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ORIGINAL CONTRIBUTION

Ahmet Koc
Abdurrahim Kocyigit
Mustafa Soran
Nihat Demir
Eylem Sevinc
Ozcan Erel
Zeki Mil

High frequency of maternal vitamin B_{12} deficiency as an important cause of infantile vitamin B_{12} deficiency in Sanliurfa province of Turkey

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A. Koc, MD, (✉) · M. Soran · N. Demir
E. Sevinc
Research Hospital
Dept. of Pediatric Hematology
Harran University Faculty of Medicine
63 100 Sanliurfa, Turkey
Tel.: +90-414/314-53 35 (Home)
+90-414/314-11 70/ 2140 (Hospital)
Fax: +90-414/315-11 81
E-Mail: ahmetkoc1@hotmail.com
or akoc@harran.edu.tr

A. Kocyigit · O. Erel
Dept. of Biochemistry
Harran University Faculty of Medicine
Sanliurfa, Turkey

Z. Mil
Health Minister Sanliurfa Maternity
Hospital
Sanliurfa, Turkey

Summary *Background* Vitamin B_{12} deficiency in infancy may cause failure to thrive, severe neurological disorders and megaloblastic pancytopenia. It is well known that infants born with deficient vitamin B_{12} storage have increased the risk of vitamin B_{12} deficiency. Vitamin B_{12} deficiency is more prevalent in infancy in Sanliurfa province (at the southeast region of Turkey). *Aim of the study* The aim of this study was to determine the frequencies of vitamin B_{12}, folic acid and iron deficiencies in pregnants and their babies at birth and to what extend the mothers' deficiency becomes effective on babies' deficiencies. *Methods* The study groups were constituted by 180 pregnant women and their single and term babies. Venous blood samples of pregnants were obtained 1–3 h before delivery and babies' cord bloods were collected at birth. Vitamin B_{12} and folic acid levels were measured with electro chemiluminiscence method; serum iron and iron binding capacities were measured by colorimetric method and complete blood counts were performed by automatic blood counter. *Results* Mean vitamin B_{12} levels in maternal and cord blood serum were 130 ± 61.7 pg/ml and 207 ± 141 pg/ml; mean folic acid levels were 8.91 ± 6.46 ng/ml and 17.8 ± 11.8 ng/ml; mean serum iron levels were 56.9 ± 37.5 μg/dl and 147 ± 43.2 μg/dl; and mean transferrin saturations were 11.8 ± 8% and 65.6 ± 24%, respectively. There were vitamin B_{12} deficiency (<160 pg/ml) in 72% of the mothers and 41% of the babies, and severe deficiency (<120 pg/ml) in 48% of the mothers and 23% of the babies. Folic acid deficiency was found in 12% of the mothers, but was not found in the babies. There were iron deficiency in 62% of the mothers and 1% of the babies. There were statistically significant correlation between maternal and cord blood serum vitamin B_{12} levels ($r = 0.395$, $P < 0.001$) and folic acid levels ($r = 0.227$, $P = 0.017$), while there were no correlation between maternal and cord blood iron levels and transferrin saturations. *Conclusion* The study results showed that vitamin B_{12} deficiency is prevalent in pregnants in this region and that 41% of infants have born with deficient vitamin B_{12} storages. Therefore, prophylactic use of vitamin B_{12} by pregnant women in Sanliurfa and other poor communities could have considerable benefits to prevent vitamin B_{12} deficiency and its complications in infants.

Key words vitamin B_{12} deficiency – pregnancy – infant – cord blood

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Introduction

Vitamin B_{12} deficiency is a rare condition in infants who are born with enough vitamin B_{12} storage. During pregnancy, vitamin B_{12} is actively transported to the fetus by the placenta. But severe deficiency may occur in infants if the mother is vitamin B_{12} deficient during pregnancy, and lactation [1–6]. It is reported that vitamin B_{12} deficiency in mother's diet at gestational period causes severe retardation of myelination of baby's nervous system and brain atrophy [7]. In infancy, vitamin B_{12} deficiency may cause failure to thrive, irritability, anorexia, delay and regression of neurological development, hypotonia, coma and convulsions, and severe megaloblastic pancytopenia because of delayed DNA synthesis and myelination defects [4–9].

Anemia, failure to thrive and neurological disorders due to vitamin B_{12} deficiency in infancy are common in the Sanliurfa Province (at the southeast region of Turkey), and some of these children are brought to the hospital in severe coma [10]. Most of these children's mothers also have vitamin B_{12} deficiency. We think that one of the possible important causes of the high frequency of vitamin B_{12} deficiency in infants is inadequate transfer of this vitamin from mothers both in pregnancy and in breast-feeding to the baby. So, we aimed to investigate vitamin B_{12} status of pregnants and their infants, and correlation of vitamin B_{12} in maternal and cord blood serum at birth. We also investigated other hematic substances, i.e., folic acid and iron, and hematologic values since nutritional deficiencies, especially iron deficiency, are high in pregnancy.

Materials and methods

The study groups were constituted by 188 healthy parturients who gave birth at the Health Minister Sanliurfa Maternity Hospital, and their babies, but 8 pairs were excluded from the study due to insufficient sampling of cord blood or broken tubes. All parturients had normal gestations lasting 38–42 weeks and gave birth to normal babies weighing more than 2500 g by uncomplicated vaginal delivery. The data associated with mothers' ages, pregnancy numbers, and medications in pregnancy were obtained from mothers and their hospital records before delivery. All pregnants gave informed consent for themselves and for their babies. The study was performed according to national and international ethical guidelines under the supervision of a medical ethic specialist.

Venous blood samples of pregnants were taken 1–3 h before delivery and babies' cord blood samples were collected at birth into two tubes one with and one without EDTA. Blood specimens in the tubes without EDTA were left to stand at room temperature for approximately 3 h and then centrifuged. The sera were collected and immediately frozen at −20 °C until tested. Vitamin B_{12} and folic acid levels were measured with electrochemiluminiscence method (Elecsys 2010), serum iron and iron binding capacities, were measured by colorimetric method (Boehringer-Meinhaim). Complete blood counts were performed by automatic blood counter (Celldyn 3500) in the same day. Vitamin B_{12} and folic acid measurements and complete blood counts were performed in all subjects; serum iron, iron binding capacities and transferrin saturations were measured in 100 of them.

Vitamin B_{12} levels lower than 160 pg/ml were accepted as deficiency and lower than 120 pg/ml were considered as severe deficiency for both pregnants and infants [11]. Serum folic acid levels lower than 4 ng/ml were accepted as deficiency and lower than 2 ng/ml were accepted as severe deficiency for both pregnants and infants [5, 12]. If serum iron level was lower than 60 μg/dl and transferrin saturation was lower than 16%, it was considered as iron deficiency for both pregnants and infants [11]. Hb levels lower than 12 g/dl in pregnants and lower than 13.5 g/dl in infants were considered as anemia. When MCV was lower than 80 fl in mothers and lower than 98 fl in infants, it was accepted as microcytosis [11].

Statistical analyses were performed by using SPSS computer program (version 11.5). The correlations between mothers' and babies' values were evaluated with Spearman correlation coefficient. Unpaired Student t test was used for comparison of mean serum concentrations of vitamin B_{12}, folic acid, iron, iron binding capacity, and transferrin saturations of pregnants and their babies. In addition, pregnants and their babies were grouped according to pregnants' ages, pregnancy numbers, vitamin B_{12} status (adequate: ≥160 pg/ml, mildly deficient: 120–160 pg/ml, and severely deficient: <120 pg/ml), and iron or multivitamin receival; and each subgroup results were also compared with other subgroups results with unpaired Student t test and one-way ANOVA test (in multiple comparisons) with Bonferroni test for post-hoc multiple comparisons. Chi Square (χ^2) test was used in comparison of deficiency rates of subgroups according to pregnants' vitamin B_{12} status.

Results

Mean age of pregnants was 27 + 5.79 years. Twenty-eight (16%) of pregnants were younger than 20 years

Table 1 Means and standard deviations of vitamin B_{12}, folic acid, iron, iron binding capacity levels, and transferrin saturations of maternal and cord blood serum

	Maternal blood	Cord blood	Correlations	
Vitamin B_{12} (pg/ml)	130 ± 61.7 (30.0–341)	207 ± 140 (30.0–897)	$r = 0.395$	$P < 0.001$
Folic acid (ng/ml)	8.91 ± 6.46 (0.50–24.0)	17.8 ± 11.8 (3.50–24.0)	$r = 0.227$	$P = 0.017$
Iron (μg/dl)	56.9 ± 37.5 (8.0–215)	147 ± 43.2 (49–263)	$r = 0.126$	$P = 0.212$
Total iron binding capacity (μg/dl)	507 ± 90.1 (210–671)	242 ± 77.0 (124–609)	$r = 0.197$	$P = 0.05$
Transferrin saturation (%)	11.8 ± 8.41 (1.0–48.0)	65.6 ± 24.1 (11.0–104)	$r = 0.105$	$P = 0.298$

The numbers in the parenthesis are minimum and maximum values

Table 2 The frequencies of vitamin B_{12}, folic acid and iron deficiencies and anemia in pregnants and their babies

	In pregnants		In babies	
	Number	%	Number	%
Vitamin B_{12} deficiency				
Mild deficiency (120–160 pg/ml)	43	24	33	18
Severe deficiency (<120 pg/ml)	87	48	41	23
Folic acid deficiency				
Mild deficiency (2–4 ng/ml)	6	3	0	0
Severe deficiency (<2 ng/ml)	16	9	0	0
Iron deficiency (Iron level <60 μg/dl, transferrin saturations <16%)	62	62*	1	1*
Anemia (Hb <12.0 g/dl in mothers, Hb <13.5 g/dl in infants)	84	48	5	3

*Measured in 100 of subject

of age, 54 (30%) were between 21–25 years of age, 59 (33%) were between 26 and 30 years of age, and 39 (22%) were in 31 years of age or older. Fifty-four (30%) of these mothers had their first pregnancy, 56 (31%) had their second or third pregnancy, 42 (23%) had their fourth or fifth pregnancy, and 28 (16%) had six or more pregnancies. Mean pregnancy number was 3.22 + 2.16.

Data of maternal and cord blood serum levels of vitamin B_{12}, folic acid and transferrin saturation were presented in Table 1. The differences between maternal and cord blood levels were significant ($P < 0.001$) for all parameters.

As shown in Table 2, the frequency of vitamin B_{12} deficiency were significantly high in both mothers and babies, while only 1% of the babies was iron-deficient and none of the babies was folic acid-deficient. Seventeen (77%) of 22 pregnants who had folic acid deficiency and 36 (58%) of 62 pregnants who had iron deficiency also had vitamin B_{12} deficiency.

Eighty-four (48%) of the pregnants had anemia (24 (13%) had Hb levels lower than 10.5 g/dl) (Table 2). Anemia was microcytic in 45 (54%) of these 84 women and normocytic in others. Only five (3%) infants had anemia and two (1%) of these infants had microcytosis.

Table 3 Mean serum vitamin B_{12} and folic acid levels and transferrin saturations of pregnants and their babies according to pregnant's vitamin B_{12} status

	Pregnants with adequate vitamin B_{12}	Pregnants with mild vitamin B_{12} deficiency	Pregnants with severe vitamin B_{12} deficiency	P
Mothers' values				
Vitamin B_{12} (pg/ml)	216^{a} (160–342)	136^{b} (122–158)	86.3^{c} (30.0–119)	<0.001*
Folic acid (ng/ml)	9.84 (0.5–24.0)	10.0 (0.5–24.0)	7.26 (0.5–24.0)	0.077
Transferrin saturation (%)	11.9 (1.0–48.0)	11.4 (3.0–35.0)	12.4 (3.0–38.0)	0.935
Newborns' values				
Vitamin B_{12} (pg/ml)	290^{d} (99.9–897)	194^{e} (101–350)	172^{f} (30.0–575)	0.002**
Folic acid (ng/ml)	18.4 (5.9–24.0)	18.1 (6.3–24.0)	15.5 (3.5–24.0)	0.069
Transferrin saturation (%)	54.2 (17.0–96.0)	60.4 (26.0–102)	64.1 (11.0–104)	0.460

†The numbers in the parenthesis are minimum and maximum values
*$P < 0.001$ for each three comparison (a with b, a with c, and b with c) with Bonferroni post-hoc test
**$P = 0.002$ for d with f, and $P = 0.04$ for d with e with Bonferroni post-hoc test

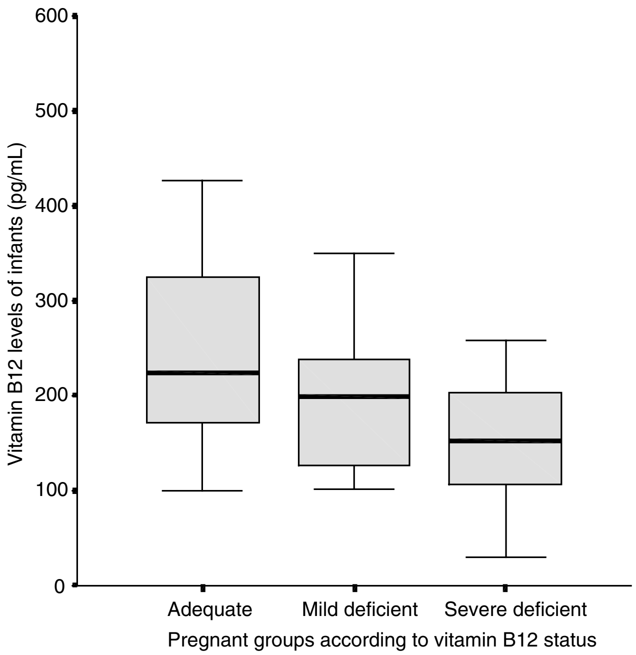

Fig. 1 Cord blood vitamin B_{12} levels according to pregnants' vitamin B_{12} status

We found a statistically significant correlation between maternal and cord blood serum vitamin B_{12} levels ($r = 0.395$, $P < 0.001$) and folic acid levels ($r = 0.227$, $P = 0.017$), while there were no correlation between maternal and cord blood serum iron levels, iron binding capacities and transferrin saturations (Table 1).

There were no statistically important correlations between both pregnants' ages and pregnancy numbers and serum levels of vitamin B_{12}, folic acid, iron, and iron saturation of mothers and infants ($P > 0.05$ for all comparison). When the infants were grouped according to pregnants' ages and pregnancy numbers, there were no significant differences between mean serum vitamin B_{12} and folic acid concentrations and transferrin saturations ($P > 0.05$ for all comparisons).

When the infants were grouped according to mothers' vitamin B_{12} status, mean vitamin B_{12} levels of the infants whose mothers were in mild and severe vitamin B_{12} deficient groups were significantly lower than mean level of the infants whose mothers were in vitamin B_{12} adequate group ($F = 6.541$, $P = 0.002$) (Table 3 and Fig. 1). There were no important differences between mean folic acid levels and transferrin saturations of infants according to pregnants' vitamin B_{12} status ($P > 0.05$ for each comparison).

The frequency of severe vitamin B_{12} deficiency status in infants whose mothers had severe vitamin B_{12} deficiency was significantly higher than the infants whose mothers had mild deficiency and had adequate vitamin B_{12} (Table 4).

According to data obtained from pregnant, 127 (71%) of them had received neither iron nor multivitamin preparation at pregnancy, while 11 (6%) had used iron and 34 (19%) had used multivitamin (5 (3%) had used each of iron and multivitamin) at least one package. Eight (4%) of the pregnants did not answer this question. There were no important differences in mean serum levels of vitamin B_{12}, folic acid and transferrin saturations between pregnants who had ever received iron or multivitamin preparations and who had not, and also between their babies ($P > 0.05$ for all comparison). These results suggested that iron or multivitamin receival by pregnants were insufficient in this region.

Discussion

This study demonstrated that the frequency of vitamin B_{12} deficiency was significantly high in pregnants of this region, and an important proportion of infants have born with deficient vitamin B_{12} storages. This results showed that vitamin B_{12} deficiency in pregnants is an important cause of biochemical vitamin B_{12} deficiency in newborns in our region, although vegetarian nutrition is uncommon.

There is little consensus on appropriate cut-off point for determining normal and abnormal vitamin B_{12} and folic acid levels. However, the levels which are frequently used for vitamin B_{12} are 160 and 200 pg/ml [11–14]. Our laboratory used <200 pg/ml as the cut-

Table 4 Vitamin B_{12} status of infants according to pregnants vitamin B_{12} status

Vitamin B_{12} status of infants	Vitamin B_{12} status of pregnants			Total (n)
	Adequate[a]	Mildly deficient[b]	Severely deficient[c]	
Adequate	42 (80%)	27 (63%)	37 (43%)	106
Mildly deficient	5 (10%)	7 (16%)	21 (24%)	33
Severely deficient	3 (6%)	9 (21%)	29 (33%)	41
Total (n)	50	43	87	180

$\chi^2 = 6.102$, $P = 0.047$ for a and b
$\chi^2 = 25.282$, $P < 0.001$ for a and c
$\chi^2 = 5.880$, $P = 0.053$ for b and c

off point for vitamin B_{12} during our investigation. But, since serum vitamin B_{12} concentrations physiologically fall during pregnancy [15–17], we accepted 160 pg/ml for vitamin B_{12} as cut-off point.

There is also no complete consensus about cut-off level of serum folic acid. In Frery et al. study [13], folic acid was considered deficient when its plasma level was less than 2.5 ng/ml. Perkins has given 2 ng/ml for normal lower limits of folic acid [11]. Whitehead et al. [5] have given 4–20 ng/ml as normal range and less than 3 ng/ml as deficiency. According to another textbook, if the serum folate concentration is more than 4 ng/ml, folate deficiency is effectively ruled out [12]. Our laboratory's lower limit of normal range for folic acid was also 4 ng/ml. Therefore, we used 4 ng/ml for cut-off point for folic acid in this study.

One of the important causes of high frequency of vitamin B_{12} deficiency in this region is inadequate consumption of animal products due to poverty. High frequency of iron deficiency, which was found in pregnants, supported this suggestion. Another important cause is the local tradition of some people at this region that, meat consumption of woman during pregnancy or lactation might be harmful to her fetus or infant. One of the other causes may be intestinal bacterial overgrowth [5], due to poor hygienic conditions of the region.

One of the nutritional characteristics of the people in this region is meat products are frequently consumed with some vegetal foods such as dry or fresh pepper and eggplant. Some foods that are usually consumed with meat may also inhibit vitamin B_{12} and iron absorption, and the subject must be investigated from this perspective. Some intestinal parasitic infections may result in vitamin B_{12} malabsorption [6], and intestinal parasitic infections, which are more common in this region, may be one of the causes of this deficiency [18, 19]. Therefore, further studies are required to determine the exact causes of vitamin B_{12} deficiency in pregnancy.

We found that cord blood vitamin B_{12} levels were significantly correlated with mothers' vitamin B_{12} levels in contrast to the cases of iron levels. Frery et al. [13] and Guerr-Shinohar et al. [20] also reported that cord blood vitamin B_{12} levels were highly correlated with mothers' vitamin B_{12} levels. Monagle et al. [3] reported that maternal vitamin B_{12} deficiency is the most frequently seen cause of infantile megaloblastosis, and 50% of these mothers were asymptomatic. It was shown that pregnants' ages or pregnancy numbers have no important effect on the infants' vitamin B_{12} levels, but pregnants' vitamin B_{12} status were significantly effective on the infants' vitamin B_{12} levels. As seen in Tables 3 and 4, especially the infants, whose mothers have severe vitamin B_{12} deficiency, are under the risk of severe vitamin B_{12} deficiency; but an important proportion of infants, whose mothers have mild deficiency may also be under the risk for severe deficiency. All these results have suggested that if mothers have inadequate vitamin B_{12} storage during pregnancy, the babies probably born with deficient vitamin B_{12} storage [1–5].

Specker et al. [21] reported that milk vitamin B_{12} was correlated with maternal vitamin B_{12} concentration and infant urinary methylmalonic acid (UMMA) concentration (an important biochemical indication of vitamin B_{12} deficiency) were inversely related to milk vitamin B_{12} concentration. Therefore, the deficiency may become more evident especially in breast-fed infants because of the low milk concentration of vitamin B_{12} [21, 22]. In contrary, although iron deficiency was more prevalent in pregnant women in our study, it was rare in infants, and this situation supports the assertion that even if mothers had iron deficiency, the fetus could get iron that was needed.

Interestingly, we found that 6% of the infants whose mothers had adequate vitamin B_{12} levels, had vitamin B_{12} levels lower than 120 pg/ml, and 10% of this infants had vitamin B_{12} levels between 120 and 160 pg/ml. We think that these pregnants might have received vitamin B_{12} sources in the final days of their pregnancy which was sufficient to correct their own serum vitamin B_{12} levels, but was not enough to correct their infants serum levels.

In some poor communities, quite high rate of vitamin B_{12} and folic acid deficiencies in pregnants have been reported [23, 24]. Ackurt et al. [25] reported that the frequencies of vitamin B_{12} and folate deficiencies in pregnant were 48.8% and 59.7% in early stages of pregnancies, 80.9% and 76.4% in late stages of pregnancy, and 60% and 73.3% in postnatal stages, respectively, in Istanbul and Izmit, two developed cities in the north-west region of Turkey. In Ackurt et al.'s study, the frequency of vitamin B_{12} deficiency in women in late stages of pregnancy was quite similar with the frequency of deficiency that was found in our study. These similar results show that vitamin B_{12} deficiency in pregnancy is not a restricted problem of south-east region, but also an important problem in the other regions of Turkey.

Generally, folic acid deficiency during pregnancy is more common than vitamin B_{12} deficiency [26]. But, the frequency of folic acid deficiency in pregnants was lower than the frequency of vitamin B_{12} deficiency, and none of the infants had folic acid deficiency at birth in this study. One of the possible causes of this result may be that the sources of folic acid [5] are more common and cheaper in our region.

This study also showed that the use of iron and multivitamin by pregnants is insufficient in this region. When it is considered that most of the physicians prescribe iron and multivitamins to pregnants, the results suggested that the insufficient follow-ups of the pregnants by the physicians, and multivitamin and iron medication is also insufficient in pregnants who reported that they receive iron or multivitamin.

It is important to diagnose vitamin B_{12} deficiency in pregnants since it can result in low vitamin B_{12} stores in infants at birth [1, 3, 5, 13, 20]. Children who are born with low vitamin B_{12} stores, if not diagnosed and treated, may show developmental and severe neurological problems within the first years of life. Treatment may resolve these complications, but permanent neurologic damage and long-term intellectual impairment may occur [2–9]. Therefore, prevention of this deficiency is an important measure for healthy development of infants and children. Ajayi et al. [27] reported that receiving the capsules that contain ferrous fumarate, folic acid, vitamin B_{12}, vitamin C, magnesium sulfate and zinc (Chemiron) by normal pregnants instead of conventional ferrous glucanate and folic acid, had better hematological effect. There is no known teratogenic effect of vitamin B_{12} if received by pregnants. In contrast, it was shown that it could reduce the teratogenic effects that induced by valproic acid and dexamethasone, and could reduce the frequency of malformation in animal experiments [28, 29]. Therefore, vitamin B_{12} administration to pregnants will be beneficial to prevent infantile vitamin B_{12} deficiency.

In conclusion, this study showed that, an important proportion of infants in Sanliurfa had vitamin B_{12} deficiency at birth due to maternal vitamin B_{12} deficiency. Due to the potential serious results of vitamin B_{12} deficiency for infants, prenatal screening studies may be performed to prevent the deficiency of vitamin B_{12} in infants. We suggest that prophylactic use of vitamin B_{12} by pregnant women, similar to iron and folic acid prophylaxis, in addition to nutrition education programs and food enrichment, will greatly benefit to prevent vitamin B_{12} deficiency and its complications in the first years of life, in Sanliurfa and other less advantaged communities.

Vitamin B_{12} can be given to pregnants in routine physician control; or it can be given by nurses or midwives in village clinics to pregnants who are not in regular physician follow-ups, at least one in each trimester of gestation as 1 mg ampoules, that is quite cheap. Vitamin B_{12} can also be given to infants at first week of life similar to vitamin K injection in poor communities. The addition of vitamin B_{12} in multivitamin preparations for infants will also have beneficial effects to prevent vitamin B_{12} deficiency in infancy.

References

1. Davis JR, Goldenring J, Lubin BH (1981) Nutritional vitamin B-12 deficiency in infants. Am J Dis Child 135:566–567
2. McPhee AJ, Davidson GP, Leahy M, Beare T (1988) Vitamin B_{12} deficiency in a breast-fed infant. Arch Dis Child 63:921–923
3. Monagle PT, Tauro GP (1997) Infantile megaloblastosis secondary to maternal vitamin B_{12} deficiency. Clin Lab Hematol 19:23–25
4. Grattan-Smith PJ, Wilcken B, Procopis PG, Wise GA (1997) The neurological syndrome of infantile cobalamin deficiency: developmental regression and involuntary movements. Mov Disord 12:39–46
5. Whitehead VM, Rosenblatt DS, Cooper BA (2003) Megaloblastic anemia. In: Nathan DG, Orkin SH, Ginsburg D, Look AT (eds) Nathan and Oski's hematology of infancy and childhood, 6th edn. W.B. Saunders Comp., Philadelphia, pp 419–455
6. Ramussen SA, Fernboff PM, Scanlon KS (2001) Vitamin B_{12} deficiency in children and adolescents. J Pediatr 138:10–17
7. Lovblad K, Ramelli G, Remonda L et al. (1997) Retardation of myelination due to dietary vitamin B_{12} deficiency: cranial MRI findings. Pediatr Radiol 27:155–158
8. Hall CA (1990) Function of vitamin B12 in the central nervous system as revealed by congenital defects. Am J Hematol 34:121–127
9. Graham SM, Arvela OM, Wise GA (1992) Long-term neurologic consequences of nutritional vitamin B_{12} deficiency in infants. J Pediatr 121:710–714
10. Koc A, Soran M, Tatli MM, Sevinc E, Vural H (1999) Vitamin B_{12} deficiency in the etiology of childhood coma. 1st National Congress of Pediatric Hematology, Antalya, Turkey
11. Perkins SL (1999) Normal blood and bone marrow values in humans. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM (eds) Wintrobe's clinical hematology, 10th edn. Williams & Wilkins, Baltimore, pp 2798–2748 (Table A.3 and Table A.17)
12. Antony AC (2000) Megaloblastic anemias. In: Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LH, McGlave P (eds) Hematology: basic principles and practice, 3rd edn. Churchill Livingstone, New York, pp 446–485
13. Frery N, Huel G, Leroy M et al. (1992) Vitamin B_{12} among parturients and their newborns and its relationship with birthweight. Eur J Obstet Gynecol Reprod Biol 45:155–163
14. Lanzkowsky P (2000) Manual of pediatric hematology and oncology. Academic Press, San Diego, pp 51–72
15. Metz J, McGrath K, Bennett M, Hyland K, Bottiglieri T (1995) Biochemical indices of vitamin B12 nutrition in pregnant patients with subnormal serum vitamin B12 levels. Am J Hematol 48:251–255
16. Allen LH (1994) Vitamin B12 metabolism and status during pregnancy, lactation and infancy. Adv Exp Med Biol 352:173–186

17. Pardo J, Gindes L, Orvieto R (2004) Cobalamin (vitamin B12) metabolism during pregnancy. Int J Gynaecol Obstet 84:77–78
18. Ulukanligil M, Seyrek A (2003) Anthropometric status, anaemia and intestinal helminthic infections in shantytown and apartment schoolchildren in the Sanliurfa province of Turkey. Eur J Clin Nutr 58:1056–1061
19. Koc A, Kocyigit A, Ulukanligil M, Demir N (2005) The frequency of vitamin B12 and folic acid deficiency in 9–12 years of age children in Sanliurfa Region and their relation with intestinal helminthes. Cocuk Sagligi ve Hastaliklari Dergisi 48:308–315 (Abstracts in English)
20. Guerr-Shinohar EM, Paiva AA, Rondo PH, Yamasaki K, Terzi CA, D'Almedia V (2002) Relationship between total homocysteine and folate levels in pregnant women and their newborn babies according to maternal serum levels of vitamin B12. BJOG 109:784–791
21. Specker BL, Black A, Allen L, Morrow F (1990) Vitamin B-12: low milk concentrations are related to low serum concentrations in vegetarian women and to methylmalonic aciduria in their infants. Am J Clin Nutr 52:1073–1076
22. Casterlina JE, Allen LH, Ruel MT (1997) Vitamin B-12 deficiency is very prevalent in lactating Guatemalan women and their infants at three months postpartum. J Nutr 127:1966–1972
23. Msolla MJ, Kinoba JL (1997) Prevalence of anaemia in pregnant women during the last trimester. Int J Food Sci Nutr 48:265–270
24. House JD, March SB, Ratnam S et al. (2000) Folate and vitamin B_{12} status of women in Newfounland at their first prenatal visit. CMAJ 162:1557–1559
25. Ackurt F, Wetherilt H, Loker M, Hacibekiroglu M (1995) Biochemical assessment of nutritional status in pre- and post-natal Turkish women and outcome of pregnancy. Eur J Clin Nutr 49:613–622
26. Lee Gr (1999) The anemias associated with renal disease, liver disease, endocrine disease, and pregnancy. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM (eds) Wintrobe's clinical hematology, 10^{th} edn. Williams & Wilkins, Baltimore, pp 1497–1517
27. Ajayi GO, Fadiran EO (1998) The effect of 61 days of combined iron (Chemiron) and single iron therapy on haemoglobin, packed cell volume, platelets and reticulocytes during pregnancy. Preliminary report. Clin Exp Obstet Gynecol 25:107–111
28. Elmazar MM, Thiel R, Nau H (1992) Effect of supplementation with folic acid, vitamin B6, and vitamin B_{12} on valproic acid-induced teratogenesis in mice. Fundam Appl Toxicol 18:389–394
29. Natsume N, Narukawa T, Kawai T (1986) Teratogenesis of dexamethasone and preventive effect of vitamin B_{12}. Int J Oral Maxillofac Surg 15:752–755