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ASSESSMENT OF THE VITAMIN B12 STATUS OF PREGNANT WOMEN AND THEIR INFANTS

GEBELERDE VE YENİDOĞANLARDA VİTAMİN B12 DÜZEYİNİN DEĞERLENDİRİLMESİ

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Abstract

Aim: Vitamin B12 deficiency is an important problem in pregnancy because it affects not only mothers but also their infants. Although vitamin B12 deficiency is seen all over the world and all age groups, its frequency is much higher in population which has low socio-economic level.
The aim of this study was to evaluate the maternal vitamin B12 status and their effect on neonatal vitamin B12 status and to detect risk factors for vitamin B12 deficiency in Bağcılar where is a low socio-economic region in Istanbul.

Materials and Methods: A total of 71 pregnant women and 71 infants were included in this study between March 2016 and March 2017. Age, gender, weight, gestational age, weight gain during pregnancy, body mass index (BMI), number of parity, socio-economic status, diet, daily vitamin intake were recorded. Blood samples for whole blood count and vitamin B12 were taken all subjects. The pregnant women and newborns were divided into groups based on their vitamin B12 levels. The risk factors were analyzed for vitamin B12 deficiency.

Results: The mean vitamin B12 level was 172.23±102 pg/ml for pregnant women. The number of pregnant women in deficient group (<200 pg/ml) were 73% and 46% of the mothers had a serum vitamin B12 level lower than 150 pg/ml. B12 level of pregnant women those who have consumed sufficient amount of animal products were found as significantly higher than the consumed insufficient (p=0.001). The mean vitamin B12 level of infants was found as 352.1±339.2 pg/ml and the number of infants in deficient group were 26.6%. Also, 14% of the infants had a serum vitamin B12 level lower than 150 pg/ml. There was no correlation between the mothers' B12 level and newborns' body measurements and gestational age

Conclusion: The prevalence of vitamin B12 deficiency in pregnant women in our region was very high and mainly cause was sub-optimal nutrition. Therefore, we suggest that the vitamin B12 status may be assess at the beginning of pregnancy in all women live in low socioeconomic region status.

Key Words: vitamin B12, pregnancy, newborn

Öz

Amaç: Gebelerde vitamin B12 eksikliği yalnızca anneleri değil aynı zamanda bebeklerini de etkileyen önemli bir sağlık sorunudur. Her ne kadar vitamin B12 eksikliği tüm dünyada ve tüm yaş gruplarında görülse de sosyoekonomik düzeyi düşük toplumlarda görülme sıklığı daha yüksektir.
Bu çalışmanın amacı, İstanbul'un sosyo-ekonomik düzeyi düşük bir bölgesi olan Bağcılar'da, gebe kadınların vitamin B12 düzeylerini belirlemek, annelerin vitamin B12 düzeyinin yenidoğan bebeklerin düzeyine etkisini ve vitamin B12 eksikliği için risk faktörlerini belirlemektir.

Materyal ve Metot: Bu çalışma Mart 2016 ve Mart 2017 tarihleri arasında 71 gebe ve 71 yenidoğan üzerinde gerçekleştirildi. Yaş, cinsiyet, ağırlık, gebelik haftası, gebelik boyunca alınan kilo, vücut kitle endeksi, doğum sayısı, sosyoekonomik durum, diyet, gebelikte vitamin alımı kaydedildi. Tüm katılımcılardan tam kan sayımı ve vitamin B12 için kan örnekleri alındı. Gebe kadınlar ve yenidoğan bebekler vitamin B12 düzeylerine göre sınıflandırıldı. Vitamin B12 eksikliği için risk faktörleri araştırıldı.

Bulgular: Gebe kadınların ortalama vitamin B12 düzeyi 172,96 ± 103 pg/ml idi. B12 yetersizliği (<200 pg/ml) saptanan gruptaki kadınların oranı %74 olarak bulundu ve bunların %46'sının vitamin B12 düzeyi 150 pg/ml 'nin altında idi. Yeterli miktarda hayvansal gıda tüketen annelerin B12 düzeyi tüketmeyenlere göre anlamlı olarak yüksek bulundu (p= 0.001). Bebeklerin ortalama vitamin B12 düzeyi 352,1 ± 339,2 pg/ml olarak bulundu ve bebeklerin %26,6'sında B12 yetersizliği saptandı. Ayrıca bebeklerin %14'ünde B12 düzeyi 150 pg/ml'nin altında idi. Annelerin B12 düzeyi ile bebeklerin doğum haftası ve vücut ölçüleri arasında ilişki saptanmadı.

Sonuç: Bölgemizdeki gebe kadınlarda vitamin B12 eksikliğinin sıklığı oldukça yüksektir ve bunun temel nedeni yetersiz beslenmedir. Bu nedenle, sosyoekonomik düzeyi düşük bölgede yaşayan tüm kadınlarda gebelik başlangıcında vitamin B12 düzeyinin değerlendirilmesi uygun olacaktır.

Anahtar Kelimeler: vitamin B12, gebe, yenidoğan.

INTRODUCTION

Vitamin B12 or "cobalamin" is a water soluble vitamin and its deficiency can lead to serious health problems both in children and adults. Although relatively rare in the developed world, vitamin B12 deficiency is an important cause of

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morbidity, especially in the developing and underdeveloped regions[1].

Vitamin B12 is an important cofactor for enzymatic reactions related to DNA synthesis, folate and cell metabolism[2,3]. Its deficiency may result in macrocytic anemia, leukopenia, thrombocytopenia and subacute combined degeneration, peripheral neuropathy, axonal degeneration. This vitamin is found mainly in foods of animal origin including meat, fish, and dairy products, so its deficiency is prevalent when intake of these foods is low[2].

In pregnancy, the placenta concentrates vitamin B 12 in fetus resulting in fetal serum levels more than maternal serum. Thus the neonatal stores are adequate for 6-12 months. Maternal depletion of the vitamin B12 results in poor vitamin B12 status in infants and they are at risk for developmental abnormalities, growth failure, and anemia. Maternal vitamin B12 deficiency generally emerges due to nutritional deficiency including vegetarian diet or sub-optimal nutrition result from a lower socioeconomic status and malabsorption. As the most infant formulas are fortified with vitamin B12, its deficiency is especially important for deficient mothers who choose to breast feed [2-5]. Manifestations of vitamin B12 deficiency in infants are usually nonspecific, such as failure to thrive, poor feeding, vomiting, irritability and weakness. Furthermore, it can present with neurological manifestations such as hypotonia, ataxia, seizures and developmental delay in infants[5,6].

The aim of this study was to evaluate the maternal vitamin B12 status and their effect on neonatal vitamin B12 status and to detect risk factors for vitamin B12 deficiency in Bağcılar where is a low socio-economic region in Istanbul.

MATERIAL AND METHODS

This study was conducted in the Departments of Pediatrics and Obstetrics and Gynecology between March 2016 and March 2017. The study protocol was approved by the local ethics committee of the university (2015-43) and informed consent was obtained for all women and their infants.

A total of 71 pregnant women and 71 of their infants were included in this study. The exclusion criteria included refusal of informed consent, mother age <18 years, complicated pregnancy, presence of systemic disease, prematurity, twin infants, major congenital abnormalities, metabolic disease and insufficient blood sample. Pregnant women who were admitted for the last follow-up before the delivery were selected at random. Age, gender, weight, gestational age, weight gain during pregnancy, body mass index (BMI), number of parity, socio-economic status, diet, daily vitamin intake were recorded. Women divided into two groups according to whether they use daily multivitamins containing B12. Consuming at least two of the animal products (meat, egg, milk, cheese and yogurt) more than three times a week was sufficient, consuming less was considered insufficient. Body mass index (BMI) was calculated by the formula (weight (kg)/height (m^2)) and classified based on the World Health Organization (WHO) classification[7]. Weight gain during pregnancy was categorized according to the 2009 Institute of Medicine (IOM) recommendations[8].

Blood samples for whole blood count and vitamin B12 were taken from the mothers within 1 month before delivery and from the infants within 1 week after delivery. Whole blood count were measured using the fluorescent flow cytometry on the XN-2000 (Sysmex, Japan) and vitamin B12 levels were measured by electro-chemiluminescence immunoassay on the Cobas E 601 (Roche, Germany) on the same day. Vitamin B12 levels were defined that <200 pg/ml (148 pmol/l) as deficiency, 200-300 pg/ml (148-221 pmol/l) as marginal status, and > 300 pg/ml (221 pmol/l) as adequate[1,4,9]. Also, we evaluated the pregnant women that had B12 level below 150 pg/ml (110 pmol/l).

In this study, statistical analysis was performed with the SPSS version 20 for Windows. Descriptive statistics are given via tables. Categorical variables were analyzed using Chi-square test. To test the differences between means, t-test, one-way ANOVA for normal data and Kruskal Wallis test for non-normal data were used. P value < 0.05 was considered statistically significant.

RESULTS

Seventy one pregnant women were included in this prospective study. The mean vitamin B12 level was 172.23±102 pg/ml for pregnant women. When the risk factors for B12 deficiency in pregnant women were evaluated, there were no statistically differences in age, BMI, weight gain, number of parity, socio-economic status, multivitamin intake. However, B12 level of those who have consumed sufficient amount of animal products were found as significantly higher than the consumed insufficient and there was a statistically difference (p=0.95, p=0.67, p=0.93, p=0.94, p=0.52, p=0.40, p=0.001, respectively). The characteristics of the groups are shown in Table 1.

Table 1. Serum Vitamin B12 Levels in Pregnant Women According to Their Characteristics.

	n (%)	Vit B12 levels (pg/ml) (mean±SD)	p value
All pregnant women	71 (100%)	172.23 ±102.61	
Age			
<30	38 (53.5%)	171.55 ± 90.91	0.95*
≥30	33 (46.5%)	172.99 ± 115.62	
BMI (kg/m^2)			
<18.5	2 (2.8%)	145.80 ± 28.99	
18.5-24.9	33 (46.5%)	156.35 ± 83.95	0.67**
25-29.9	25 (35.2%)	194.68 ± 127.85	
≥30	11 (15.5 %)	172.96 ± 103.13	
Weight gain			
Insufficient	14 (19.2%)	181.33 ± 101.81	
Sufficient	29 (40.8%)	169.35 ± 72.42	0.93**
Excessive	28 (39.4%)	172.23 ± 102.61	
Number of Parity			
1	30 (42.2%)	168.88 ± 85.34	0.94**
2	25 (35.2%)	176.24 ± 129.65	
≥3	16 (22.5%)	178.96 ± 111.42	
Socio-economic status			0.52*
Low	36 (50.7%)	164.47 ± 90.50	
Moderate	35 (49.3%)	179.59 ± 113.63	
Multivitamin intake			
Yes	61 (85.9%)	168.91 ± 85.35	0.40*
No	10 (14.1%)	195.88 ± 165.33	
Consumption of animal products			0.001*
Sufficient	33 (46.4%)	221.32 ± 119.34	
Insufficient	38 (53.6%)	131.85 ± 61.85	

**Two-Sample T-Test, **One-way Analysis of Variance,*

The number of pregnant women in deficient group (<200 pg/ml) were 52 (73.2%) and significantly higher than other groups (p=0.00) and their mean vitamin B12 level significantly lower (129.2 ± 42 pg/ml) than marginal status (253.19 ± 30.96 pg/ml) and sufficient group (472.47 ± 169.24 pg/ml) (p=0.00). Also, we found that 34 (46%) of the mothers had a serum vitamin B12 level lower than 150 pg/ml. When we analyzed the groups in terms of hematological parameters (hemoglobin; Hb, hematocrit; Hct, mean corpuscular volume; MCV, MCH, MCHC, RDW), we found no

significant differences (p=0.60, p=0.51, p=0.79, p=0.42, p=0.36, p=.0.39, respectively) (Table 2).

Table 2. Maternal groups and their laboratory results according to Vitamin B12 status.

	Deficient	Marginal status	Sufficient	p
Number of pregnant Women (n, %)	52 (73.2%)	15 (21.1%)	4 (5.6%)	0,00*
Vit B12 (mean±SD)	129.2 ± 42.3	253.1 ± 30.9	472.4 ± 169.2	0.00**
Hb (g/dl) (mean±SD)	11.76 ± 1.50	12.27 ± 1.58	12.5 ± 2.57	0.60***
Hct (%) (mean±SD)	35.54 ± 3.97	36.1 ± 4.3	36.6 ± 4.2	0.51***
MCV (mean±SD)	99.9 ± 9.5	88.5 ± 6.7	91.0 ± 4.1	0.79***

Abbreviations: Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volüme
Chi-square test, **Kruskal-Wallis test, * One-way Analysis of Variance*

The number of newborn in this study were 71. The mean gestational age and birth weight of infants were found as 38.2±1.2 weeks and 3260.9±447 g. The number of female were 40 (56%) and males were 31 (44%). The mean vitamin B12 level of infants was found as 352.1±339.2 pg/ml. The infants divided into three groups according to vitamin B12 level. The number of infants in deficient group (19; 26.6%) were lower than marginal status (26; 36.6%) and sufficient group (26; 36.6%), but there was no statistically difference (p= 0.06). Also, we found that 10 (14%) of the infants had a serum vitamin B12 level lower than 150 pg/ml. The mean vitamin B12 level in deficient group (136.4±48.7 pg/ml) was significantly lower than marginal status (249.9±26.8 pg/ml) and sufficient groups (610.9±454 pg/ml) (p= 0.001). There were no differences in terms of gestational age, gender, weight, length, head circumference and laboratory parameters among the groups (p=0.59, p=0.93, p=0.94, p=0.28, p=0.11, p=0.30, p=0.61, p=0.21, respectively) (Table 3). We found a statistically significant correlation between the mothers' and newborns vitamin B12 levels (Pearson correlation test: p=0.03, r: 0.26), but there was no correlation between the mothers' B12 level and newborns' weight, length, head circumference and gestational age (p=0.1, p= 0.51, p=0.79, p=0.2 respectively).

Table 3. Infant groups and their clinical characteristics, laboratory results according to Vitamin B12 status.

	All infants	Deficient	Marginal status	Sufficient	p
Number of infants (n, %)	71 (100%)	19 (26.6%)	26 (36.6%)	26 (36.6%)	0.06*
Gestational age (week)	38.2±1.2	38.1 ± 1.5	38.4 ± 0.9	38.3 ± 1.3	0.59**
Gender					
Male	31 (44%)	9 (47.4%)	11 (42.3%)	11 (42.3%)	0.93*
Female	40 (56%)	10 (52.6%)	15 (57.7%)	15 (57.7%)	
Birth weight (g)	3260.9±447	3242 ± 437	3284 ± 459	3250 ± 457	0.94**
Birth length (cm)	49.7±1.8	49.2±2	49.9±1.9	49.8±1.6	0.28**
Head circumference (cm)	34.2±1.3	33.6±1	34.3±1.7	34.4±0.9	0.11**
Vit B12 (pg/ml) (mean±SD)	352.1±339	136.4 ± 48.7	249.9 ± 26.8	610.9 ± 454	0.001**
Hb (g/dl) (mean±SD)	17.5±2	17.23 ± 2.3	17.31 ± 2.1	18.06 ± 1.7	0.30***
Hct (%) (mean±SD)	52.5±5	52.50 ± 4.1	51.72 ± 6.5	53.31 ± 5.2	0.61***
MCV (mean±SD)	104.8±5	105.9 ± 3.9	105.5 ± 3.9	103.2 ± 6.6	0.21***

Abbreviations: Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume
Chi-square test, **Kruskal-Wallis Test, * One-way Analysis of Variance*

When the effect of mothers' consumption of animal product on their infants' vitamin B12 levels were evaluated, the mean vitamin B12 levels of newborns whose mothers are consumed sufficient amount of animal products was higher than insufficient group (396.2±36 and 312.3±32 pg/ml, respectively). However, there was no statistically difference (p= 0.3).

DISCUSSION

Vitamin B12 deficiency is an important problem in pregnancy because it affects not only mothers but also their infants. Although vitamin B12 deficiency is seen all over the world and all age groups, its frequency is much higher in population which has low socio-economic level[1-4]. The Institute of Medicine reported that the "Recommended Daily Allowance" (RDA) ranges from 0.4 mcg for age< 6 months to 2.4 mcg for adults and they suggested that the "Estimated Average Requirement" (EAR) and RDA during pregnancy women be 2.2 µg/day and 2.6 µg/day, respectively[10]. The level of vitamin B12 deficiency are not clearly defined, however the cut-off value for vitamin B12 is frequently used as 200 pg/ml[1,9-11]. Previous studies showed that serum vitamin B12 concentration decreases physiologically during pregnancy, so serum B12 levels above 150 pg/ml may not indicate the B12 deficiency in pregnant women[11-13].

In a study from Canada, the prevalence of vitamin B12 deficiency during pregnancy has been reported as 7.4%[14]. However, in the studies conducted in Venezuela, India, and Nigeria, its prevalence was found as 61%, 42% and 32%, respectively[15-17]. A systematic review revealed that the prevalence of vitamin B12 deficiency is common in pregnant women and the plasma B12 levels gradually decreasing during pregnancy[18].

There is a limited number of studies on vitamin B12 deficiency in pregnant women and their infants in Turkey. In 2004, Koc et al[19]. found that vitamin B12 levels were lower than 160 pg/ml in 72% of mothers and 41% of their infants in Şanlıurfa region. In 2010, Önal et al.[20] reported that 81.6% of mothers had levels below 300 pg/ml and 42% of their infants had levels below 200 pg/ml in İstanbul province. In further study by Halicioglu et al. (2012)[21]. found that, 47.6% of mothers in İzmir had serum B12 levels < 160 pg/ml. In a study conducted in Samsun province in 2014, vitamin B12 deficiency (<200 pg/ml) in pregnant women were found to be 58.1%[22]. In our study, mean vitamin B12 level was found to be 172.23 ±102 pg/ml in pregnant women and 352.1±339.2 pg/ml in their infants. Vitamin B12 deficiency (<200 pg/ml) in women and infants were 73.2% and 26.6%, respectively. Also, when we evaluated the pregnant women that had B12 level below 150 pg/ml, we found that 46% of the mothers and 14% of the infants had a serum vitamin B12 level lower than 150 pg/ml. All of these studies show that vitamin B 12 deficiency is common and a serious problem in pregnant women and their infants in Turkey.

The risk factors for B12 deficiency includes poor nutritional status, poverty, vegan diet, impaired gastric or intestinal absorption, congenital/inherited disorders, medications and aging[1,2,4,12]. In previous studies, it was reported that sub-optimal nutrition secondary to low socio-economic status can affected the serum B12 level[21,22]. In this present study, we found no differences in terms of age, BMI, weight gain, number of parity. However, the serum vitamin B12 levels of women who had consumed sufficient animal-source foods significantly higher than the women who had consumed insufficient. It is known that the best sources of vitamin B12 include animal foods as meat, fish and dairy products. Although the difference was not in terms of socioeconomic status, all pregnant women in our study had

low or moderate incomes. We think that the low socioeconomic level of the region we are in may explain the nutritional status and the level of vitamin B12 of mothers and their infants.

The vitamin B12 support in pregnant women is important in populations with low socioeconomic level because of sub-optimal nutrition. In our study, 86% of pregnant women used multivitamin preparations containing B12 and there was no difference in terms of serum B12 level between women who did and did not use. The amount of vitamin B12 of the prescribed multivitamins ranged 2.5 to 4 µg/day, however only 7 patients (11%) used medicines regularly.

Previous studies reported that infants' B12 levels were correlated with mothers' levels and low concentration of B12 in pregnant women was a risk factor for their babies[13]. When we evaluated the relationship between infants' and their mothers' vitamin B12 level, we found a positive correlation between the mothers' and their infants' B12 level. Also, the infants of mothers that consumed sufficient animal-source foods had higher than other infants, although there was no significant difference.

There are some studies that evaluating the effect of B12 deficiency on intrauterine growth and prematurity. In a study, Muthayya et al[23]. showed that the deficiency of vitamin B12 in pregnant women may related with fetal growth restriction. In a meta-analysis, Rogne et al[24]. reported that lower maternal B12 level in pregnancy increased the risk of prematurity. However, Sukumar et al[18]. and Halicioglu et al[21]. reported that there is no association between B12 level and growth restriction. In another study, Chen et al. showed that higher B12 concentrations was not reducing the risk of preterm birth.[25] Similarly, we found no association between maternal B12 level and body measurements at birth or gestational age. **Also,** when the infants groups were evaluated according to B12 levels, the difference was not found between groups in terms of gender, gestational age, birth weight, length, head circumference.

Severe B12 deficiency affects the bone marrow in patients and it may causes macrocytic anaemia, leukopenia or neutropenia, and thrombocytopenia. However, 30% of affected patients may have a normal hemoglobin and mean corpuscular volume. Therefore, the diagnosis of B12 deficiency should not depend on the hematologic parameters[3,4]. In our study, the difference was not found between groups in terms of laboratory parameters in women and infants.

Suboptimal B 12 status is very common and it affects of 30%-60% of the pregnant women in countries with low socio-economic status. B12 deficiency can lead to serious health problems in infants; the neurological and intellectual development is particularly vulnerable. Therefore, using the expanded newborn screening may be considered for early diognosis. Thus, serious health problems can be prevent[26,27].

There are some limitations in our study. We could not evaluate the serum homocysteine level in the study group and this study was included a single district that has low socio-economic status. Also, the number of women who did not receive multivitamin support was low. Therefore, further studies are needed to evaluate the limitations of this study.

The data in present study showed that the prevalence of vitamin B12 deficiency in pregnant women was very high and mainly cause was sub-optimal nutrition. For this reason, pregnant women whose have low socioeconomic status should be supported with multivitamin preparations included vitamin B12 or food fortifications. However, the optimal dose in population that vitamin B12 deficiency is common is not clearly and there is not data to support the administration of high dose vitamin B12 to all pregnant women. Therefore, we suggest that the evaluation of B12 status at the beginning of pregnancy in women.

The authors declare that there is no conflict of interest.

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