

The importance of micronutrient deficiency in the etiology of anemia in the first trimester pregnancy

Deha Denizhan Keskin¹, Seda Keskin², Orkun Çetin², Fatma Ferda Verit Atmaca²,
Oğuz Yücel², Özhan Özdemir³

¹Clinics of Obstetrics & Gynecology, Bayrampaşa State Hospital, Istanbul, Turkey

²Clinics of Obstetrics & Gynecology, Süleymaniye Maternity Training and Research Hospital, Istanbul, Turkey

³Clinics of Obstetrics & Gynecology, Ankara Numune Training and Research Hospital, Ankara, Turkey

Abstract

Objective: To determine the frequency of anemia in pregnant women admitted to our hospital for the purpose of examination in the first trimester, to determine the location of micronutrient deficiencies in the etiology of anemia and to make analysis of demographic factors associated with anemia.

Methods: This study included 366 pregnant women below 12 weeks of gestation between November 2011 and February 2013. Pregnant women together with demographic data were examined in terms of hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folate, vitamin B12 levels. Tests were statistically evaluated with demographic analysis.

Results: The mean maternal hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folate, and vitamin B12 levels were respectively 12.6±1.02 g/dl, 36%±4.12, 76.63±44.76 µg/dl, 302.28±93.14 ng/dl, 19.35±20.43 ng/ml, 11.2±8.31 ng/ml and 187.2±101.14 pg/ml. The study evaluated 344 pregnant women and anemia was detected in 79 of them. In our study, the frequency of anemia was calculated to be 22.96%. Analyzing the etiology of anemic pregnant women, iron deficiency anemia was diagnosed in 35 patients (44.3%), vitamin B12 deficiency in 44 patients (55.7%), combination of vitamin B12 and iron deficiency was found in 9 patients. None of the patients were found to have folic acid deficiency.

Conclusion: The frequency of anemia in pregnant women was found as 22.96%, which shows that the vitamin B12 deficiency is important in the etiology of anemia as frequent as iron deficiency.

Key words: Pregnancy, anemia, micronutrient deficiency.

Gebeliğin ilk trimesterindeki anemi etyolojisinde mikrobesein eksikliğinin önemi

Amaç: İlk trimester muayenesi amacıyla hastanemize başvuran gebelerde anemi sıklığını belirlemek, mikrobesein eksikliklerinin anemi etyolojisindeki yerini saptanmak ve anemiyle ilişkili demografik faktörlerin analizlerini yapmak.

Yöntem: Kasım 2011 - Şubat 2013 tarihleri arasında polikliniğimize başvuran 12 ve altı gebelik haftasındaki 366 gebe çalışmaya dahil edildi. Gebelere ait demografik verilerle beraber, hemoglobin, hematokrit, serum demir, total demir bağlama kapasitesi, ferritin, folat, B12 vitamini seviyeleri incelendi. Tetkikler demografik analizlerle beraber istatistiksel olarak değerlendirildi.

Bulgular: Çalışmaya katılan gebelerin ortalama hemoglobin, hematokrit düzeyleri, serum demir, total demir bağlama kapasitesi, ferritin, folat ve B12 vitamini düzeyleri sırasıyla 12.6±1.02 g/dl, %36±4.12, 76.63±44.76 µg/dl, 302.28±93.14 ng/dl, 19.35±20.43 ng/ml, 11.2±8.31 ng/ml ve 187.2±101.14 pg/ml olarak bulundu. Çalışmamızda değerlendirmeye alınan 344 gebenin 79'unda anemi saptandı. Anemi prevalansı % 22.96 olarak hesaplandı. Anemik gebelerdeki etyoloji incelendiğinde, 35 hastada demir eksikliği (%44.3), 44 hastada B12 vitamini eksikliği (%55.7), 9 hastada ise B12 vitamini ve demir eksikliği bir arada bulundu. Hiçbir hastada folik asit eksikliğine rastlanmadı.

Sonuç: Çalışmaya dahil edilen gebelerde anemi sıklığı %22.96 olarak saptanmış olup, etyolojide demir eksikliği kadar B12 vitamini eksikliğinin de rol oynadığı gösterilmiştir.

Anahtar sözcükler: Gebelik, anemi, mikrobesein eksikliği.

Correspondence: Deha Denizhan Keskin, MD. Bayrampaşa Devlet Hastanesi, Kadın Doğum Kliniği, Bayrampaşa, Istanbul, Turkey.
e-mail: dehara@myynet.com

Received: June 21, 2013; **Accepted:** August 8, 2013

Available online at:
www.perinataljournal.com/20130212005
doi:10.2399/prn.13.0212005
QR (Quick Response) Code:



Introduction

Healthy nutrition during pregnancy is essential in many aspects. Healthy nutrition is required for fetus development, maternal health, successful delivery and lactation process. Also, proper nutrition during pregnancy decreases postpartum obesity risk and provides a positive contribution to maternal health in the long-term.^[1]

During the adaptation period at pregnancy, significant changes occur at vitamin and mineral levels in maternal blood. Vitamin B12 and folate levels increases 50% during pregnancy compared to pre-pregnancy period. Serum iron levels also tend to decrease.^[1,2]

According to the data of WHO, approximately one third of women population in the world and more than half of the pregnant women are anemic. At first and second trimesters, hemoglobin value being lower than 11 g/dl and hematocrit value being lower than 33% is interpreted as anemia. At third trimester, hemoglobin value being lower than 10.5 g/dl and hematocrit value being lower than 32% is interpreted as anemia.^[1,3,4]

In 50% of women not considered as anemic, and in 90% of pregnant women were found to have extremely low ferritin levels, which means iron deficiency.^[5]

Deep anemia causes serious cardiac failure even in small amounts of bleeding during miscarriage or delivery, and may increase maternal mortality up to five times. It also causes fetal complications (such as preterm labor, intrauterine growth retardation, and low birth weight) as well as maternal complications (such as preeclampsia, eclampsia, and sepsis).^[3,4]

Plasma volume increases about 50% during pregnancy to provide fetal development and placental blood flow. Since the increase in erythrocyte mass is lower, maternal hematocrit decreases. This is called physiologic anemia of pregnancy. Hematocrit level reaches the lowest level at third trimester, especially between 30th and 34th weeks.^[6,7]

Other factors causing anemia during pregnancy are insufficient nutrition and emptied iron balance of body due to repeating and frequent pregnancies.^[8,9]

In our country, there have been many regional studies aimed to present anemia prevalence. The prevalence of anemia in our country varies according to regions, and rates have been reported between 29.4% and 95.2% in various studies.^[10-15] In this study, it was aimed to determine the frequency and etiology of anemia in

pregnant women admitted to our clinic, and to determine demographic factors associated with anemia.

Method

Our study included 366 pregnant women below 12 weeks of gestation with age ranging between 16 and 44 who admitted to Bayrampasa State Hospital for the first time between November 2011 and February 2013. Women who had any systemic disease, vaginal bleeding for an obstetric reason in current pregnancy, and who started to have any iron and/or multi-vitamin supplement were excluded from the study. Our study is retrospective and required approval of ethics committee has been obtained.

According to the data of CDC (Centers for Disease Control), pregnant women with hemoglobin value lower than 11 g/dl and hematocrit value lower than 33% were interpreted as anemia. Values for serum folate and vitamin B12 below 3 ng/ml and 200 pg/ml, respectively, were considered as deficiencies. Informed consent forms were received from all these pregnant women and they were asked to fill a form including their demographic data. The form included information of age, hometown, obstetric history, educational status, and average income level. As a laboratory examination, patients were evaluated in terms of their hemoglobin (Hb), hematocrit (Htc), serum iron (Fe), total iron binding capacity (TIBC), ferritin, folate and vitamin B12 levels. Twenty-two patients were removed from the study since their blood had hemolysis.

Hemogram and hematocrit were studied by Swelab alpha device; serum iron and total iron binding capacity were studied by Prestige 24I device; ferritin, folate and vitamin B12 were studied by Unicel DxI 800 device.

Data obtained by forms and examinations were evaluated. Constant variables were indicated as mean and standard deviation. Data was evaluated by SPSS (Statistical Package for the Social Science) 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Pregnant women included in the study were separated into age groups for evaluation. Mean age of patients was found as 29.08±6.79. Also, gestational week, gravid, and parity of pregnant women are given in the **Table 1.**

Mean hematocrit levels and standard deviations were calculated according to the age groups. Anemia prevalence was analyzed in the basis of the age groups (Table 2). Accordingly, anemia prevalence was found to be high in the age groups 21-25 and 26-30 as 34.64% and 33.78%, respectively. Mean hematocrit levels were found to be coherent in age groups. Anemia was detected in 79 of 344 pregnant women included in the study. So, anemia prevalence was calculated as 22.96%.

In 21 cases in our study, serum iron levels were found to be lower than 37 µg/dl. Therefore, iron deficiency was seen in 6.1% of the pregnant women in our study.

Analyzing the etiology of anemic pregnant women, iron deficiency anemia was diagnosed in 35 patients (44.3%), vitamin B12 deficiency in 44 patients (55.7%), combination of vitamin B12 and iron deficiency was found in 9 patients (11.4%). None of the patients were found to have folic acid deficiency (Table 3). Age and blood parameters of pregnant women included in the study were evaluated separately in women with and without anemia (Table 4). The mean maternal hemoglobin, hematocrit, serum iron, total iron binding capacity, ferritin, folate, and vitamin B12 levels were respectively 12.6±1.02 g/dl, 36%±4.12, 76.63±44.76 µg/dl, 302.28±93.14 ng/dl, 19.35±20.43 ng/ml, 11.2±8.31 ng/ml and 187.2±101.14 pg/ml (Table 3). When hematological parameters of these women were compared, it was seen that statistically and significantly mean serum iron level was lower and total iron binding capacity was higher in pregnant with anemia.

When pregnant women with and without anemia were compared in terms of their hometowns, obstetric histories, educational status and average income level,

Table 1. Age, gestational week, gravida, parity evaluation.

	Mean	Min.	Max.
Age	29.08±6.79	16	45
Gestational week	8±3	5	12
Gravida	1.5±1.2	1	9
Parity	0.8±0.9	0	5

Table 2. Anemia prevalence according to age groups.

Age	Mean hematocrit	Anemia rate
16-20	36.19±3.98	20.30
21-25	35.55±3.86	34.64
26-30	35.78±4.00	33.78
31-35	35.95±3.98	27.60
36-40	36.60±4.42	20.91
41-45	37.29±4.86	20.18

Table 3. Hemoglobin (Hb), hematocrit (Hct), folate, and vitamin B12 levels.

	Mean	Min.	Max.
Hb	12.6±1.02	6.8	17.1
Hct	%36±4.12	19.1	49.8
Folate	11.2±8.31	3.4	22.27
Vitamin B12	187.2±101.14	18	1521

there was statistically no significant difference between two groups.

Discussion

According to WHO, anemia is a health issue seen in 21-80% of women population in the world. While ane-

Table 4. Comparison of age and blood parameters in groups with and without anemia.

	Mean	With anemia	Without anemia
Age	29.08±6.79	28.66±6.39	29.22±6.93
Iron	76.63±44.76	53.54±21.61	97.23±26.41
TIBC	302.28±93.14	417.23±87.56	261.67±105.65
Ferritin	19.35±20.43	5.45±4.11	27.56±9.59
Folate	11.2±8.31	16.92±9.78	17.12±5.98
Vitamin B12	187.2±101.14	210.23±118.56	237.89±87.13

TIBC: total iron binding capacity.

mia rate of women is 14% in European countries, it is 25% in Turkey. In terms of etiology, 40-89% of anemia cases are caused by iron deficiency anemia.^[16] According to the data of WHO, iron deficiency anemia affecting 30% of world population affects 51% of pregnant women.^[17] Especially in underdeveloped countries, anemia is more prevalent and at more serious levels. In the study performed by Malhotra in 2002, it was found that anemia rate during pregnancy was 72.5% in India.^[18] As the development level increases, anemia frequency decreases. Anemia during pregnancy in Korea was found to be 35.3% in the study performed by Choi.^[19] In the studies performed in developed European countries, anemia rates were reported as 7-16%.^[20,21]

Anemia was found in 79 of 344 pregnant women included into our study and therefore anemia prevalence was calculated as 22.96%. Analyzing the etiology of anemic pregnant women, iron deficiency was diagnosed in 35 patients (44.3%), vitamin B12 deficiency in 44 patients (55.7%), combination of vitamin B12 and iron deficiency was found in 9 patients (11.4%). None of the patients were found to have folic acid deficiency.

When Turkish studies performed on anemia frequency during pregnancy are analyzed, it is seen that there is no large-scale research that will represent Turkish population. Anemia frequency in Turkey varies according to the regions, and the rates range between 29.4% and 95.2%.^[10-15] Compared to these rates, the anemia rate found by our study (22.96%) has been observed lower than other studies.

Al Khatib et al. reported in their study performed in Lebanon that 7.7% of women who were at fertility age but not pregnant had iron deficiency, 25.9% of them had folic acid deficiency and 39.4% of them had vitamin B12 deficiency.^[22] In a study performed in Africa, only 23% of the cases had anemia due to iron deficiency, 32% of them had anemia due to iron deficiency together with the deficiency of other micronutrients (folate, vitamin B12, vitamin A), and 26% of them did not have any iron deficiency but had micronutrient deficiency.^[23]

Non-existence of folic acid deficiency in our study can be explained by the sufficient folic acid supplement provided in our clinics both before pregnancy and during the first trimester. In a study performed in Adana/Turkey, the relationship between increase of pregnancy number and anemia was found statistically

significant.^[12] In a study performed in Elazığ/Turkey, statistically no significant relationship was found between pregnancy number and anemia frequency.^[11] In our case, statistically no significant relationship was found between pregnancy number and anemia frequency.

In our study, no question was asked for nutrition. However, income levels of pregnant women that reflect their nutrition condition indirectly were asked and no relationship was found between income level and anemia frequency.

According to the Population and Health Survey of Turkey conducted in 1998, adolescent pregnancy frequency is 14% in Turkey. It was seen that mean age in the study group was 30.69 ± 7.17 and 73% of patients were in the age group 20-35. It was observed that 3.7% of pregnant women had adolescent pregnancy.^[24]

Conclusion

Consequently, anemia frequency during pregnancy was found to be lower in this study compared to the country data. Significance of the vitamin B12 deficiency as much as iron deficiency in etiology is one of the results of our study. In two third of anemic pregnant women had low vitamin B12 level. This emphasizes the importance of multi-vitamin supplement as well as the nutrition during pregnancy. Studies with larger amount of cases are required in order to present regional differences in the prevalence across the country.

Conflicts of Interest: No conflicts declared.

References

1. World Health Organization (WHO). Pregnancy, childbirth and newborn care. Essential care practice guide. New York: WHO; 2000.
2. Economides DL, Kadir RA, Lee CA. Inherited bleeding disorders in obstetrics and gynaecology. *Br J Obstet Gynaecol* 1999;106:5-13.
3. Milman N, Bergholt T, Byg KE, Eriksen L, Graudal N. Iron status and iron balance during pregnancy. A critical reappraisal of iron supplementation. *Acta Obstet Gynecol Scand* 1999;78:749-57.
4. Nelson-Piercy C. Handbook of obstetric medicine. New York: Martin Dunitz; 2003. p. 250-68.
5. Tunalı A. Kan hastalıkları. Bursa: Güneş Kitabevi; 1990. p. 699-716.
6. JHyttén F, Paintin DB. Increase in plasma volume during normal pregnancy. *Obstet Gynaecol Br Emp* 1963;70:402-7.

7. Steer PJ. Maternal hemoglobin concentration and birth weight. *Am J Clin Nutr* 2000;71(5 Suppl):1285S-7S.
8. Fich CA, Cook JD. Iron deficiency. *Am J Clin Nutr* 1984;39:471-7.
9. Allen LH. Pregnancy and iron deficiency: unresolved issues. *Nutr Rev* 1997;55:91-101.
10. Beştepe G, Bilgin N. Afyon ili 2 ve 4 no'lu sağlık ocaklarındaki gebelerde anemi prevalansı ve anemiye etkileyen bazı faktörlerin incelenmesi. *Sağlık ve Toplum* 2002;12:43-53.
11. Piriñçi E, Açık Y, Bostancı M, Eren S, Beritanlı H. Elazığ il merkezinde yaşayan gebelerde anemi prevalansı. *Fırat Üniversitesi Sağlık Bilimleri Dergisi* 2001;15:449-54.
12. Oruç O, Tuncer A, Apan E. Ulusal Halk Sağlığı Kongresi Bildiri Kitabı. İstanbul, 1996. p. 374-8.
13. Mersin S, Kuş C, Yeşildal N, Mayda A, Şerifi B. 8. Ulusal Halk Sağlığı Kongresi Bildiri Kitabı. Diyarbakır, 2002. p. 257-60.
14. Pekcan G, Karaağaoğlu N. State of nutrition in Turkey. *Nutrition and Health* 2000;14:41-52.
15. Toksöz P, İçlin E, Özcan M. Diyarbakır Bağlar Sağlık Ocağı bölgesinde gebe kadınlarda anemi prevalansı. *Beslenme ve Diyet Dergisi* 1990;19:61-9.
16. WHO. The prevalence of anemia in women. A tabulation of available information. Geneva: WHO; 1992.
17. Fairbanks VF, Beutler E. Williams hematology. 5th ed. New York: Mc Graw-Hill; 1995. p. 490-506.
18. Malhotra M, Sharma JB, Batra S, Sharma S, Murthy NS, Arora R. Maternal and perinatal outcome in varying degrees of anemia. *Int J Gynaecol Obstet* 2002;79:93-100.
19. Choi JW, Kim CS, Pai SH. Erythropoietic activity and soluble transferrin receptor level in neonates and maternal blood. *Acta Paediatr* 2000;89:675-9.
20. Massot C, Vanderpas J. A survey of iron deficiency anaemia during pregnancy in Belgium: analysis of routine hospital laboratory data in Mons. *Acta Clin Belg* 2003;58:169-77.
21. Meier PR, Nickerson HJ, Olson KA, Berg RL, Meyer JA. Prevention of iron deficiency anemia in adolescent and adult pregnancies. *Clin Med Res* 2003;1:29-36.
22. Al Khatib L, Obeid O, Sibai AM, Batal M, Adra N, Hwalla N. Folate deficiency is associated with nutritional anaemia in Lebanese women of childbearing age. *Public Health Nutr* 2006;9(7):921-7.
23. van den Broek NR, Letsky EA. Etiology of anemia in pregnancy in south Malawi. *Am J Clin Nutr* 2000;72(1 Suppl):247S-256S.
24. Türkiye Aile Sağlığı ve Planlaması Vakfı. Aile planlaması hizmetleri ve isteyerek düşükler. Ankara: Türkiye Aile Sağlığı ve Planlaması Vakfı; 1998.