standard deviation (SD) and mean (min–max) values are given as descriptive statistics. A p value <0.05 was considered significant for all statistics. In the assessment of correlation coefficients, r=0–0.30 was considered as absence of correlation, r=0.31–0.40 was considered as very weak correlation, r=0.41–0.50 was considered as weak correlation, r=0.51–0.75 was considered as moderate correlation, r=0.76–0.85 was considered as strong correlation, and r=0.86–1 was considered as very strong correlation.

Results

The mean age of the pregnant women was 27.7±5.4 years. Forty-four (17.6%) of the pregnant women had low SEL, 56 (22.4%) had low-moderate SEL, 73 (29.4%) had moderate-high SEL, and 77 (30.8%) had high SEL. Seventeen (6.8%) of the pregnant women were illiterate. One hundred fifty-one (60.4%) were primary school graduates, 55 (22%) were secondary school graduates, 27 (10.8%) were higher education graduates. It was the first delivery for 126 (50.4%) of the pregnant women, the second delivery for 83 (33.2%), the third delivery for 24 (9.6%), the fourth delivery for 10 (4%), and the fifth or above delivery for 7 (2.4%).

Table 1. Hematologic values in pregnant women and newborns

Variable	Pregnant women Mean±SD (n=250) Median (min.–max.)	Newborns Mean±SD (n=250) Median (min.–max.)
Hemoglobin (g/dL)	11.7±1.2 11.9 (8.5–14.5)	15.9±1.7 15.7 (11.5–20)
Hematocrit (%)	35±3 35 (24–43.7)	47.8±5.6 47.1 (32.8–63)
Red blood cells (million/mm³)	3.95±0.9 3.97 (2.85–4.9)	4.47±0.5 4.40 (3.12–5.86)
MCV (fl)	88.4±5.9 89 (63–101.4)	107.2±4.8 107 (90.1–128)
RDW (%)	14.3±2.1 13.8 (11.8–28)	16.9±1.4 17 (12–25)
Vitamin B12 (pg/mL)	118.2±53.7 108.3 (40–380)	169.1±78.9 153.5 (53–527)
Folic acid (ng/mL)	7.1±4.4 6.5 (1–20)	14.2±4.6 14.5 (3.6–20)
Ferritin (ng/mL)	32. ±30.9 25.5 (2.18–205)	121.4±76.8 108.5 (11–404)

SD: Standard deviation; Min.: Minimum; Max.: Maximum; MCV: Mean corpuscular volume; RDW: Red cell distribution width

When the pregnant women were interrogated in terms of the use of vitamin and iron preparations, it was learned that 22 (8.8%) pregnant women did not use iron, 61 (24.4%) used iron preparations irregularly, 167 (66.8%) used iron preparations regularly, 21 (4.4%) did not use vitamin preparations, 50 (20%) used vitamins irregularly, and 179 (71.6%) used vitamins regularly.

Sixty-two (24.8%) of the pregnant women were anemic. Sixteen (6.4%) pregnant women were found to have microcytosis, and three (1.6%) were found to have macrocytosis. Vitamin B12 level was sufficient only in 24 pregnant women (9.6%). Vitamin B12 levels were found to be below 200 pg/mL in 226 pregnant women (90.4%). Folic acid deficiency was found in 56 (22.4%) of the pregnant women. Ferritin levels were found to be low in 70 (28%) pregnant women. The hematologic values in the pregnant women are shown in Table 1.

No clinical correlation was found between the women's vitamin B12, ferritin, and Hb levels and SEL, though there was a statistically significant correlation (r=0.068, r=0.137, r=0.170, respectively; p=0.282, p=0.030, p=0.007, respectively). A very weak positive significant correlation was found between the pregnant women's folic acid levels and SEL (r=0.357, p=0,00). A statistically significant differ-

Table 2. The mothers' hemoglobin, vitamin B 12, folic acid values according t0 education levels

Education level	Hemoglobin (g/dL) Mean±SD (n=250) Median (min.–max.)	Ferritin (ng/ml) Mean±SD (n=250) Median (min.–max.)	Vitamin B 12 (pg/mL) Mean±SD (n=250) Median (min.–max.)	Folic acid (ng/mL) Mean±SD (n=250) Median (min.–max.)
Illiterate	11.4±1.3 (8.9–13.5)	36.3±47.5 (5.7–205)	127.6±43.4 122 (62–225)	5.6±5.3 3.9 (1–20)
Primary school	11.6±1.2 (8.5–14.5)	29.3±28.8 (2.1–199)	112.1±55.1 103 (40–380)	6.7±4.4 5.9 (1–20)
Secondary school	11.9±0.9 (9.6–13.7)	35±26.5 (6.4–134)	119.5±51.1 110 (47–342)	7.7±3.9 7.6 (1.5–20)
Higher education	12.2±1.1 (9.6–14.5)	42.5±36.7 (10–168)	143.6±49.9 132 (63–238)	9.0±4.6 8.1 (1.7–19)
	p=0.07	p=0.022[a]	p=0.004[b]	p=0.004[c]

SD: Standard deviation; Min.: Minimum; Max.: Maximum; a, b, and c: Statistically significant difference at a level of p<0.05

Table 3. Cord blood vitamin B 12 and folic acid levels according to the vitamin use of the pregnant women

Vitamin use	Vitamin B 12 (pg/mL)		Folic acid (ng/mL)	
	Mean±SD (n=250)	Median (min.–max.)	Mean±SD (n=250)	Median (min.–max.)
Regular	167.5±75.7	148 (58–527)	15.2±4.4	16 (3.9–20)
Irregular	174.3±86.8	163.5 (53–410)	12.1±4.3	12 (3.6–20)
Not using vitamin preparation	170.7±89.1	160 (94–505)	10.2±4.1	9.2 (5–20)
	p=0.919		p<0.001[a]	

SD: Standard deviation; Min.: Minimum; Max.: Maximum; a: Statistically significant difference at α level of p<0.05, level 0.016 (p<0.016, between women using vitamin preparations regularly and those who were using vitamin preparations irregularly and not using vitamin preparations)

ence was found between the women's vitamin B12 and folic acid levels by education level, whereas no significant difference was found between their Hb levels (p=0.004, p=0.004, p=0.070, respectively). A statistically significant difference was found in terms of ferritin according to Kruskal– Wallis variance analysis (p=0.022). According to the post-hoc Dunn test, a statistically significant difference was found between the primary school graduates and higher education graduates (p=0.037) (Table 2).

In terms of vitamin use, no statistically significant difference was found between the mothers' vitamin B12 levels (p=0.837), but a statistically significant difference was found between the folic acid levels (p<0.001). According to the post-hoc Dunn test, this difference in folic acid levels was present between women who used folic acid regularly and those who used folic acid irregularly or did not use folic acid (p=0.001, 0.001, respectively). When the pregnant women's ferritin and Hb levels were compared in terms of iron use, a statistically significant difference was found for both (p=0.0001, p=0.0001, respectively). According to the post-hoc Dunn test, this difference was present between the women who used iron preparations regularly and those who used iron preparation irregularly or did not use iron preparations for both ferritin and hemoglobin levels (p=0.001, 0.001, 0.001, 0.007, respectively). A difference was found between the babies' folic acid levels according to the mothers' use of folic acid (p=0.0001). According to the post-hoc Dunn test, this difference was present between women who used folic acid regularly and those who used folic acid irregularly and did not use folic acid (p=0.001, 0.001, respectively). No significant difference was found in terms of vitamin B12 levels (p=0.919) (Table 3).

One hundred twenty-three (49.2%) of the newborns were female and 127 (50.8%) were male. Eight (3.2%) of the newborns were anemic, 181 (90.4%) had vitamin B12 deficiency, and 69 (9.6%) had normal vitamin B12 levels. Folic acid deficiency was not found in any of the newborns and seven newborns (2.8%) had low levels of ferritin. The hematologic values of the newborns are shown in Table 1.

Table 4. Relationship between maternal and cord blood vitamin B12, folic acid, ferritin, and hemoglobin levels

Variable	Maternal Mean±SD (n=250)	Cord blood Mean±SD (n=250)	r	p
Vitamin B 12 (pg/mL)	118.2±53.7	169.1±79.1	0.675[a]	<0.001
Folic acid (ng/mL)	7.1±4.4	14.2±4.6	0.499[b]	<0.001
Ferritin (ng/mL)	32.5±30.9	121.1±76.8	0.052	0.412
Hemoglobin (g/dL)	11.7±1.2	15.9±1.7	0.116	0.067

SD: Standard deviation; a: Statistically significant moderate correlation; b: Statistically significant weak correlation

Table 5. Vitamin B12, folic acid and ferritin levels in newborns with vitamin B12 deficiency status in pregnant women

Cord blood values	Maternal vitamin B 12 status		p
	Sufficient Mean±SD Median (min.–max.) (n=24)	Deficient Mean±SD Median (min.–max.) (n=226)	
Vitamin B12 (pg/mL)	290.7±107.6 265.5 (141.0–527.0)	156.2±63 146.0 (53.0–508.0)	<0.001[a]
Folic acid (ng/mL)	14.8±3.9 14.9 (7.3–20.0)	14.1±4.7 14.4 (3.6–20.0)	0.647
Ferritin (ng/mL)	93±46.4 82.1 (20.0–170.0)	124.4±78.8 110.5 (11.0–400.0)	0.102

SD: Standard deviation; a: Statistically significant difference at a level of p<0.001

A moderately strong positive correlation was found between the mothers' and newborns' vitamin B12 levels (r=0.675, p=0.0001). A weak positive correlation was found in terms of folic acid levels (r=0.499, p=0.0001). There was no significant correlation in terms of ferritin and Hb levels (r=0.052, r=0.116, respectively; p=0.412, p=0.067, respectively) (Table 4). Vitamin B12 deficiency was present in 78% of the newborns whose mothers had vitamin B12 deficiency. Vitamin B12 levels were found to be sufficient in 87.5% of the babies whose mothers had normal vitamin B12 levels during pregnancy. When the babies were grouped according to the vitamin B12 level in their mothers, a statistically significant difference was found (p=0,0001), but there was no statistically significant difference in terms of folic acid and ferritin levels (p=0.360, p=0.495, respectively) (Table 5). No statistically significant difference was found between the ferritin and Hb levels of the babies whose mothers did and did not have anemia during pregnancy (p=0.223, p=0.143, respectively).

Among the mothers of infants aged between 6 and 9 months, prenatal measurement values showed vitamin B12 deficiency in 86 (91.5%) mothers, folic acid deficiency in 17 (18.1%) mothers, low ferritin levels in 25 (26.6%) mothers, and anemia in 19 (74.5%) mothers. Cord blood measurements in the infants showed vitamin B12 deficiency in 70 (74.5%) infants and anemia in four (4.3%) infants. Folic acid deficiency and low ferritin levels were not found in any of the infants.

Anemia was found in 21 (22.3%) of the infants and ferritin levels were low in 14 (14.9%). Folic acid deficiency was found in one (1.06%) infant and vitamin B12 deficiency was found in 38 (40.1%) infants. The level of vitamin B12 was sufficient in 56 (59.6%) infants. The mean values for vitamin B12, folic acid, ferritin, Hb, and MCV were found as 219,9±102,9 pg/mL, 14,1±4,5 ng/mL, 35,3±26,6 ng/mL, 11,2±0,8 g/dL and 77,2±3,5 fl, respectively. When the infants' cord blood values and follow-up values were compared, a significant difference was found between vitamin B12 and ferritin values (p=0.0001, p=0.0001, respectively), but no difference was found in terms of folic acid (p=0.199).

No statistically significant difference was found between the infants' vitamin B12, folic acid, ferritin, and Hb values according to the mothers' SEL (p=0.062, p=0.161, p=0.489, p=0.530, respectively). No statistically significant difference was found between the infants' vitamin B 12, folic acid, ferritin, and Hb values according to the mothers' education status (p=0.605, p=0.844, p=0.469, p=0.753, respectively). A weak positive correlation was found between the newborns Hb values at birth and at the age of 6–9 months (r=0.463, p=0.0001. A weak positive correlation was found

Table 6. Cord blood and maternal vitamin B12 levels by vitamin B12 levels in infants

Vitamin B12 (pg/mL)	Vitamin B12 in infants		p
	Sufficient Mean±SD Median (min.–max.) (n=56)	Deficient Mean±SD Median (min.–max.) (n=38)	
Cord blood	180.85±72.5 176.0 (75.0–410.0)	127.7±47.6 131.5 (53.0–319.0)	<0.001[a]
Maternal blood	126.1±63.8 112.5 (44.0–380.0)	96.9±42.5 91.5 (47.0–226.0)	0.012[b]

SD: Standard deviation; a: Statistically significant difference at a level of p<0.001; b: Statistically significant difference at a level of p<0.05

in terms of vitamin B12 (r=0.408, p=0,0001), and a very weak positive correlation was found between the mothers' values measured at birth (r=0.315, p=0.02).

A significant difference was found between the infants who received iron supplements at appropriate doses and infants who received iron supplements at inappropriate doses or did not receive iron supplements in terms of ferritin and Hb values (p=0,0001, p=0.007, respectively). The mean values for Hb and ferritin were found as 11.3±0.7 g/dL and 42±28.8 ng/mL, respectively, in infants who received iron supplements at appropriate doses, and 10.9±0.9 g/dL and 20.4±11.2 ng/mL, respectively, in infants who received iron supplements at inappropriate doses or did not receive iron supplements. A statistically significant difference was found between the levels of vitamin B12, folic acid, and ferritin in infants who received appropriate supplementary food and infants who received inappropriate supplementary food or no supplementary food (p=0.024, p=0.012, p=0.042, respectively). The mean levels of vitamin B12, folic acid, and ferritin were found as 227±101.2 pg/mL, 14.5±4.4 ng/mL, and 36.9±27.1 ng/mL, respectively, in infants who received appropriate supplementary food, and 152.5±100.5 pg/mL, 10.3±4.2 ng/mL, and 20.9±14.9 ng/mL, respectively, in infants who did not receive appropriate supplementary food.

When cord blood vitamin B12 levels in the infants and the mothers' vitamin B12 levels in the prenatal period were compared according to the status of vitamin B12 deficiency in the infants, a statistically significant difference was found between the groups (p=0,0001, p=0.012, respectively) (Table 6).

Discussion

Vitamin B12 deficiency was described by Jadhav et al. (8) for the first time in 1962. In children, primary deficiency is rare, and deficiency generally develops as a result of deficiency in the mother or juvenile pernicious anemia. Deficiency during pregnancy and the lactation period causes vitamin B12 deficiency in the fetus and newborn, due to a reduction in vitamin B12 content in breastmilk. In neonates born with normal vitamin B12 stores, deficiency does not occur for 6–8 months even if dietary intake is inadequate or absorption is deficient. On the other hand, babies born from mothers with vitamin B12 deficiency are born with insufficient stores, and these babies who are breastfed will not be able to receive sufficient amounts of vitamin B12 because the content in breastmilk will be low. In these infants, signs of deficiency will occur in the first six months of life (9, 10).

Our study showed that the rate of vitamin B12 deficiency was high in pregnant women and newborn babies in our region, and vitamin B12 levels in newborns were closely correlated with maternal levels. Our study is important in terms of demonstrating the vitamin B12 levels in newborns in this region, associating these levels with maternal levels and obtaining blood samples from a high number of babies.

In many studies performed previously, it was demonstrated that the most important reason for deficiency in the neonatal period and infancy was maternal deficiency (10–13). In our study, vitamin B12 deficiency was found with a rate of 90.4% in the pregnant women and with a rate of 72.4% in the newborns in our region. Folic acid deficiency was found with a rate of 22.4% in the pregnant women, but it was not observed in the newborns. In Şanlıurfa, Koç et al. (10) found vitamin B12 deficiency with a rate of 72.3% in pregnant women and with a rate of 41.2% in newborns; they did not observe folic acid deficiency in newborns. Özdemir (14) found vitamin B12 deficiency with a rate of 72% in 50 pregnant women in Istanbul, and did not find folic acid deficiency in any of these women. They found vitamin B12 deficiency with a rate of 56% and folic acid deficiency with a rate of 2% in the neonates born from these women. In another study conducted in Istanbul with 250 pregnant women and newborns, vitamin B12 insufficiency was found in 81.6% of the mothers and in 42% of the babies (15). In a screening study conducted by Ertaş et al. (16) in primary health care centers in Şanlıurfa with 211 healthy infants aged 6–11 months, vitamin B12 deficiency was found with a frequency of 40%. Vitamin B12 deficiency was observed with a rate of 75% in the mothers of the babies who were found to have deficiency, whereas this rate was 51.1% in the mothers of babies who had normal vitamin B12 levels; the difference was found to be statistically significant ($p<0.05$).

In our study, a moderately strong positive correlation was found between the vitamin B 12 levels in the pregnant women and newborns. Similarly, Koç et al. (10), Guerra-Shinohara et al. (13), Monsen et al. (17), and Guiglani et al. (18) found a correlation between the vitamin B 12 levels of mothers and newborn babies ($r=0.395$, $r=0.68$, $r=0.51$, $r=0.730$, respectively; $p<0.001$, $p<0.01$, $p<0.001$, $p<0.01$, respectively). In our study, a weak correlation was found between the levels of the mothers and babies in terms of folic acid levels. Similarly, Koç et al. (10), Guerro-Shinohara et al. (13), and Guiglanive et al. (18) found a positive correlation between the folic acid levels in pregnant women and newborns ($r=0.227$, $r=0.55$, $r=0.361$, respectively; $p=0.017$, $p<0.01$, $p<0.01$, respectively).

In our study, anemia was found in 24.8% of the pregnant women and low ferritin levels (iron deficiency) were found in 28%. In Istanbul, Büyükyazı et al. (19) reported anemia with a rate of 27.5% and iron deficiency with a rate of 43.7%; Pehlivanoğlu (20) reported anemia with a rate of 14.7% and iron deficiency with a rate of 23.2%; Özdemir (14) reported anemia with a rate of 28% and iron deficiency with a rate of 38%; and Karaalp et al. (21) reported anemia in 19.7% of 2801 pregnant women. In Izmir, Umay (22) reported anemia with a rate of 30% and iron deficiency with a rate of 18.5%. In Erzurum, Eryılmaz (23) reported anemia with a rate of 12.4% and iron deficiency with a rate of 85.1%. In Ankara, Erdoğan (24) reported anemia with a rate of 10.6% and iron deficiency with a rate of 40.7%. In Şanlıurfa, Koç et al. (10) reported anemia with a rate of 48% and iron deficiency with a rate of 62%. In Van, the rate of iron deficiency was found with a rate of 40% in 700 pregnant women (25). These values show that anemia in pregnancy is a problem for all regions, though the rates vary.

Although anemia was present in 24.8% of the pregnant women, Hb was found to be low in 3.2% of the newborns. While iron deficiency was present in 28% of the pregnant women, this rate was found as 2.8% in the newborns. Reduced ferritin levels were not observed in any of the babies born from pregnant women who had normal ferritin levels. A statistically significant difference was found between the levels of vitamin B12 and folic acid in terms of the education levels of the pregnant women. The rate of using vitamin preparations regularly was higher in the pregnant women who were secondary school and higher education graduates compared with those who were primary school graduates, especially those who were illiterate. We thought that this difference in terms of vitamin B12 and folic acid was also associated with the increase in awareness of adequate nutrition and purchasing power with increased education levels, as well as regular use of vitamins. In our study, we found that there was no significant difference between ferritin and Hb levels in terms of education and SEL. Similarly, in a study conducted by Eryılmaz (23) in Erzurum, no significant difference was found in terms of ferritin and Hb levels according to the pregnant women's education status. In a study conducted by Polat et al. (26) in Sivas, it was reported that the rate of anemia was higher in women who lived in villages, who were illiterate, who had a parity of 5 and more, and who did not receive care in the prenatal period. In our study, we associated the finding that there was no significant difference between ferritin and Hb in terms of education and SEL, with the fact that access to prenatal care was easier due to lower population density and convenient geographic conditions in our region.

We observed that folic acid levels were higher in pregnant women who used vitamins regularly compared with those who used vitamins irregularly or did not use vitamins. In addition, we found that regular use of vitamins created a statistically significant difference in folic acid levels in cord blood ($p=0,0001$). Although vitamin B12 was also present among the vitamin preparations used in obstetrics outpatient clinics, we did not observe the same difference for vitamin B12 ($p=0.837$). We thought this was associated with insufficient amount of vitamin B12 in vitamin preparations used during pregnancy.

When we grouped the mothers according to vitamin B12 status, in our study, we observed that cord blood vitamin B12 levels were higher in babies whose mothers had sufficient vitamin B12 levels compared with the group whose mothers had deficient vitamin B12 levels, and the difference was statistically significant. Similarly, Koç et al. (10) divided mothers into three groups as sufficient deficiency, moderate deficiency, and severe deficiency according to vitamin B12 status, and reported a statistically significant difference between the babies whose mothers had sufficient levels of vitamin B12 and those whose mothers had severe vitamin B12 deficiency ($p=0.002$).

We found anemia in 22.3% of 94 infants who presented for the follow-up visits. Iron deficiency anemia is the most frequent hematologic disease of childhood. It is most commonly observed between the ages of 6 months and 24 months; it arises from rapid growth and deficiency in intake. In our study, we found iron deficiency in 14.9% of 94 infants. Almost one-third (30.9%) of the infants were not receiving iron at appropriate doses. We observed that the mean ferritin and Hb values were higher in infants who were receiving iron supplements at appropriate doses.

Vitamin B12 levels were found to be deficient in 181 (72.4%) of 250 infants and normal in 69 (27.6%). Among the infants who presented for the follow-up visits, B12 level was found to be deficient in 38 infants (40.4%) and normal in 56 infants (59.6%). Folic acid deficiency was found in only one infant. In a study conducted by Yetim et al. (27) in Istanbul, vitamin B12 deficiency was found with a rate of 93% in pregnant women, with a rate of 61% in cord blood, and a correlation was found between the levels in pregnant women and cord blood levels. In a study conducted in infants aged 1–6 months who were at term and being exclusively breastfed in India (n=100), the prevalence of vitamin B12 deficiency was found as 57%, and deficiency in the mothers was found with a rate of 46%; a correlation was observed between the maternal levels and the levels in the babies, especially in the period below 3 months (28).

We found that the mean ferritin, vitamin B12, and folic acid levels were higher in the infants who received appropriate supplementary food and the difference was statistically significant. This finding supports that timely initiation of appropriate supplementary food is important following encouragement of breastfeeding in the first six months.

In Şanlıurfa, Minnet et al. (29) showed damage in DNA using alkaline mononuclear cell electrophoresis in the DNA of 94 patients who were diagnosed as having vitamin B12 deficiency aged between 1 month and 15 years, and that this damage improved to an important extent following vitamin B12 treatment for one week. In addition, it was observed that there was no relationship between the dimension of damage and the degree of deficiency, and DNA damage could develop even in mild deficiency. In a study conducted by Sinclair et al. (30) with sheep, intense epigenetic modifications related to increased adipose tissue, insulin resistance, modified immune functions, and increased blood pressure were found in adulthood in babies born when vitamin B12, folic acid, and methionine were reduced in maternal diet in an 8-week period before conception.

We found a statistically significant difference between the cord vitamin B12 blood levels and follow-up vitamin B12 levels in infants. The mean follow-up vitamin B12 value was higher compared with the mean cord blood vitamin B12 value. We associated this with the fact that the infants were being fed appropriate supplementary food, though they were influenced by maternal deficiency. We found no significant differences when we compared the Hb, ferritin, folic acid, and vitamin B 12 values according to maternal education status and family SEL. We associated this with the easy accessibility to healthcare services due to geographic conditions and low population density in our region, though maternal education and family SELs were low.

When we classified the infants according to vitamin B12 deficiency, we observed that the mean cord blood vitamin B12 value in the group with sufficient vitamin B12 level was higher compared with the group with vitamin B12 deficiency, and the difference was statistically significant (p=0,0001). This showed that infants with low values at birth had a higher risk in terms of developing vitamin B12 deficiency. Similarly, we observed that the mothers of infants who had sufficient vitamin B12 levels in the follow-up had higher levels compared with the mothers of the infants who had vitamin B12 deficiency (p=0.012). In a study conducted in 114 healthy primigravida pregnant women, it was shown that the vitamin B12 levels at the 6th month were correlated with the values throughout pregnancy and the values at the 6th postnatal week. In the same study, a reduced vitamin B12 level at the 18th gestational week was defined to be a risk factor for biochemical vitamin B12 deficiency at the 6th month (31). This showed that maternal vitamin B12 levels were important for newborns to be born with sufficient amounts of vitamin B12 and for persistence of transmission by breastmilk in sufficient amounts, and pregnant women should be evaluated and supported in this aspect, and should be educated in terms of nutrition.

Our study is important in terms of demonstrating that vitamin B12 deficiency in newborns and pregnant women in our region is more prevalent than predicted, values in newborns are influenced by maternal deficiency, and this influence continues in infancy because of decreased transmission by breastmilk, inappropriate supplementary food, maternal feeding habits, and reduced consumption of food of animal origin.

Ethics Committee Approval: The study was approved by the Ethics Committee of Trakya University (2008/66).

Informed Consent: Written informed consent was obtained from the pregnant woman and mothers.

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