ORIGINAL RESEARCH

Bagcilar Med Bull
DOI: 10.4274/BMB.galenos.2024.2024-02-020

Effect of Iron Deficiency Anemia on Fetal and Maternal Morbidity

Demir Eksikliği Anemisinin Fetal ve Anne Morbiditesi Üzerine Etkisi

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Abstract

Objective: To investigate the effect of third-trimester iron deficiency anemia on fetal and maternal morbidity.

Method: A total of 240 pregnant women whose third trimester hemoglobin level was found to be <11 g/dL in the retrospective review of medical records were included in the study. Pregnant women who had blood samples taken at least twice for the diagnosis of anemia in the third trimester constituted the study group. Pregnant women whose gestational weeks were matched and without anemia were included as the control group. Multivariate logistic regression analysis was performed to identify independent risk factors for anemia after adjusting for age and body mass index (BMI).

Results: The rates of cesarean delivery, preterm labor, placental abruption, premature membrane rupture, low birth weight, and admission to intensive care due to fetal distress were significantly higher in the anemic group than in the non-anemic group. Vaginal birth rates in the anemic group (29.2%) were significantly lower than those in the non-anemic group (50%). While 170 patients in the anemic group underwent cesarean section (70.8%), 120 patients in the non-anemic pregnant group underwent cesarean section (50%). Logistic regression analysis revealed that high gravidity (95% confidence interval 1.176-2.677), parity (95% confidence interval 1.138-2.033), and gestational weeks (95% confidence interval 1.003-1.006), were independent risk factors for anemia severity after adjustment for potential confounders, including age and BMI.

Conclusion: Anemia during pregnancy increases cesarean delivery rates and decreases vaginal birth rates. Gravidity, parity, and gestational age increase the severity of anemia regardless of age and BMI. Treating anemic pregnant women with iron supplementation may reduce cesarean section rates and increase normal birth rates in a more cost-effective manner.

Keywords: Cost effectivity, feto-maternal morbidity, iron deficiency anemia, third trimester

Öz

Amaç: Üçüncü trimester gebelerde demir eksikliği anemisinin fetal ve maternal morbidite üzerine etkisini araştırmak.

Yöntem: Tıbbi kayıtların retrospektif olarak incelenmesinde üçüncü trimester hemoglobin düzeyi <11 g/dL olan 240 gebe çalışmaya dahil edildi. Üçüncü trimesterde anemi tanısı için en az iki kez kan örneği alınan gebeler çalışma grubunu oluşturdu. Gebelik haftaları uyumlu, anemisi olmayan gebeler kontrol grubu olarak alındı. Yaş ve vücut kitle indeksi (VKİ) ile ayarlama yapıldıktan sonra anemi için bağımsız risk faktörlerini belirlemek amacıyla çok değişkenli lojistik regresyon analizi yapıldı.

Bulgular: Sezaryen doğum, erken doğum, plasentanın ayrılması, erken membran rüptürü, düşük doğum ağırlığı ve fetal distres nedeniyle yoğun bakıma alınma oranları anemik grupta anemik olmayan gebelere göre anlamlı olarak daha yüksekti. Anemik grupta vajinal doğum oranları (%29,2), anemik olmayan gruba (%50) göre anlamlı derecede düşüktü. Anemik grupta 170 hastaya (%70,8) sezaryen yapılırken, anemik olmayan gebelerde 120 hastaya (%50) sezaryen uygulandı. Lojistik regresyon analizi, yüksek gravidanın (%95 güven aralığı 1,176-2,677), paritenin (%95 güven aralığı 1,138-2,033) ve gebelik haftalarının (%95 güven aralığı 1,003-1,006) doğum sonrası anemi şiddetinin bağımsız risk faktörleri olduğunu ortaya çıkarmıştır.

Sonuç: Gebelik anemisi sezaryen doğum oranlarını artırmakta ve vajinal doğum oranlarını azaltmaktadır. Gravidite, parite ve gebelik yaşı, yaş ve VKİ'den bağımsız olarak aneminin şiddetini artırır. Anemik gebe kadınların demir takviyesi ile tedavi edilmesi, sezaryen oranlarını azaltabilir ve normal doğum oranlarını daha uygun maliyetli bir şekilde artırabilir.

Anahtar kelimeler: Demir eksikliği anemisi, feto-maternal morbidite, maliyet etkinliği, üçüncü trimester

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Cite this article as: Özyurt R, Bulutlar E. Effect of Iron Deficiency Anemia on Fetal and Maternal Morbidity.

Introduction

Anemia occurs when hemoglobin (Hb) is below the values determined by age and gender (1). The World Health Organization (WHO) defined anemia as a Hb concentration below 12 g/dL in women and 13 g/dL in men (2,3). Anemia is characterized by decreased oxygen-carrying capacity of erythrocytes to tissues. Decreased tissue oxygenation is reflected in patients with delay or difficulty in performing the functions of the cells. Although anemia can be seen in all age groups, children, pregnant women, and the elderly are the most affected. Although it varies from country to country, anemia is observed in approximately 38% of all pregnant women (4-6). The prevalence of anemia in pregnancy in industrial societies is one third of the developing countries (6,7). Anemia in pregnant women presents a spectrum ranging from simple clinical symptoms to preterm labor and maternal or fetal death. Newborns of untreated anemic pregnant women are often born with low birth weight. An increase in maternal morbidity and mortality occurs in proportion to the amount of blood lost by anemic pregnant women during vaginal delivery or cesarean section (8). The increase in plasma volume due to physiological changes during pregnancy intensifies anemia dilutionally. Therefore, patients experience clinical symptoms due to a decrease in oxygen capacity from the second trimester.

Apart from previous studies, there are no comprehensive data on the prevalence of anemia in pregnant women in Turkey. Turkey is in the category of developing countries, and the prevalence of pregnancy anemia is quite high, and this incidence decreases or increases according to geographical regions. In addition, because the diagnosis of anemia is made according to the Hb values in different trimesters, it is difficult to comment on the true prevalence of anemia in pregnancy. It is possible to encounter pregnancy anemia in roughly 28-40% of all pregnant women (9-11). This study was planned to investigate the effects of demographic parameters such as age, parity, and body mass index (BMI) on the prevalence of anemia, fetomaternal, and adverse pregnancy outcomes in pregnancy.

Materials and Methods

This retrospective study was initiated after the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee decided that it was ethically appropriate with the decision dated 07.07.2010 and numbered 2/19. In the review of medical records, pregnant women in the third trimester with an Hb value of <11 g/dL were included in the study. The Declaration of Helsinki was followed throughout the study. A total of 240 third trimester patients whose Hb values were compatible with anemia who applied to the Pregnancy Polyclinic of the University of Health Sciences Turkey, İstanbul Training and Research Hospital, Department of Obstetrics and Gynecology between 2015 and 2022 were selected as the study group.Two hundred forty healthy pregnant women without anemia were taken as the control group. In the third trimester, blood samples were taken at least twice for the diagnosis of anemia. According to the WHO, if the Hb value was <11 g/dL in any trimester, anemia was diagnosed, so patients below this value were considered to have anemia during pregnancy. Patients diagnosed with anemia in the first or second trimester were excluded from the study because they were given iron replacement. Between 28-42 weeks of gestation were considered as the third trimester. Multiple pregnancies, pregnant women who received iron replacement therapy in the first trimester, those having gestational diabetes, hypertension, systemic diseases and fetal anomalies were not included in the study.

Term singleton pregnant women between the ages of 18 and 40 years without systemic diseases, multiple pregnancies, placental adhesion anomalies, or Hb synthesis diseases were included in the study. Patient data were retrospectively scanned from medial records. Those over the age of 40 years, those who had blood transfusion in the last 3 months, and those with hematological disease who had multiple pregnancy detected on ultrasonography were excluded from the study.

Fetomaternal outcome, delivery types, hypertension, gestational diabetes, preeclampsia, ablatio placentae, polyhydramnios or oligohydramnios, premature rupture of membranes, preterm delivery, fetal birth weight, and intensive care unit rates were recorded. Gestational age at birth was defined by routine ultrasound scanning in the first trimester (between 0-13+6 weeks of gestation) (12,13). Anemia was diagnosed according to the WHO criteria, and participants were divided into mild, moderate, and severe (3). Table 1 shows the anemia groups according to Hb values. If the fetal weight was 4000 g or more, macrosomia was diagnosed. Fetal weight <2500 g was considered as low birth weight. Patients who gave birth before 37 weeks of gestation were defined as having a premature birth. Gestational diabetus (GDM) was diagnosed with 50 g and 75 g OGCT performed between 24 and 28 weeks. The diagnosis of hypertensive diseases was made by clinical evaluation, blood, and urinalysis.

Statistical Analysis

The number of participants was determined by power analysis using G*Power version 3.1.9.4. Cohen's d effect size was 0.80; α value 0.05; The power (1-β) value was taken as 0.80, and the number of samples required for one-tailed statistical comparison of anemic and non-anemic groups was calculated as n=240 for each group (12). Data were analyzed using the SPSS version 22.0 statistical package program (Statistical Package for Social Sciences, version 22.0, SPSS Inc, Chicago, III, USA). Shapiro-Wilk test was used to determine the data distribution pattern. Variables with normal distribution were analyzed by independent sample t-test, and non-normal variables were analyzed with Mann-Whitney U test or Kruskal-Wallis test depending on the number of groups. Multivariate logistic regression analysis was performed to identify independent risk factors for anemia after adjusting for age and BMI. Data are given as mean ± standard deviation for continuous variables and as frequency (percentage) for categorical variables. Two-tailed p-values of $p<0.05$ were considered significant.

Results

According to the WHO classification of anemia, the number of patients with mild anemia (53.3%) was significantly higher than that of patients with moderate (30%) and severe anemia (16.6%) (Table 1). As can be clearly seen in Table 2, no significant difference was found between the demographic characteristics of the anemic and non-anemic groups. When the perinatal outcomes of the groups were compared, cesarean section rates were found to be significantly higher in the anemic group than in the non-anemic group. There was no significant difference between the groups in terms of vaginal delivery rates. Oligohydramnsiosis and GDM rates were similar in both groups. The premature birth rate was higher in the anemic group. Ablatio placenta and preterm prematüre rupture of membrane (PPROM) were higher in anemic patients. The rate of low birth weight was higher in newborns in the anemic group. Fetal distress and neonatal intensive care unit were higher in anemic pregnant women (Table 3). Multivariate logistic regression analysis revealed that high gravidity (95% confidence interval 1.176-2.677), parity (95% confidence interval 1.138-2.033), and gestational weeks (95% confidence interval 1.003-1.006), were independent risk factors for anemia severity after adjustment for potential confounders, including age and BMI (Table 4).

Discussion

Iron deficiency anemia continues to be an important public health problem in obstetric practice because of the decrease in normal birth rates and the increase in costs associated with cesarean delivery. Our study was designed to analyze the morbidities observed in patients diagnosed with third trimester anemia and their newborns. Independent variables contributing to anemia severity were also determined by multivariate analysis. Because iron replacement was performed in these patients, our results cannot be compared with those of the control group. Because iron deficiency was determined according to WHO criteria and classified as mild, moderate, or severe, it was

Table 1. Anemia groups according to the Hb values

	Mild	Moderate	Severe	
Hemoglobin values	100-109 g/L	70-79 g/L	<70 g/L	
*Anemic group (n=240)	128 (53.3%)	72 (30%)	40 (16.6%)	Results are given as numbers (%)
*Non-anemic group (n=240)	Hb values were within physiological limits.			

*WHO (World Health Organization) hemoglobin concentrations for the diagnosis of anemia and assessment of severity. Edited by the World Health Organization, 2011. Hb: Hemoglobin

Table 2. Demographic characteristics of anemic and non-anemic pregnant women

	Pregnant women with anemia	Non-anemic pregnant women	p-values
N	240 (50%)	240 (50%)	
Age	28.0±4.02 (27-30)	28.8±3.09 (26-32)	0.08
Gravidity	2.05±0.11 (1-3)	1.98±0.02 (1-3)	0.50
Parity	1.20±0.20 (1-1.4)	0.98±0.03(0-1)	0.34
BMI	22.0±405	22.8±3.06	0.20
Gestational week	28.4±4.11	29.2±4.30	0.45

BMI: Body mass index, results are given in means ± standard deviation or n (%). P-values of >0.05 were considered insignificant

Table 3. Perinatal and maternal morbidities in anemic and healthy pregnant women

	Anemic (240)	Non-anemic(240)	p-values
C/S	170 (70.8%)	120 (50%)	**0.01**
Vaginal birth	70 (29.2%)	120 (50%)	**0.01**
Oligohydramnios	48 (20.8%)	48 (20%)	0.56
Preterm birth	36 (15%)	24 (10%)	**0.04**
GDM	24 (10%)	24 (10%)	0.30
Hypertensive disorders	22 (9.1%)	28 (11.6%)	0.43
Abruptio placenta	6 (2.5%)	0 (0%)	**0.01**
PPROM	12 (5%)	8 (3.3%)	**0.02**
Low birth weight (<2500 g)	20 (8.3%)	15.8 (6.6)	**0.03**
Fetal distress	46 (19.1%)	36 (15%)	**0.01**
NICU admission	24 (10%)	16 (6.6%)	**0.02**

C/S: Ceserean section, GDM: Gestational diabetes mellitus, PPROM: Preterm premature rupture of membrane, results are given in numbers (%). A p-value of <0.05 was considered significant for all bold values, NICU: Neonatal intensive care unit

Table 4. Logistic regression analysis of the effects of gravididy, parity, and gestational weeks on anemia severity after adjustment for age and BMI

	Unadjusted		Adjusted (1)	
	OR (95% CI)	p	OR (95% CI)	p
Gravidity	1.151 (1.132-2.216)	**<0.001**	1.738 (1.176-2.677)	**<0.01**
Parity	1.518 (1.122-2.232)	**<0.01**	1.324 (1.138-2.033)	**<0.05**
Gestational weeks	1.003 (1.001-1.008)	**<0.01**	1.004 (1.003-1.006)	**<0.05**

OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, A p-value of <0.05 was considered significant for all bold values

possible to compare the relationship between anemia severity and perinatal and maternal outcomes (12).

Iron deficiency remains an important public health problem in developing countries. It is possible to encounter anemia in different prevalences in every society according to geography, culture, economy, and education level. The decrease in daytime performance due to the decrease in the oxygen carrying capacity of the patient causes early fatigue and activity restriction. The co-existence of pregnancy and anemia causes worsening of the clinical picture. Fetal development is affected at different stages, as maternal iron stores will be depleted due to the increased need for iron during gestational weeks. Sometimes, lack of amniotic fluid and hypertensive changes due to vascular bed damage cause worsening of the clinical picture. An increase in cesarean delivery rates due to fetal distress. Owing to all these negative effects, anemic pregnant women are more prone to morbidity than healthy controls in terms of both maternal and fetal outcomes (9-11). In a study by Breymann (14) it was determined that maternal anemia may have both maternal and fetal effects, and it was shown that enzymatic functions, mental functions, muscle and cardiac effects on the mother may occur, and these effects indirectly affect the fetus. Fetally, it has been reported that there are risks of fetal tension retardation, preterm birth, and may even be associated with a developing preeclampsia (14).

The prevalence of iron deficiency anemia has decreased in the last two decades in our country. Close monitoring of pregnant women in terms of anemia in health centers has become a state policy. Providing the necessary drugs for iron replacement free of charge to patients with iron deficiency and strict controls after treatment played an important role in reducing the incidence of the disease. For all these reasons, while the prevalence of anemia in our country used to be quite below the European average, it has now approached the developed country averages over the years. However, it still continues to be an important public health problem in our country, especially in the pregnant population (15,16). Despite all these advances in diagnosis and treatment, pregnancy anemia continues to increase both fetal and maternal morbidity. The prevalence of anemia-related PPROM and placental diseases continues to increase. Because these obstetric problems increase the cesarean section rates, morbidities such as bleeding and infection are still increasing. The intensive care needs of bloodless mothers are considerably higher than those of

healthy newborns. This increases both neonatal morbidity and the cost (9,11).

The fact that gestational anemia plays a critical role in determining the mode of birth requires that this public health problem be treated. In the current study, 170 patients (70.8%) in the anemic group underwent cesarean section, whereas this rate was 120 (50%) in the non-anemic group. Anemia has led to a 20% increase in cesarean delivery rates. When iron deficiency anemia in pregnancy is treated with conventional iron preparations, the rate of patients having a normal vaginal birth will be higher than that after cesarean delivery (17-20). Considering the cost of a cesarean birth to the hospital and the country, correcting anemia with iron supplementation would be a more cost-effective approach. Detecting anemic patients by conducting iron deficiency screening programs before or during pregnancy can be made a state policy. To reduce the rate of cesarean section due to anemia, it should be made easier for pregnant women to use iron preparations.Thus, the expenses that the patient and the social insurance institution will pay due to the cesarean section surgery and the duration of hospital stay should be minimized.

Conclusion

The acceptance of pregnancy anemia as an important disease by health professionals at all stages, starting from primary care physicians, will be an important step toward a solution. The foundations of a society rising thanks to healthy generations and mothers will be possible by treating this clinical picture in every region of our country. As the prevalence of anemia will decrease and normal birth rates will increase, the morbidity and costs associated with cesarean section will also decrease.

Ethics

Ethics Committee Approval: This retrospective study was initiated after the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee decided that it was ethically appropriate with the decision dated 07.07.2010 and numbered 2/19.

Informed Consent: Not necessary for this manuscript.

Authorship Contributions

Concept: R.Ö., E.B., Design: R.Ö., E.B., Data Collection or Processing: R.Ö., E.B., Analysis or Interpretation: R.Ö., E.B., Literature Search: R.Ö., E.B., Writing: R.Ö., E.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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